THE INVESTIGATION OF THE SENSITIVITY GRADIENT OF THE VISUAL FIELD, AS A FUNCTION OF STIMULUS DYNAMIC RANGE, IN THE NORMAL AND ABNORMAL EYE

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The study utilized the advanced technology provided by automated perimeters to investigate the hypothesis that patients with retinitis pigmentosa behave atypically over the dynamic range and to concurrently determine the influence of extraneous factors on the format of the normal perimetric sensitivity profile.

The perimetric processing of some patients with retinitis pigmentosa was considered to be abnormal in either the temporal and/or the spatial domain.

The standard size III stimulus saturated the central regions and was thus ineffective in detecting early depressions in sensitivity in these areas. When stimulus size was scaled in inverse proportion to the square root of ganglion cell receptive field density (M - scaled), isosensitive profiles did not result, although cortical representation was theoretically equivalent across the visual field. It was conjectured that this was due to variations in the ganglion cell characteristics with increasing peripheral angle, most notably spatial summation. It was concluded that the development of perimetric routines incorporating stimulus sizes adjusted in proportion to the coverage factor of retinal ganglion cells would enhance the diagnostic capacity of perimetry. Good general and local correspondence was found between perimetric sensitivity and the available retinal cell counts.

Intraocular light scatter arising both from simulations and media opacities depressed perimetric sensitivity. Attenuation was greater centrally for the smaller LED stimuli, whereas the reverse was true for the larger projected stimuli. Prior perimetric experience and pupil size also demonstrated an eccentricity - dependent effect on sensitivity. Practise improved perimetric sensitivity for projected stimuli at eccentricities greater than or equal to 30°; particularly in the superior region. Increase in pupil size for LED stimuli enhanced sensitivity at eccentricities greater than 10°. Conversely, microfluctuations in the accommodative response during perimetric examination and the correction of peripheral refractive error had no significant influence on perimetric sensitivity.

Automated perimetry, intraocular light scatter, retinitis pigmentosa,
cortical representation, learning - effect.

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1. AUTOMATED PERIMETRY

1.1 Introduction

The visual field is a topographical representation of the functional integrity of the visual system. Classically, it has been defined as "that portion of space in which objects are visible at the same moment during steady fixation of gaze in one direction" (Traquair 1927). It has been traditionally likened to an island of vision in a sea of blindness, such that large and bright stimuli can be seen at the periphery of the visual field, whilst small and dim stimuli may only be seen if they are situated proximal to the visual axis. Disturbances at any stage of visual processing are characteristically reflected in the form of the visual field; the measurement of the visual field is therefore not only of intrinsic value but also of great diagnostic importance.

1.1.1 History

The measurement of visual fields, perimetry, was introduced as a clinical method by Von Graefe (1856) who used a black board, the tangent screen, over which the stimuli were moved. Subsequently, Aubert and Foerster (1857) devised the first semi - circular arc perimeter which could be pivoted about it's centre so that each meridian could be tested out to 90° from fixation. In this way the entire visual field for each eye could be evaluated, although the quality of the assessment was coarse since the visual fields were measured with only one type of stimulus. Bjerrum (1889) recognized this anomaly and demonstrated that a more detailed assessment of the visual field could be obtained by using several different sized stimuli to measure sensitivity. All of these early field testing techniques, however, utilized poorly controlled stimulus parameters which resulted in inconsistent results and poor repeatability.

In 1945, Goldmann introduced the hemispheric test area which permitted control of the background luminance and included a system to determine the luminance of the stimulus and a means of

monitoring the patient's fixation (Goldmann 1945a; 1945b). In this way the examination conditions were standardized and facilitated quantitative kinetic visual field investigation.

The method of perimetry using static stimuli was introduced by Sloan (1939) using an arc perimeter. It was not until the development of the hemispheric Tubinger perimeter in the early 1960's by Aulhorn and Harms, however, that static perimetry became a viable technique. The Tubinger perimeter provided the advantages of standardization inherent in Goldmann perimetry without the problems associated with kinetic perimetry (outlined in section 1.1.2). Static perimetry is, however, time - consuming and requires both a skilled patient and a skilled perimetrist (Leydhecker 1983).

Automated perimeters were developed in order to obviate the problems incurred in manual visual field testing. The ultimate aim was to produce a means of measuring visual fields accurately at minimum cost and time; within these guidelines automation was demonstrated to be feasible (Greve et al 1976).

Early attempts at automation were not without problems (Harrington and Flocks 1954); it was not until the introduction of the Octopus, developed as a result of extensive innovative work (Fankhauser et al 1972; Koch et al 1972), that automation became a viable clinical technique. Subsequently, various groups of workers developed and utilized instrument prototypes (Spahr 1975; Heijl and Krakau 1975; Greve et al 1976) to determine, for example, the effectiveness of various test logics, patient - instrument interaction and the efficacy of detection of visual field defects compared to the standard manual instruments. The currently available automated perimeters have a basis in these prototypes but have been extensively modified in the light of subsequent clinical experience.

1.1.2 Static And Kinetic Perimetry

Early perimetry was almost exclusively based upon the kinetic examination technique, which

determines the limits of the visual field by moving stimuli of constant luminance from the periphery to the centre of the visual field until they are reported as seen. The area contained within these limits is known as the isopter for that specific stimulus; several isopters using different stimulus sizes may be plotted during a single examination. Kinetic perimetry is rapid because the stimulus is continuously presented, however, it is susceptible to variations in patient reaction time and in the speed and direction of stimulus movement, which all contribute to produce unreliable results particularly when the visual field sensitivity is reduced (Aulhorn 1969; Fankhauser 1969; Greve 1973). Indeed, when a moving stimuli is just below threshold it will excite a series of receptors infraliminally; in the periphery where spatial summation is relatively high, summation of these successive infraliminal stimuli can occur to produce a response, so that shallow depressions in sensitivity may be missed (Greve and Verriest 1971; Greve 1973). Kinetic perimetry is thus not satisfactory for the detection of small shallow defects, particularly central and paracentral defects or those with a varying sensitivity distribution within a defect, but is the method of choice for the definition of the limits of larger visual field defects (Greve 1973).

The measurement of the differential light threshold ($\Delta L/L$), where (ΔL) is the increment threshold and (L) the background luminance, using stationary stimuli is termed static perimetry. This technique was introduced by Sloan (1939) and was subsequently developed over the period 1950 - 1972 by the fundamental work of Harms and Aulhorn. Stimulus luminance is increased discreetly in steps of a given magnitude rather than continuously, because the temporal interaction and the reaction time of both the subject and the examiner may influence threshold perception (Greve 1973). The size of the luminance steps is determined by the intra - individual variation of threshold measurements and the significance ascribed to slight depressions in sensitivity. The stimulus duration is limited by local adaptation. Inter - stimulus duration is usually in the region of 2 s (Greve 1973). The magnitude of the luminance steps, the intervals between the steps, and the patient's reaction time make the static method a time - consuming procedure. Static perimetry has been shown, however, to be more precise than kinetic perimetry (Harms 1952; Drance, Wheeler and Patullo 1967; Aulhorn and Harms 1972). Indeed, several workers have reported that the static technique of visual field examination is superior to the kinetic in having the ability to detect the

small, isolated scotoma that are often the first and only sign of glaucomatous damage (Drance, Wheeler and Patullo 1967; Aulhorn and Harms 1972; Greve and Verduin 1977).

The combination of static and kinetic perimetry in the detection and assessment phases of perimetry has been advocated by several workers as the most effective means of visual field examination (Harms 1957; Schmidt 1965; Greve 1973). The detection phase determines whether there is a significant reduction in sensitivity and the assessment phase determines the shape and extent of the visual field defect (Greve 1982). In this way, kinetic perimetry can be utilized to examine the blindspot and the periphery in the detection phase, whilst static perimetry can be utilized to qualitatively and quantitatively assess the central regions in the detection and assessment phases.

1.2 Automated perimetry

Accurate manual visual field testing is compounded because the technique is non - standardized, labour - intensive and time - consuming. The introduction of automated perimetry, in which part or all of the visual field examination is performed by a computer instead of a human examiner, has standardized the visual field examination by eliminating intra - and inter - examiner variations in technique, which are fundamental sources of variation in visual field measurement (Berry et al 1966; Henson 1983; Ross et al 1984). Furthermore, since automated perimeters can be operated by technical assistants the need for skilled personnel is overcome, rendering the technique more cost - effective (Johnson and Keltner 1980; Henson 1983; Heijl 1984).

The incorporation of highly sophisticated software has permitted the employment of relatively intricate test strategies and a wide choice of stimulus parameters (Heijl 1977a; Greve 1982) and offers the advantages inherent in the computer analysis of large amounts of data (Fankhauser et al 1972). Automation also permits flexibility in the testing routine via modification of the program, and the facility to optimize a given examination routine to the suspect pathology (Henson 1983). The quality of precise spatial mapping of the visual field incorporated in the software, facilitates a detection rate of sensitivity loss which has been demonstrated to be superior to conventional manual

methods (Koerner et al 1977; Johnson et al 1979). The stimuli can be presented in random order which significantly improves patient fixation (Krakau 1978; Aulhorn et al 1979; Keltner and Johnson 1981) and minimizes the influence of expectancy (Keltner and Johnson 1981). This facilitates the detection of defects and avoids the introduction of variations in local adaptation into the examination; interestingly, it also has the effect of enlarging the size of field defects compared to those measured when the stimuli are exposed in regular sequence (Heijl and Krakau 1977). The excess of computer capacity can additionally be employed for novel types of graphical output and to monitor variables such as screen intensity and eye position (Johnson and Keltner 1980; Henson 1983).

1.3 Stimulus parameters

The choice of stimulus parameters incorporated in automated perimeters has been based largely upon manual perimetry research aimed at extending the dynamic range, although engineering considerations and compatibility with previous instruments have had some influence.

The dynamic range has been defined as the measurement range over which the neuro - visual system can be tested, using specific equipment with a given set of variables (Fankhauser 1979). It relates to the effective range of measurement (between the maximum possible stimulus luminance (ΔL_m) and the threshold stimulus luminance (ΔL_o)) and pertains to the interaction between the perimeter and the patient, rather than the entire operational range of either the neuro - visual system or of the equipment. Attenuation of the dynamic range due to equipment limitations, or due to inappropriate choice of experimental variables, reduces the effectiveness of visual field assessment of regions in which sensitivity has fallen below the limits imposed by this range (Fankhauser 1979). Since ΔL_o increases with increasing background luminance (L), a large dynamic range is obtained by maximising ΔL_m and minimising L. ΔL_m is, however, determined by constraints related to the design of the perimetric apparatus.

1.3.1 Stimulus

The stimulus can be generated by a projection system or by either light emitting diodes (LEDs) or by fibre optics and light guides.

A projection system is considered superior to other methods of stimulus generation (Tate and Lynn 1977) and has the obvious advantage of flexibility (Heijl 1984). The luminance of the stimulus is determined by the luminous intensity of the light source which is varied by neutral density filters and the aperture of the projection system. The incorporation of small stepping motors into the system allows the stimulus to be projected to any location in the visual field. The maximum stimulus luminance (ΔL_m) is, however, governed by factors such as the quantity of light scattered beyond the geometrical boundaries of the stimuli (stray light) which may produce artifactual threshold stimulation, in addition to the practical constraints of the instrument. Wilson (1968) reported that for a high background luminance of 629 asb, scattered light from a bright stimulus can artificially reduce the depth and area of scotomatas. Subsequent studies on the manual Tubinger perimeter at a 10 asb background luminance (Weale and Wheeler 1977) and the Octopus at a 4 asb background luminance (Fankhauser and Haeberlin 1980) confirmed these initial findings and led Fankhauser (1979) to propose that a ΔL_m of 1000 asb was adequate in terms of dynamic range and minimized stray light when used in conjunction with a 4 asb background luminance.

The size of projection stimuli can be altered; the choice of the ideal stimulus size has, however, been the subject of much controversy. Increasing the stimulus diameter provides a larger dynamic range (Fankhauser 1979; Heijl 1985). Indeed, by increasing the stimulus size from 0.108° (Goldmann standard I) to 0.431° (Goldmann standard III) under the conditions of the Octopus, it is possible to extend the dynamic range from between 3 - 12 dB by virtue of spatial summation (Fankhauser 1979). Spatial summation can be described by Ricco's Law:

$$\Delta L \cdot A = \text{constant}$$

where ΔL is the increment threshold and A is the stimulus size. Spatial summation increases with eccentricity, with decrease in stimulus duration, with decrease in adaptation level and with decrease in stimulus size (Barlow 1958; Gougnard 1961; Fankhauser and Schmidt 1960; Sloan 1961).

A further advantage of larger stimulus sizes is the diminished influence of optical blur due to the defocus or light diffusion (Jennings and Charman 1981a; Atchison 1987) which may arise due to media opacities or retinal oedema. It has been reported that stimuli larger than 0.431° are practically unaffected by up to 3 D of blur in the central field whilst larger stimuli also act like a filter, separating pre - receptor from receptor and post - receptor disturbances (Sloan 1961; Greve 1973; Atchison 1987) .

It has been demonstrated, however, that the accuracy with which a defect can be measured increases as the stimulus size decreases (Greve 1973). Indeed, this finding is in agreement with that of Gramer et al (1981) in a study of glaucomatous fields. Greve (1973) proposed that small stimuli subtending 0.1° - 0.17° were preferable for the investigation of field defects, particularly since he reported that the inter - and intra - individual variations were not stimulus size dependent. Conversely, Fankhauser (1979) advocated that 0.431° (size III) stimuli were the best choice for routine automated perimetry, and Radius (1978) demonstrated using manual perimetry that larger stimulus sizes were most appropriate for the perimetric assessment of cataractous eyes. Indeed, the majority of automated projection perimeters offer a choice of stimulus sizes but designate size III as the default value (Heijl 1985); furthermore, all normative data available is for stimulus size III. Minimum stimulus size is also limited by the contrast function of the eye (Fankhauser 1969; Greve 1973), which is approximately 0.1° at the fovea (Campbell and Green 1965).

Interestingly, Crick and Crick (1981) proposed that "sine bell stimuli" which contain a minimum of high spatial frequency components (effectively large stimuli with blurred borders) should be utilized in perimetry. These workers suggested that such stimuli minimize the need for a refractive correction and are unaffected by visual acuity. They have not, however, been implemented in the design of commercially available perimeters.

The main disadvantage of projection systems are cost, complicated and vulnerable mechanical construction and slowness (Heijl 1984). A further disadvantage is that the stepping motors which control where the stimulus is projected in the visual field are slightly audible as they move which may result in the patient becoming conditioned to respond (Taylor et al 1984).

LEDs and light guides when used as stimulus generators are mounted in holes in the perimeter bowl. Since each stimulus is fixed, a limit is automatically imposed upon the number of stimulus locations that can be tested; flexibility may only be increased by rotating the whole bowl or by using additional fixation targets. Geometric size is fixed and intensities have to be individually calibrated during manufacture. LEDs can be easily controlled over a high intensity range without the use of filters but have a narrow light emission which makes their mounting critical. This can be circumvented by utilizing a semi - translucent film to cover the stimuli as in the Competer, Peritest and Perimat perimeters. The LEDs of the Topcon perimeter are lit at the same level as the bowl luminance so that a true increment threshold (ΔL) is measured. Indeed, if as in the Dicon, the LEDs are not covered by a translucent film, each stimulus position will be visible as a black hole, which will lead to changes of local adaptation and the intensity of the stimulus when lit will not be added to an even background so that a true increment threshold will not be measured (Heijl 1985). A further alternative type of stimulus is the fibre optic, which provides the stimulus illumination from a single tungsten light source; these were used in the early Fieldmaster perimeters and more recently in conjunction with a diffusing surface in the Tubinger 2000 perimeter.

1.3.2 Stimulus duration

The duration of the stimulus exposure is considered to be less significant than background luminance and stimulus size in the consideration of the dynamic range of the perimeter. Temporal summation is described by Bloch's law:

$$\Delta L \cdot T = \text{constant}$$

where T is the duration of the stimulus. Bloch's law only applies for stimuli of duration of less than, or equal to, the critical time (during which temporal summation is complete) after which only partial temporal summation is operative. The critical time varies with eccentricity, adaptation level and stimulus size (Barlow 1958; Saunders 1975) but is generally considered to be of the order of 80 ms. Investigations using manual perimetry have, however, demonstrated that some temporal summation may occur centrally after 100 ms (Dannheim and Drance 1971a). Indeed, Harms (1952) stated that stimulus duration had no effect on the differential threshold when it was 100 ms or longer and should never be more than 1 s duration; he suggested a standard stimulus duration of 1 s. It has been proposed, however, that longer stimulus durations may allow the patient fixation to wander and may effectively lengthen the examination (Greve 1973). A further argument against long stimulus exposures is that they facilitate abnormal temporal summation, which is manifested as an increase in summation (Wilson 1970) and which may compensate for the decrease in differential light sensitivity in a diseased eye. The characteristics of temporal summation in both normal and abnormal eyes, however, remain controversial (Dannheim and Drance 1971a).

Greve (1973) reported that normal inter - individual differences in temporal summation were small and suggested that electro - magnetic shutters facilitating short stimulus presentations were most suitable. Indeed, the majority of commercially available automated perimeters employ relatively short stimulus presentations (see Table 1.1.).

1.3.3 Background luminance

Early automated perimeters utilized low background luminances to extend the dynamic range of the particular instrument (Spahr 1973; Heijl and Krakau 1975) which was frequently less than required, due to the output of the projection bulb. Fankhauser (1979) reported that the combined effect of decreasing the background luminance from 40 asb to 4 asb, and increasing stimulus diameter from 0.108° to 0.431° extended the dynamic range by 17 dB. Stimulus light output is, however, now no longer a problem due to better designed instrument components, so that factors other than dynamic range must be considered, such as the optimum stimulus combinations necessary for early detection

	Octopus 201	Dicon AP3000	Humphrey 620	Topcon SBP1000
HARDWARE				
Stimulus				
Type	projection	LED uncovered	projection	LED backlit
Size	0 - V	1.613 mm (II)	I - V	2 mm (II)
Colour	white	570 nm	red, blue, green or white	585 nm
Duration	0.1 s	0.05 - 2 s	0.2 s	0.2 - 3.2 s
Inter - stimulus duration	modified to patient response time	0.05 - 10 s	modified to patient response time	0.2 - 3.2 s
Maximum luminance	1000 asb	10,000 asb	10,000 asb	425 asb
Bowl				
Luminance	4 asb	0, 10, 31.5 or 45 asb	31.5 asb	31.5 asb
Radius	50 cm	33 cm	33 cm	33 cm
Fixation	monitor	monitor Heijl - Krakau	telescope	monitor Heijl - Krakau
SOFTWARE				
Strategy	4 - 2 - 1 double staircase bracketing	4 - 2 ascending method of limits	4 - 2 - 2 double staircase bracketing	4 - 2 -1 treble staircase bracketing
Fluctuation analysis	yes	limited	yes	none

Table 1.1 Summary of the main hardware and software characteristics of the automated perimeters employed in the study

of visual field loss.

Several workers have proposed that visual field investigation in the scotopic and mesopic ranges is desirable in the detection and the differential diagnosis of many ocular conditions (Jayle and Aubert 1958; Greve 1979; Hara 1979). Indeed, it is well established that dark - and light - adapted static perimetry permits visual disability assessment and classification of sub - types in retinitis pigmentosa (Marmor et al 1983) and this has been subsequently confirmed by Jacobson et al (1986) using a modified Humphrey Field Analyser automated perimeter. Shiga (1968) reported that increasing the adaptation level resulted in the depression of isopters in the early stages of retinal and third neuron disease, but had no effect on the fields of homonymous quadrantanopia. Similarly, it has been demonstrated that the detection of early neurological defects (Paige 1985) and of progressive cone dysfunction (Elenius and Leinonen 1986) is enhanced at high background luminances of 629 asb. Conversely, it has been suggested that perimetric investigation at lower adaptation levels permits early detection of glaucomatous visual field defects (Fellman and Lynn 1985; Drum et al 1986; Starita et al 1987). Studies on the influence of background luminance on the spread of results associated with the threshold response have also reported equivocal results: with decreased background luminance, Aulhorn and Harms (1967) found an increase in fluctuations, and Jayle et al (1965) reported a decrease in fluctuations whilst Fankhauser and Schmidt (1960) and Greve (1973) reported no significant difference with change in background luminance.

Decreasing the background luminance from the photopic to the mesopic and scotopic ranges alters the basic operating curve of the retina (Aulhorn and Harms 1972). In the photopic range the Weber - Fechner law holds:

$$\Delta L/_{L} = \text{constant}$$

where ΔL is the increment threshold and L is the background luminance. At the lower border of the scotopic range ΔL becomes a constant, independent of L, for threshold excitation. The relationship describing the transition has been suggested to take the form of:

$$\Delta L/L + ID = \text{constant}$$

where ID is the photon noise of the eye. It is frequently stated, however, that the Rose - de - Vries law where:

$$\Delta L/\sqrt{L} = \text{constant}$$

is operational in the low photopic and mesopic regions, although Barlow (1972) suggested that the Weber - Fechner law may be applicable in the scotopic region and that the Rose - de - Vries law may hold in the photopic region.

It has been suggested that the Rose - de - Vries law holds for the adaptation levels of the current automated perimeters (Fankhauser 1979) however, this has never been substantiated, with many workers considering the levels to conform to the Weber - Fechner law (Aulhorn and Harms 1972; Greve 1973; Klewin and Radius 1986).

Numerical comparison between instruments is confounded by variations in the stimulus combinations particular to each perimeter (see Table 1.1) and also by the nomination of different measurement scales. Sensitivity is most commonly quantified in decibels (dB), which are logarithmic units and are not directly related to the luminance values of the stimulus or the background unless a reference value is specified. Since the stimulus combinations of each instrument vary, the reference conditions between instruments are non - uniform. Thus, for example, 0 dB on the Octopus automated perimeter refers to a 1000 asb stimulus upon a 4 asb background, and on the Humphrey Field Analyser refers to a 10,000 asb stimulus on a 31.5 asb background.

1.4 Strategies

An examination strategy is the course of decisions and actions which occur in order to detect or assess a visual field defect. In the detection phase the sole purpose is to determine whether a defect is present. Since threshold testing is time - consuming, many perimeters employ suprathreshold strategies as the procedure for detection. In general, suprathreshold static strategies utilize stimulus luminances that are at a level assumed to be brighter than normal sensitivity and are presented at relatively few stimulus locations.

1.4.1 Suprathreshold

Single level suprathreshold screening employs a single stimulus intensity to test locations in the visual field (Keltner et al 1979; Johnson et al 1979). This has proved to be a very rapid method of perimetric screening as compared to traditional manual Goldmann procedures (Bebie et al 1976a; Fankhauser 1979) although doubt has been expressed regarding the specificity of this type of one - level screening (Gramer and Kriegelstein 1981; Gramer et al 1982).

Keltner et al (1979) demonstrated that more accurate results could be obtained if screening is performed with two different stimulus luminances, the central field being tested with dim stimuli and the peripheral field with bright stimuli, this was termed two - zone testing.

"Threshold related suprathreshold testing", a strategy which presents stimuli the luminance of which are graded to allow for the variation in sensitivity of the hill of vision with eccentricity, was advocated by Greve (1980). The strategy relies on a built - in standard sensitivity profile (hill of vision) for the patient. There is, however, an inter - individual variation in sensitivity between people with normal visual fields which is reported to be of the order of 2 dB (Verriest and Israel 1965; Greve and Wijnans 1972) although Heijl (1984) suggested that it may exceed 10 dB due to age, media opacities or miosis. To overcome this inter - individual variation, the threshold may be measured at a small number of points prior to supraliminal screening. The appropriate supraliminal

screening intensities are then calculated by the computer on the basis of the data programmed into it for the normal decay of sensitivity with eccentricity and for the desired level of supraliminality (often 0.5 log units to 0.8 log units above threshold), although Greve (1980) advocated that a suprathreshold stimulus of 0.4 log units was acceptable. There are still some problems, however, incurred with this approach, since if the initial threshold determinations are either faulty or performed in areas with pathologically increased thresholds, the choice of supraliminal screening intensities may be erroneous. Most automated perimeters attempt to eliminate this risk by performing threshold determinations at 2 - 4 locations at a given eccentricity and select the location with maximum sensitivity. The accuracy of the initial threshold determinations may be increased by using a test logic which crosses the threshold more than once (Heijl 1977a) or by repeating threshold determinations (Heijl 1985).

1.4.2 Threshold

In manual static perimetry, the methods of threshold determination are variations on traditional psychophysical techniques, such as the "method of limits" (Guilford 1954) although the staircase method (Stiles and Crawford 1934) in spite of it's apparent superiority has been little used (Spahr 1975). Threshold determination by the latter method is more exacting and can only be usefully employed with the help of a computer (Fankhauser et al 1972; Koch et al 1972). Automated perimeters generally employ one of two procedures to measure detection thresholds:

A) The "method of limits", which consists of an ascending series of stimuli, whose luminance is increased from an infraliminal level until it is perceived. The first stimulus is chosen approximately 2 - 4 dB below the mean threshold for the corresponding age group (at that eccentricity) and stimulus luminance is increased in constant and predetermined steps.

B) The "repetitive up and down method" or bracketing technique, which is considered to be almost optimal (Spahr 1975). The first stimulus is selected from the mean of thresholds for a given eccentricity for a given age group. If the first stimulus is not perceived the next stimulus

is increased by 4 dB, otherwise it is reduced by 4 dB. This process is repeated with the correction interval generally decreasing by half each time until the threshold has been crossed twice, designated 4 - 2 - 1 where the final 1 dB resolution is achieved by interpolation as in the Octopus (Figure 1.1), or where the threshold is crossed three times, also designated 4 - 2 - 1, as in the Topcon perimeter, where the final 1 dB increment is a measured rather than an interpolated increment. The number of stimuli which must be presented in order to achieve the end - point is according to Spahr (1975), approximately 4 or 5. Most automated perimeters employ a version of the bracketing technique with different correction intervals (Table 1.1).

The average number of stimuli required for the "repetitive up and down method" is greater than for the "method of limits", however, the latter is less reliable (Bebie et al 1976a). Indeed, the gain of information per response for the bracketing strategy is only slightly below that of the optimal strategy (Bebie et al 1976a). The optimal strategy was developed by Spahr (1975) who applied the principles of mathematical information theory in order to obtain optimal information gain per response. Interestingly, Gandolfo et al (1985) using the automated Goldmann perimeter (Perikon - Optikon) demonstrated that the mean sensitivity and the short - term fluctuations measured by either the double resolution method of limits, "the up and down method" or "the method of limits" obtained manually, were not significantly different.

For both the "method of limits" and the "repetitive up and down method" the problem with selecting the first stimulus on the basis of age - matched normal values, is the presence of interindividual variations in normal sensitivity as previously discussed in this section. Preliminary knowledge of the average sensitivity function at the measured visual field locations, and of factors such as fluctuations and false responses, permits an almost optimal presentation pattern of stimuli which is only limited by instrumental factors; foreknowledge of the average sensitivity function also influences the first luminance step (Spahr 1975). False responses may be either negative, where the patient fails to respond even though the stimulus is well above the previously determined threshold, or positive, where a stimulus is "perceived" even though no stimulus was presented. The precision of computerized threshold determinations can also be increased by allowing the process to

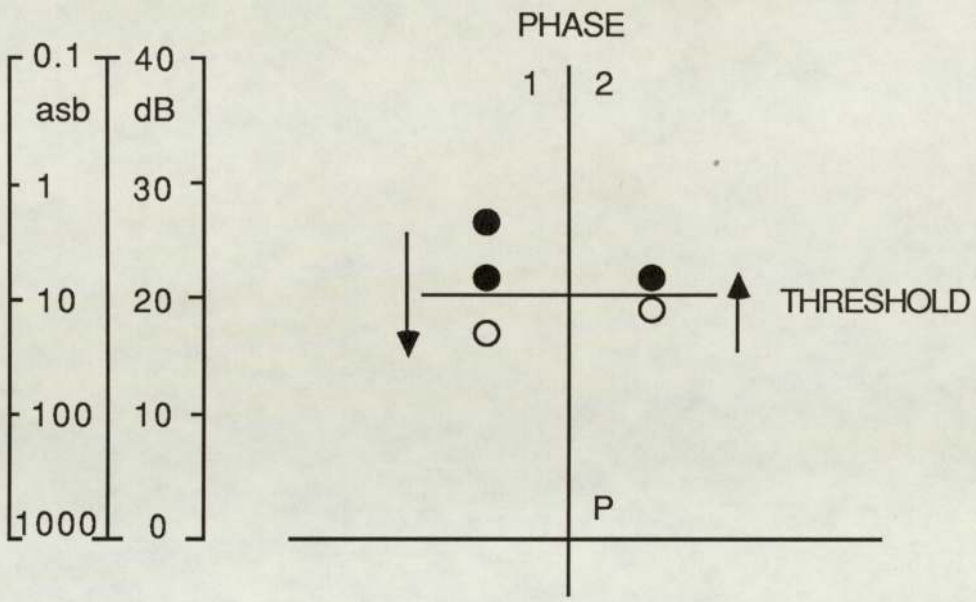


Fig. 1.1 Schematic representation of the "repetitive up and down method" or bracketing technique, employed in quantitative Octopus perimetry. The threshold is crossed twice, first in steps of 4 dB and then in steps of 2 dB. The final 1 dB step is achieved by interpolation.

continue through several reversals at each tested point, but this requires more stimulus presentations and increased examination time (Heijl 1977b; Bebie et al 1976a). In addition, most algorithms have a tolerance for patient errors, more so in complex programs where the threshold is crossed several times before it is determined (Bebie et al 1976a; Heijl 1977a).

1.4.3 Grid configuration

The probability of detecting small depressions in differential light sensitivity by static perimetry depends essentially upon the number of stimulus locations examined, however, the arrangement of the examination grid for a given number of stimulus locations is very important (Greve 1975; Bebie et al 1976b; Fankhauser and Bebie 1979). It was demonstrated that for scotomata of radius greater than 1°, a regular, rectangular grid of 6° resolution, such as the square grid of the Octopus, has twice the detection probability of a grid which tests the same area along two meridians assuming a radial resolution of 1.5° (Fankhauser and Bebie 1979). These authors found that for visual field losses of radius less than 1°, detection probability was extremely low and independent of the type of grid. Indeed, Greve (1975) demonstrated that to detect a 3° circular defect with a probability of 95%, a total of 452 stimuli would be required. Since the purpose of visual field examination is the detection of visual field defects in a relatively short time, a compromise must be established between the conflicting needs of accurate detection and speed. Gutteridge (1984) stated that there are 3 possible alternatives:

1) Systemic sampling.

2) Higher density sampling of areas of the visual field where depressions in sensitivity occur more frequently.

3) A combination of systemic sampling and higher density sampling.

The first alternative has been adopted in several automated perimeters such as the Competer and the

Peritest - first phase in which stimuli are evenly spaced on several concentric circles around fixation, or in the Octopus and Humphrey Field Analyser in which the stimuli are arranged in a square grid configuration. Interestingly, King et al (1986) demonstrated that a grid resolution as fine as 6° is still inadequate for identification of scotomas of the size and depth of the physiologic blind spot in the central field.

The second alternative is employed by several automated perimeters such as the Dicon and in semi - automated instruments such as the Friedmann Visual Field Analyser I and II. The areas which are usually sampled with a higher density are the fixation region, arcuate region, horizontal and vertical midlines and around the blindspot. In other areas, the separation between stimulus locations is greater because visual field losses are less likely to occur there. Indeed, Weber and Dobek (1986) demonstrated that the most effective method of detecting glaucomatous losses using the square stimulus configuration of the Humphrey Field Analyser was to utilize a grid interval of 3° within the central 10°, a grid interval of 4.2° in the 10° - 20° area and a grid interval of 6° in the 20° - 30°. Unfortunately, such software is not currently available for threshold perimetry.

The third alternative of sampling the visual field with a combination of systemic sampling and higher density sampling is employed in automated perimeters such as the Ocuplot and the Fieldmaster series. Indeed, the systemic investigation of the central field and the sampling of selected regions of the periphery (such as the nasal periphery) was advocated for the detection of glaucomatous defects with the Armaly - Drance method of static and kinetic perimetry (Rock et al 1971; 1973; Armaly 1972)

1.5 Fluctuations

The advent of automated perimetry has permitted easy access to numerical threshold values and has provided a means of quantification of the visual field and potential to analyse results (Gloor et al 1981; Henson and Chauhan 1985; Flammer 1986).

Fluctuations in perimetric sensitivity arise, in common with all threshold psychophysical measurements, from the statistical nature of the patient's threshold response. The threshold luminance can be statistically defined as that luminance which is perceived at a 50% probability. In order to increase the probability of a "seen" response from 16% to 84% the stimulus luminance has to be raised by a factor of approximately two to four. The accuracy of thresholds derived from five to seven presentations, which is routine in standard static procedures, will thus be poor. These threshold fluctuations frequently submerge scotoma in the threshold noise which thus become undetectable; alternatively normal threshold shifts may be interpreted as reductions in sensitivity. The magnitude of these effects is generally underestimated, and can only be controlled by statistical evaluation of the threshold fluctuations and by determining the magnitude of the sensitivity loss (Fankhauser and Bebie 1979).

The individual fluctuation at a given eccentricity which arises during a single automated visual field examination is termed the short - term fluctuation (Bebie et al 1976b; Flammer, Drance, Fankhauser and Augustiny 1984). This is estimated in the base programs of the Octopus as the root mean square of the differences between duplicate measurements at 10 selected test locations.

$$SF = \sqrt{1/m \sum_{i=1}^{m} \{ \sum_{r=1}^{R} (x_i - y_i)^2 /R-1 \}}$$

where x_i is the threshold in dB obtained from first testing at a given point i, y_i is the threshold obtained from second testing, R is the number of repetitions (phases), r is one repetition and m is the total number of stimulus locations.

The additional threshold variation observed from one examination to another (separated by a period of hours to years) is called the long - term fluctuation (Bebie et al 1976b; Flammer, Drance and Zulauf 1984). The long - term fluctuation has been described as having two components; homogeneous, which affects all parts of the field equally, and heterogeneous which affects different areas by different amounts and is thought to be influenced by various diseases of the visual system (Flammer, Drance and Zulauf 1984). The components of short - and long - term fluctuations are

significantly positively correlated, but the relationship is not robust enough to accurately predict in an individual the long - term fluctuation from the short - term fluctuation (Flammer, Drance and Zulauf 1984).

The extent of the short - term fluctuation is mainly determined by the level of the differential light threshold (Flammer, Drance, Fankhauser and Augustiny 1984), however, there are a large number of related factors. The thresholding strategy has been demonstrated to influence the short - term fluctuation for automated perimetry (Bebie et al 1976b; Flammer, Drance, Fankhauser and Augustiny 1984; Parrish et al 1984; Lewis et al 1986; Brenton and Argus 1987). In contrast, Zingirian et al (1985) using automated perimetry, found that the strategy exerted no influence on the threshold fluctuations. Interestingly, Koerner et al (1977) reported that there was no difference between the fluctuations obtained with static manual and automated perimetry. Fluctuations decrease with experience of the manual (Aulhorn and Harms 1967) and the automated (Wilensky and Joondeph 1984) perimetric task and increase with fatigue of the subject for manual (Haidor and Dixon 1961; Ronchi and Salvi 1973) and for automated perimetry (Heijl 1977b; Flammer, Drance and Schulzer 1984). Conversely, Rabineau et al (1985) using automated perimetry demonstrated that during a period of one hour fatigue did not influence the short - term fluctuations in normal subjects. Pupil size has a negligible effect on fluctuations in normals but in glaucoma, decrease in pupil size was found to increase the short - term fluctuation for automated perimetry (Flammer, Drance, Fankhauser and Augustiny 1984). Some workers have found that short - term fluctuation varies from one stimulus location to another for manual (Aulhorn and Harms 1967; Greve and Wijnans 1972; Werner and Drance 1977; Donovan et al 1978) and for automated perimetry (Van den Berg et al 1985; Brenton and Phelps 1986; Lewis et al 1986; Heijl et al In press). Other workers have shown, however, that eccentricity has no influence on short - term fluctuations out to an eccentricity of 30° (Flammer, Drance, Fankhauser and Augustiny 1984; Flammer and Zulauf 1985). Decreased sensitivity, was generally found to result in, and be predated by, an increase in fluctuations for manual (Werner and Drance 1977; Koerner et al 1977; Werner et al 1982) and for automated perimetry (Koerner et al 1977; Holmin and Krakau 1981; Heijl and Drance 1983; Flammer, Drance, Fankhauser and Augustiny 1984; Flammer et al 1985), in particular with

increased intraocular pressure (Werner and Drance 1977; Flammer, Drance, Fankhauser and Augustiny 1984; Gloor et al 1984; Rabineau et al 1985; Sturmer et al 1985).

The homogeneous component of the long - term fluctuation has been shown to be significantly related to the variation in the short - term fluctuation and is greater when the intraocular pressure is elevated and when the retinal sensitivity is reduced (Flammer, Drance and Zulauf 1984). This latter finding is in general agreement with that of Ross et al (1984) who demonstrated that long - term fluctuations measured for manual kinetic perimetry were of greater magnitude in subjects with retinitis pigmentosa than in normals.

Clinically, both short - term and long - term fluctuations are relevant in that they limit the accuracy of threshold determination during field testing (Flammer 1985) and may be misinterpreted as early changes in the visual field.

1.6 Data representation and visual field indices

1.6.1 Data representation

Traditionally, perimetric data has been represented by various forms of graphs. Kinetic manual perimetry is generally represented by isopters, although graphics tablets which compute the area contained within an isopter have been recently introduced (Kosaki and Nakatani 1983). The introduction of automated perimetry has, however, permitted easy access to large amounts of numerical data which have been represented in a variety of forms.

The raw numerical data provides the most accurate information, however, it is difficult to interpret (Greve 1982). The gray scale plot, in which the sensitivity values are represented by a series of symbols, is one of the more common representations, and is more easily visualized by defocusing or viewing from a distance (Fankhauser et al 1977; Jay and Yavitz 1981). The gray scale representation does, however, incur some interpretation problems, particularly in the interpolation

of the raw data. The interpolated sensitivities are derived from measured sensitivities at the four neighbouring points using coordinate differences as weighting factors, and are only slightly less accurate than direct measurements when the inter - stimulus grid does not exceed a separation of 6° (Fankhauser and Bebie 1979). Several workers believe that this form of representation despite the inherent inaccuracies is the most useful representation with which to recognize visual field changes easily and quickly, although it does trade intelligibility against information content (Fankhauser and Bebie 1979; Flammer 1986). In addition, gray scales vary between perimeters due to the nomination of different dB scales and choice of different symbols.

Three - dimensional graphs are an alternative means of representing the differential light sensitivity data derived by both manual and automated perimetry (Flammer et al 1981; Hart and Hartz 1982; Hart and Burde 1983; Accornero et al 1984; Swann and Bloesch 1986; Haas et al 1986; Jaffe et al 1986). These plots are analogous to the two - dimensional gray scales but possess the added advantage of an instantaneous visualization of the topography of the visual field particularly in the vertical dimension. Nevertheless, comparison of plots from one publication to another reveals considerable differences in terms of such features as the degree of vertical scaling, the resolution of the plot and the techniques used to remove the hidden surfaces. It is apparent, therefore, that there is a need for standardization of these plots in order for them to become a meaningful method of data representation.

1.6.2 Visual field indices

The techniques for data representation in the two - or three - dimensional form do not, however, provide the clinician with any additional raw data and do not in their current form, represent diffuse damage and fluctuations adequately (Flammer 1986). These representations of the data facilitate the identification of clear - cut visual field changes such as the classical nerve fibre bundle - type defects as well as generalized depressions of the hill of vision. The availability of numerical threshold data provided by automated perimeters, together with the computer capacity of the instrument, permits mathematical and statistical manipulations of the data to calculate visual field indices.

The mean sensitivity (MS) represents the mean of the differential light sensitivity at all the tested locations in the visual field and can be defined as:

$$MS = {}^{1}/_{m} \cdot \sum_{i=1}^{m} x_{i}'$$

where m is the number of stimulus locations and $x_{i'} = {}^{1}/_{R} \cdot \sum x_{ik} \cdot x_{ik}$, the average of local sensitivity results x, at stimulus location i for replication k and R is the number of replications (independent measurements within the same session).

Computation of the M.S. does not involve the use of any age - corrected normal values, and is independent of the short - term fluctuation and the heterogeneous component of the long - term fluctuation if the number of stimulus locations is large enough (Flammer, Drance and Schulzer 1984).

The mean defect (M.D.) is the mean of the difference between the measured sensitivity values and the established normal sensitivity values for the locations tested. The M.D. is a representation of the average loss over the whole field and does not provide localized information and is defined as:

$$MD = {}^{1}/_{m} \cdot \sum_{i=1}^{m} (z_i - x_i)$$

where x_i is the threshold measurement at test location i and z_i is the age corrected normal value at test location i. The M.D. will be most elevated by diffuse depression of the differential light threshold and is relatively unaffected by the short - term fluctuations.

The Defect Volume (D.V.) utilizes an alternative approach, and describes the total defect intensity for separate areas and the whole visual field. The D.V. can be defined as the fall in volume of the three - dimensional representation of the visual field which arises due to a depression in the normal differential light sensitivity (Van den Berg et al 1985). The D.V. is calculated from the normal

volume of the visual field (estimated on the basis of the patient's non - pathological visual field areas) minus the sum of the actually measured threshold values (Langerhorst et al 1985). The standard error in D.V. can be estimated by:

$$DV = \sqrt{n'^2 \cdot \partial^2 / (2n - 2) + n' \cdot \partial^2}$$

where n and n' are the values representing the normal and depressed test locations and ∂ and ∂' are the respective standard errors.

The loss variance (L.V.) represents the local nonuniformity of a visual field defect (Flammer 1984). It is small if the visual field damage is evenly distributed across the field, but is very large in the presence of deep scotomatas. Double determinations are not required for the calculation of L.V. which permits a reduction in the duration of the programs. The L.V. can be defined as:

$$LV = {}^{1}/_{(m - 1)} \sum_{i=1}^{m} (x_i + MD - z_i)^2$$

The L.V. may be increased by threshold fluctuations or by real depressions in sensitivity.

The corrected loss variance (C.L.V.) helps to separate the real depressions in sensitivity from deviations due to threshold fluctuations (Augustiny and Flammer 1985). The threshold fluctuations or scatter are calculated by means of double determinations, it is then possible to determine how much of the L.V. is due to scatter and how much is due to an additional component expressing the real local deviation. The C.L.V. can be defined as:

$$CLV = LV - {}^{1}/_{r} (SF)^2$$

This index is corrected for the short - term fluctuation. When used in conjunction with the M.D. it helps to differentiate between generalized depressions and localized defects.

A further interpretation of the data utilizes the third moment and the skewness of the distribution of the local deviations from normal, which are denoted M3 and Q respectively (Brechner and Whalen 1984). These calculations raise the differences between the measured value and the normal value, for a given stimulus location, to the third power. This has the effect of greatly increasing the impact of a small group of depressed values on the final global statistic. In addition, elevation to the third power allows all the negative differences to retain their original sign. Supernormal values resulting from inherent patient variability affect the final statistic along with the subnormal or depressed values.

The third central moment (M3) is sensitive to deviations present at a small number of stimulus locations and therefore may be helpful in the detection of very early visual field defects. M3 can be defined as:

$$M3 = {}^{1}/_{m} \sum_{i=1}^{m} (z_i - MD - x_i)^3$$

Skewness (Q) provides very similar information to M3 but is a standardized measure and can be defined as:

$$Q = {}^{M3}/_{\sqrt{(LV)}^3}$$

The M3 and Q indices are thought to be more sensitive to localized defects but less affected by diffuse defects than the M.D., L.V. and C.L.V. (Brechner and Whalen 1984).

These visual field indices do not account for the spatial arrangement of visual field loss. This is possible by the calculation of the spatial correlation (S.C.), which is low if the defects are distributed all over the field randomly and becomes larger if the defects are clustered (Bebie 1985). S.C. can be defined as:

$$SC = {}^{1}/_{p} \sum_{(ij)} (z_i - MD - x_i)(z_j - MD - x_i)$$

where p is the number of pairs involved in the summation and ij indicates a summation over pairs of adjacent test locations.

The problem which confounds the use of such statistical tests for clinical decisions, however, is that they are generally based upon inadequate empirical knowledge of the statistics of normal fields and of those with early visual field defects. The use and interpretation of these statistical tests must thus be exercised with caution.

1.6.3 Commercially available analytical programs

In response to the increased interest in the statistical analysis of visual field data a number of user - specified software programs have been designed. These programs have been developed as a result of the innovative work by a number of researchers using the Octopus automated perimeter and more recently using the Peritest and Perimat automated perimeters.

JO and STATJO is a package designed for the Octopus which consists of an examination program JO and an analysis program STATJO. Sensitivity is determined twice at each of 49 stimulus locations and calculates visual field indices, for example, the mean sensitivity and the short - term fluctuation. This permits the evaluation of short - term fluctuations, the influence of examination time, reaction time and false - positive and false - negative responses in addition to measurement of the differential light threshold (Flammer, Drance, Jenni and Bebie 1983). Similar software packages are currently being developed for other perimeters.

The program SARGON was developed for the Octopus to make it possible to design user - defined programs and to store them permanently for subsequent applications (Jenni et al 1983). This program permits the user to design a flexible problem - orientated distribution of up to a maximum of 66 stimulus locations within a radius of 60° (Fankhauser and Jenni 1981). The usual 4 - 2 - 1 bracketing strategy is employed for the locations tested, but the location, sequence and number of determinations are governed by the user. Similar custom programs are available on the Dicon

AP3000 (ZETA program), Humphrey Field Analyser and Competer perimeters.

Program SAPRO is a spatially adaptive routine written for the Octopus 201, which identifies areas of abnormal values in standard testing, and subsequently allows examination of these areas with finer stimulus grids at two or three levels of resolution (Fankhauser et al 1981). The SAPRO program classifies the differential sensitivity of a particular stimulus location into one of three ranges rather than determine the individual differential sensitivity values.

The F - Program was developed for the Octopus to provide high resolution programs (maximum resolution 0.2°) which consist of linearly arranged stimulus locations which may be selected at any orientation in the visual field (Fankhauser et al 1981). The measurements in the case of the F - programs are real threshold measurements, performed by the normal or shortened repetitive bracketing procedure described by Spahr (1975) and Bebie et al (1976a). The program permits the measurement of differential light sensitivity, the local as well as the overall fluctuations, calculation of M.S., and for comparison purposes, the local age - corrected normal sensitivity values (Fankhauser et al 1981).

The DELTA program was introduced as a prototype version for the Octopus (Bebie and Fankhauser 1981; Gloor et al 1980; 1981) and performs data reductions such as M.S., M.D., S.F. and L.F. Furthermore, the program will execute statistical t tests on visual field data selected from two examinations to determine whether any variation in M.S. has occurred and thus provides an index of the long - term fluctuation (Fankhauser and Jenni 1981).

More recently, the program G1 has been introduced for the Octopus, which measures 60 stimulus locations out to an eccentricity of 26° either once or twice as desired (Flammer 1984). The C.L.V. index may be calculated if the stimulus locations have been determined twice, however, if only one measurement has been executed at each location, then only the M.D., L.V., M3 and Q indices are calculated.

The Defect Volume (D.V.) program is currently available on the Peritest and Perimat perimeters (Greve 1985), and calculates the D.V. and the standard error in D.V. (described in section 1.6.2).

1.7 Factors influencing visual field assessment

Various studies of the topography of the normal visual field have been undertaken to obtain age - related normative data, to which the potentially abnormal visual fields can be compared. Such studies have been performed for the Humphrey Field Analyser (Brenton and Phelps 1986; Katz and Sommer 1986), for the Octopus (Haas et al 1986; Jaffe et al 1986) and for the Dicon (Jacobs and Patterson 1985) automated perimeters, although normative data is not available for other automated perimeters such as the Perimat, the discontinued Perimetron and the various versions of Fieldmaster.

Normative values cannot, however, be considered in isolation without evaluating the influence of various factors inherent in the subjective measurement of the visual field.

1.7.1 Influence of optical defocus

Harms (1950) using static manual perimetry demonstrated that uncorrected refractive errors decreased the differential light threshold out to an eccentricity of 10°. Similarly, Fankhauser and Enoch (1962) showed that the differential light threshold measured with Goldmann stimulus size I out to an eccentricity of 30° was markedly affected by defocus. This is in agreement with the manual findings of Sloan (1961) for Goldmann stimulus sizes I and II and with the automated findings of Benedetto and Cyrlin (1985) for stimulus size III (Goldmann III equivalent). Indeed, the latter workers reported that sensitivity at fixation was depressed to a greater extent than more peripheral locations when measured with stimulus size III. Serra (1983) reported that the effect of positive lenses on manual kinetic perimetric thresholds for stimulus II_{2e} was to produce narrowing of the isopter in a series of normal presbyopic subjects.

Accommodative spasm or fatigue can also induce depression in central sensitivity (Tate 1985) the former being common in young uncorrected hyperopes and the latter in undercorrected presbyopes.

1.7.2 Variation with age

Studies with manual kinetic perimetry demonstrated a general contraction of the visual field with age (Feree et al 1929; Goldmann 1945a; Weekers and Roussel 1945; Drance, Berry and Hughes 1967). These findings were more recently confirmed when manual kinetic visual field data was analysed in terms of the area enclosed by the kinetic isopters (Williams 1983) and in the volume of the 3 - dimensional representation (Suzumura et al 1985). Sensitivity loss with aging was found to occur first at the central isopter and spread towards the periphery, with general sensitivity loss manifested after 60 years of age (Suzumura et al 1985).

Studies with manual static perimetry reported that the average differential light sensitivity decreases with age (Goldmann 1945a; Jayle 1960) although the slope and shape of the visual field remain the same. The concept of a hill of vision as a uniform profile which decreases in sensitivity with increasing age was, however, demonstrated to be erroneous using automated perimetry (Jacobs and Patterson 1985). Indeed, Katz and Sommer (1986) reported that the retinal sensitivity was not equally depressed at equivalent degrees of eccentricity from fixation, but was decreased to a greater extent in the superior hemi - field. This was in agreement with Haas et al (1986) who reported that sensitivity was depressed to a greater extent in the superior field and also in the central and peripheral regions, with the pericentral regions affected last. Jaffe et al (1986) demonstrated that the age - related decline in sensitivity increased with eccentricity, and was twice as rapid at 30° than at fixation, resulting in a steepening of the sensitivity profile. These workers attributed these age - related changes to a functional or anatomic loss of photoreceptors, ganglion cells and higher structures.

1.7.3 Influence of pupil size

Variations in pupil size have several implications in perimetry. The pupil may either enhance or degrade the image quality and also controls the amount of light which reaches the retina. The effectiveness of the pupil to facilitate light entry is diminished at oblique angles, since the available area of the pupil decreases more slowly than the cosine of the angle of eccentricity (Spring and Stiles 1948; Jay 1962). The reduction in pupillary area decreases the effective illumination with increasing eccentricity, however, the reduced retinal image projection has been shown to compensate for this (Drasdo and Fowler 1974; Holden et al 1987) so that retinal illumination is approximately constant out to an eccentricity of 80° (Bedell and Katz 1982; Koojiman 1983).

Empirical clinical observations have suggested that the inter - individual differences in pupil size encountered within the normal clinical range have a negligible effect on the kinetic visual field threshold determined manually (Drance, Berry and Hughes 1967; Williams 1983). Drug induced miosis, however, produces isopter contraction out to an eccentricity of 30° (Day and Scheie 1953) and also across the full field (Engel 1942; Kolker and Hetherington 1976; Harrington 1981; Shields 1982). Furthermore, the area of existing glaucomatous field defects can be increased and defects simulating glaucomatous field loss may result from drug induced miosis (Engel 1942; Forbes 1966). Indeed, McCluskey et al (1986) reported that the decrease in pupillary area (for pupillary miosis < 2.4 mm) was significantly correlated with the reduction in kinetic isopter area.

Reductions in pupil size, modified by pharmacological preparations, were reported to produce a maximum depression in static perimetric sensitivity of 0.14 log units out to an eccentricity of 25° (Bedwell and Davies 1977). Similarly, Greve (1973) reported a 0.2 log unit depression in static perimetric sensitivity out to an eccentricity of 25° with decrease in pupil size.

Studies using automated perimetry, have demonstrated that in normal eyes, inter - individual differences in pupil size do not influence mean sensitivity (Brenton and Phelps 1986) nor the magnitude of the short - term fluctuations (Flammer, Drance, Fankhauser and Augustiny 1984).

Drug induced miosis, however, has been reported to depress the mean sensitivity by 0.2 log units measured with static automated perimetry (Fankhauser 1979) out to an eccentricity of 30°, whilst Mikelberg et al (In press) have reported a good correlation between pharmacologically modified pupil area and mean sensitivity out to an eccentricity of 26°.

1.7.4 Influence of training

The influence of training on the manual static perimetric threshold has been investigated by few workers. Aulhorn and Harms (1967) reported an increase in perimetric sensitivity with practise, which was of greatest magnitude in the early sessions, plateaued in subsequent sessions, and was independent of eccentricity.

Similarly, the influence of training on static thresholds determined by automated perimetry has not been extensively investigated. Gloor et al (1981), in a retrospective study with the Octopus with glaucomatous subjects, demonstrated the presence of a 2 dB learning - effect out to an eccentricity of 30°. Conversely, a learning - effect was not demonstrated out to an eccentricity of 30° in the retrospective studies of Gramer et al (1986) with the Octopus and of Kosoko et al (1986) with the Humphrey Field Analyser. Interestingly, several studies have acknowledged the presence of a learning - effect, but believe that it is eliminated by either excluding the first (Flammer, Drance, Fankhauser and Augustiny 1984) or the first two examinations (Wilensky and Joondeph 1984). Furthermore, it has been suggested that any improvement in sensitivity is counterbalanced by a decrease in sensitivity associated with a fatigue effect arising from the examination itself (Katz and Sommer 1986). The findings pertaining to the effect of practise on the differential light sensitivity measured with automated perimetry therefore remain equivocal.

1.7.5 Other Factors

Ethyl alcohol has little influence on the manual perimetric performance of normal eyes. For a 0.05% blood alcohol level, a small increase in central static sensitivity was reported for both

mesopic and photopic adaptation levels together with an enlargement of the blindspot; with kinetic perimetry the central and intermediate isopters were contracted (Gandolfo 1983). Similar findings were demonstrated for a 0.08% blood alcohol level using Octopus perimetry, where the differential light sensitivity remained unchanged, although a decrease in cooperation was manifested by an increase in short - term fluctuations and in the number of false - negative and - positive responses (Zulauf et al 1986).

Short - term treatment with diazepam in young individuals does not significantly influence the outcome of automated perimetry; mean sensitivity was slightly depressed with diazepam treatment, but the short - term fluctuations, false - negative and false - positive responses and the learning - effect remained unaffected (Haas and Flammer 1985). Similarly, Martin and Rabineau (1987) demonstrated that the use of the nonselective betablocker, timolol, on normal subjects did not significantly influence any of the visual field parameters measured in automated perimetry.

In normal subjects the diurnal variation in mean sensitivity out to an eccentricity of 30° measured with the Octopus is small (Mizutani and Suzumara 1985), however, some ocular hypertensive patients demonstrated large variations in mean sensitivity which corresponded to the diurnal variation in intraocular pressure. These authors suggested that those subjects who demonstrated a diurnal variation in mean sensitivity were likely to develop glaucoma.

2. RATIONALE FOR THE RESEARCH

2.1 Aims of the study

The study arose from the work undertaken in the Department in conjunction with the Birmingham and Midland Eye Hospital (B.M.E.H.) in which visual fields derived by conventional kinetic and semi - automated static manual techniques were compared to those of a pioneering automated perimeter, the Octopus 201 (Flanagan et al 1984a; 1984b; Wild et al 1984). From this earlier work a hypothesis had been proposed that different combinations of stimulus parameters presented by a given instrument can, in certain ocular and/or neurological disorders, be manipulated to provide diagnostic information additional to that obtained from the conventional perimetric examination. In particular, it was reported that some patients with retinitis pigmentosa (R.P.) behaved atypically over the dynamic range (Flanagan et al 1984b). At the same time however, it had also been recognized that patient specific variables such as, for example, intraocular light scatter arising from cataract may influence the results in perimetry (Barnes et al 1985; Wild et al 1986).

The aim of the current study was therefore twofold: firstly, to investigate the sub - hypothesis that patients with R.P. behave atypically over the dynamic range and secondly, to concurrently investigate the influence of extraneous factors on the format of the normal perimetric profile.

It was intended that the research should be undertaken both at the Retina Department of the B.M.E.H. and at the Department of Vision Sciences, Aston University. Patients with abnormal ocular conditions were to be drawn from the B.M.E.H. and were selected with the knowledge and cooperation, of the consultant ophthalmologists. Normal subjects, for control purposes, were to be selected from the University clinics and from the undergraduate and academic populations of the university. The study was to specifically involve two distinctly different automated perimeters, namely, the Octopus 201 at the B.M.E.H. which employs projected stimuli, and the Dicon AP3000 at Aston University which utilizes LED stimuli. These perimeters were selected in order to

investigate the role of the two different stimulus configurations in the particular perimetric assessment. In addition, it was proposed to utilize the manual Goldmann bowl perimeter, Tubinger bowl perimeter and the Friedmann Visual Field Analyser II (F.V.F.A. II) as necessary.

2.2 Procedures

It was intended that the two aims of the study should be investigated concurrently. The detailed aspects of the experimental design were determined as the study progressed. Certain decisions were made prior to commencement of the practical investigations, whilst others were implemented in the light of experience gained during the course of the study.

It was envisaged that the format of the perimetric sensitivity profile in patients with R.P. would be investigated under various states of parametric adjustment, which included variation in stimulus size, stimulus duration and adaptation level, and the use both of static and kinetic stimuli. Since no single automated perimeter permits variation of all these parameters a combination of perimeters was employed. These included, in addition to the Octopus 201 and the Dicon AP3000 automated perimeters, manual static and kinetic perimetry with the Goldmann bowl perimeter and manual static perimetry with the Tubinger bowl perimeter.

At the outset of the study it was recognized that the current lack of understanding of the mechanisms generating the perimetric response in normal eyes posed problems in the interpretation of the responses in the abnormal eye, such as those reported by Flanagan et al (1984b). It was felt that the preliminary stages of the study also should address this problem. High resolution assessment of perimetric sensitivity across the entire visual field as a function of stimulus size was determined in a series of normals using the Octopus 201 perimeter, in order that the resultant sensitivity profiles could be scaled, such that cortical representation across the visual field was theoretically constant (M - scaling). M - scaling of the perimetric profiles, with respect to spatial stimulus parameters, did not result in the expected isosensitive profiles. This finding stimulated further investigations. The F.V.F.A. II clinically produces an isosensitive profile in normal

subjects by presenting larger stimuli in the periphery compared to those in the central regions. The sizes of the stimuli were measured to determine whether they increased as a function of cortical magnification with eccentricity or whether the relationship followed an alternative power function. The results from these two investigations indicated that the sensitivity to conventional perimetric stimuli depended upon a likely interaction between ganglion cell density and the spatial summation properties of the ganglion cells. To test these conclusions, the investigation was repeated using a parametric adjustment which facilitated less spatial summation, namely a higher adaptation level and longer stimulus duration. Since an automated perimeter employing the stated parametric adjustment was then unavailable, arrangements were made for the relevant data to be collected by a former post graduate student from the Department, Dr. J.G. Flanagan now at the University of Waterloo, Ontario, Canada. The latter study was undertaken using the Humphrey Field Analyser 620 for a further sample of subjects and was matched to the original Octopus study with respect to procedure and analysis. Dr. Flanagan was blind as to the purpose of the experiment and was not involved in the experimental design, analysis or consideration of the data. The investigation validated the previous conclusion that the spatial characteristics of ganglion cells had an important role in the processing of perimetric spot stimuli.

Subsidiary peaks in perimetric sensitivity recorded by the Octopus 201 were found across the visual field, which corresponded to local elevations in the rod density data of Osterberg (1935) and the ganglion cell density data of Oppel (1967). This led to investigation of the relationship between the topographical variations in the visual field profile and those of the ganglion cell, rod and cone densities.

Two major extraneous factors, namely, degradation of the perimetric profile due to intraocular light scatter arising from media opacities and the possible improvement in perimetric sensitivity arising from prior perimetric experience, were also acknowledged as having an important role in the perimetric assessment of patients. The effect of these variables on the format of automated perimetric profiles was relatively unknown. Concurrent investigations were therefore undertaken to determine the influence of these factors.

It became apparent that there was no definitive means of determining the influence of intraocular light scatter on perimetric sensitivity. One approach was to investigate light scatter in a series of patients with unilateral media opacities, however, the integrity of the visual system behind the media opacity could not be guaranteed. An alternative possibility was to induce intraocular light scatter using a simulating cell placed in front of the normal eye. The validity of such a simulation as an accurate reflection of the visual degradation produced by media opacities, however, was open to conjecture. It was firstly decided to induce intraocular light scatter in normal subjects using scattering solutions contained in plano cells. Numerous trials were undertaken in order to select a suitable solution which consistently scattered light within the limits required by the experiment. Having derived the relationship between perimetric attenuation and intraocular light scatter in normals, the results were compared with those obtained for a series of patients with actual media opacities. Ideally, the patients should have had unilateral media opacities so that the clear eye could act as a control, however, such patients were found to be scarce. Consequently, it was decided to expand the scope of the study to include patients who exhibited asymmetry in the degree of media opacity between the two eyes, or who exhibited media opacities in one eye and an intraocular lens (permitting good visual function) in the other. The influence of adaptation level and stimulus configuration on the degree of perimetric attenuation arising from intraocular light scatter was assessed using the standard stimulus parameters with the Dicon AP3000 at 2 adaptation levels and with the Octopus 201 using the standard stimulus parameters.

The influence of prior perimetric experience on sensitivity was assessed over the full field using projection perimetry in a series of normal subjects who were inexperienced in perimetric techniques. It was apparent that numerous experimental designs could have been employed. It was decided to assess the influence of repeated examinations (undertaken on consecutive days) on the perimetric sensitivity of the right eye alone. The Octopus 201 was selected for the investigation as it provides the facility to measure the entire visual field in one program.

It was acknowledged that the quantitative profiles of the normal control subjects and the perimetric assessment of the abnormal subjects could also be intrinsically influenced by individual variations

in peripheral refractive error, pupil size and accommodative level. The significance of these factors in perimetric assessment was determined in separate samples of normal observers.

The effect of peripheral refractive error on perimetric sensitivity was assessed in a series of normal emmetropic subjects using the Octopus 201 such that the influence of stimulus size could be determined. Peripheral refraction was measured with a modified version of the commercially available optometer, the Canon Autoref R - 1. This instrument was selected since it employs an infra - red method of measurement which does not influence pupil size.

The influence of changes in pupil size and accommodative status were determined using the Dicon AP3000 autoperimeter which facilitates investigation of the effect of adaptation level and requires a high level of accommodation by virtue of the 33 cm bowl radius compared to that of the 50 cm bowl radius of the Octopus 201 perimeter. The study was conducted on normal emmetropic subjects and the pupil size and accommodative status of the subjects was modified using appropriate topical ophthalmic drugs.

It was considered that the LEDs of the Dicon AP3000 perimeter, which have been described as "black hole" LEDs, because they do not incorporate a device to mask the aperture in which they are situated, may produce a measurement of sensitivity unique to that perimeter. During the later stages of the study the opportunity to use the Topcon SBP1000 autoperimeter presented itself. The Topcon employs LED stimuli similar to those of the Dicon, but without the "black hole" effect because they are backlit to match the surrounding luminance. The format of the perimetric profiles measured with "black hole" LED stimuli and backlit LED stimuli was compared.

Progress throughout the course of the study was relatively unimpeded. The only major problem arose in the selection of patients. All patients were required to be volunteers and had to be approached by letter. The response rate, to a request to participate in the study was approximately 50%. This led to difficulties in the selection of patients with relatively rare ocular conditions, in particular those patients with truly monocular cataracts.

3. CORTICAL REPRESENTATION OF THE PERIMETRIC PROFILE

3.1 Introduction

It is well established that a topographically organized representation of the visual field is maintained through many stages of processing in the mammalian visual pathway. The scale of these topographic representations varies with visual field location, such that the central areas have a much larger representation than the peripheral regions. This emphasis on central vision is apparent at the retinal level where it is manifested by large regional variations in the density of ganglion cells (Van Buren 1963; Oppel 1967) and of cones (Osterberg 1935); similar variations in the density of the amacrines and of the bipolars would be expected although quantitative data in human has yet to be determined. The rod population (Osterberg 1935), however, does not reflect this central enhancement. The anatomical emphasis is further endorsed by Woolsey et al (1942) who suggested that the scaling factor for a variety of sensory representations is related to the peripheral innervation density rather than to the physical size of any portion of the peripheral structure.

3.2 Studies of cortical representation in animals

The earliest attempts to quantify the scaling of the visual field at the cortex were reported in animals. Talbot and Marshall (1941) devised an index of cortical representation expressed as the angle, measured radially from the centre of gaze, which is represented on each millimetre of the cortex. They demonstrated in the rhesus monkey, that a circle subtending 1 minute of arc at the fovea was magnified 10,000 times and covered a 0.5 mm diameter of the cortex. Daniel and Whitteridge (1961) utilized the reciprocal of this index and defined the cortical magnification factor (denoted by M) as the linear extent of striate cortex, in millimetres, corresponding to one degree of arc in visual space. From cumulative results for various monkeys and baboons, Daniel and Whitteridge (1961) produced an estimate for M of 5.6 mm deg^{-1} at the fovea. A foveal value of the order of 6 mm deg^{-1} at the fovea has also been reported for the squirrel monkey (Cowey 1964).

Subsequent studies have provided estimates of the linear magnification factor for the foveal representation in macaque striate cortex and these span a seven - fold range in M: namely, 4.5 mm deg^{-1} (Hubel and Wiesel 1974), 13 mm deg^{-1} (Tootell et al 1982; Van Essen et al 1984) and 30 mm deg^{-1} (Dow et al 1981).

Many of the earlier animal studies observed that M in monkey (Daniel and Whitteridge 1961; Whitteridge and Daniel 1961; Rolls and Cowey 1970) and visual acuity in human (Weymouth 1958) declined in a similar manner with increasing eccentricity. The monotonic decrease in visual acuity with increasing eccentricity has been quantitatively related to the concomitant reduction in retinal cone (Osterberg 1935) and ganglion cell (Weymouth 1958; Van Buren 1963) density. In addition, Rolls and Cowey (1970) demonstrated that between 10° and 50° eccentricity along the horizontal meridian, the cortical magnification was approximately proportional to retinal ganglion cell density. Within the central 10°, however, this relationship is not valid as the ganglion cells are displaced from their receptive fields by an indeterminate amount.

More recently it has been suggested that the amplification of the central region of the visual field at the primate striate cortex does not arise solely because of increased central ganglion cell density but is subject to the central magnification provided by subcortical structures (Cynader and Berman 1972; Malpeli and Baker 1975; Myerson et al 1977; Perry and Cowey 1985). An enhanced central representation at the superior colliculus in macaca mullatta has been reported by Cynader and Berman (1972) which is in accord with the findings of an enhanced central representation at the lateral geniculate body and at the superior colliculus in macaca mullatta (Malpeli and Baker 1975). In the afoveate owl monkey, Myerson et al (1977) demonstrated that the proportion of the cells in striate cortex devoted to central vision is much larger than the comparable proportion of retinal ganglion cells. A similar enhancement has also been reported for the macaque (Van Essen et al 1984; Perry and Cowey 1985).

The most direct data on human M is that reported by Brindley and Lewin (1968), who implanted electrodes in the occipital pole of a blind patient and mapped the cortical phosphenes produced by the stimulation along the inferior meridian. Cowey and Rolls (1974) utilized this data and related the linear separation of each stimulating electrode pair to the angular separation of the corresponding phosphene. By this means they calculated values of M for locations out to an eccentricity of 30° along the inferior meridian. Comparing these values with estimates of peripheral visual acuity for man derived by Wertheim (1894), Cowey and Rolls demonstrated a monotonic decline of M from 4 mm deg^{-1} at 2° eccentricity to 0.5 mm deg^{-1} at 25° eccentricity in the inferior field. By extrapolation they predicted a foveal value of 15.1 mm deg^{-1}. It has been suggested, however, for the cat (Wilson and Sherman 1976; Tusa et al 1978) and for man (Drasdo 1977) that the areal cortical magnification, M^2 rather than M is directly proportional to the projected ganglion cell density (cells deg^{-1}) in visual space for peripheral angles greater than 10°.

Drasdo (1977) was the first to estimate the value of M in man across the entire visual field including the central 10°. Based on the assumption that $M^2 = gD$ where D is the density of retinal ganglion cells and g is a constant, and by using data on ganglion cell receptive field density, the anatomical obstacle posed by the foveal excavation of ganglion cells was obviated. Drasdo plotted the best available estimates of human ganglion cell density (Vilter 1954; Van Buren 1963; Oppel 1967), took a mean line between the data points for each meridian and corrected these for the optical magnification of the eye (Drasdo and Fowler 1974). By extrapolation to the foveal region, by means of Polyak's (1957) data for the central - most cone density, Drasdo obtained an M - value for the foveal area of 11.5 mm deg^{-1}, and fitted an equation to the data (which was valid for the central 40°):

$$V = k[\, 1 - SE(1 - 3E^2 \,.\, 10^{-5} + 8(SE)^{5.5} \,.\, 10^{-10})]$$

where V provides an estimate of $1/\sqrt{D_r}$ at an eccentricity E, and S varies as a function of meridian:

$S_{(temporal)} = (0.46 - 0.00043E)$

$S_{(nasal)} = (0.50 + 0.0019E)$

$S_{(superior)} = (0.62 + 0.0033E)$

$S_{(inferior)} = (0.66 - 0.0006E)$

The values obtained were found to be highly correlated with established visual acuity values (Wertheim 1894; Dunsky 1980) and additionally with estimates of M derived from migraine scotoma dimensions (Richards 1971) and from the cortical phosphene distributions (Brindley and Lewin 1968). The use of the central - most cone density as an index of the central ganglion cell receptive field density is, however, dependent upon the assumption that the ratio of foveal cones to ganglion cells is one to one (Polyak 1941; Missotten 1974). Recent evidence suggests, however, that in monkey this ratio is nearer 1 to 1.6 (Van Essen and Anderson 1986) although this has yet to be confirmed in human.

Some doubt was expressed regarding the validity of Drasdo's findings by Hughes (1978). He argued that the ganglion cell distributions, on which Drasdo based his conclusions, were obtained by unreliable techniques which did not measure shrinkage or have a consistent criterion for the type of ganglion cell counted and should not be pooled since they differed by more than 100 - fold at some eccentricities. Drasdo (1978) countered this argument by pointing out that the data had not been pooled, that shrinkage corrections had been made and that Oppel's (1967) final ganglion cell count fell short of Van Buren's (1963) by only 40%.

Rovamo and Virsu (1979) although in agreement with the general principles of Drasdo (1977) considered that Polyak's (1957) cone densities were too high. They included the cortical magnification data of Hubel and Wiesel (1974) and used an averaged value of foveal cone density obtained from the results of Polyak (1957) and Rolls and Cowey (1970) to devise four equations, one for each principal meridian of the visual field. These equations related M_E, the magnification at a given eccentricity E, to the magnification at the central fovea M_O; a value of 7.99 mm deg^{-1} was obtained for the fovea.

$$M_{E\ (nasal)} = (1 + 0.33E + 0.00007E^3)^{-1} M_O$$

$$M_{E\ (temporal)} = (1 + 0.29E + 0.000012E^3)^{-1} M_O$$

$$M_{E\ (superior)} = (1 + 0.42E + 0.00012E^3)^{-1} M_O$$

$$M_{E\ (inferior)} = (1 + 0.42E + 0.000055E^3)^{-1} M_O$$

3.4 M - scaling of visual function

The quantification of M in human has made it feasible to investigate how various stimulus parameters should be scaled in order to obtain equal sensitivity across the visual field. It has been proposed that if stimuli were magnified at peripheral visual field locations, in inverse proportion to the human M, then sensitivity would become independent of eccentricity (Rovamo and Virsu 1979). This process has been termed M - scaling.

Utilizing their revised values of M published in 1979, Rovamo and Virsu (1979) demonstrated that the photopic contrast sensitivity function across the entire visual field could be made similar, if the cortical representations of the stimulus gratings were made equivalent by means of M - scaling and thus independent of eccentricity. High spatial frequencies were not M - scaled successfully, however, and it was proposed that this arose because the high frequency images were subject to greater optical degradation. These investigations were subsequently extended to the temporal characteristics of contrast sensitivity; area, spatial frequency and cortical velocity were successfully M - scaled to produce equal sensitivity at all eccentricities (Virsu et al 1982). It was concluded that foveal and peripheral photopic vision were qualitatively similar in spatio - temporal visual performance (Rovamo and Raninen 1984).

The process of M - scaling has been successfully applied to a variety of other psychophysical functions although the scaling factors employed to produce isosensitivity have varied. Foster et al (1981) successfully scaled the fine - grain movement illusion across the visual field using the M values of Cowey and Rolls (1974), whereas, at suprathreshold stimulus levels, motion and displacement thresholds (Wright and Johnston 1983) and lower thresholds for motion (Johnston and

Wright 1983) were scaled successfully using Rovamo and Virsu's (1979) values of M. Noorlander et al (1983) estimated the scaling factor for colour contrast gratings by calculating the ratio between the foveal and the peripheral stimulus sizes which yielded identical colour discrimination and found that the ratio correlated well with Drasdo's M values. Conversely, Rovamo (1983) altered the grating area and spatial frequency of luminance modulated chromatic gratings in proportion to 1/M using the M values of Rovamo and Virsu (1979) and produced equal sensitivity at all eccentricities, except for the high spatial frequencies over 1 cycle mm^{-1}. The incompleteness of the scaling was attributed to optical attenuation and increasing ganglion cell summation in the periphery. McKee and Nakayama (1984) demonstrated that although differential velocity threshold plotted as a function of stimulus velocity increased with eccentricity, the functions could be normalized by expressing stimulus velocity with reference to the fall in acuity with eccentricity (resolution units sec^{-1}). They considered the acuity gradient to be a psychophysical estimate of the cortical magnification factor. Utilizing an alternative paradigm, namely the detection of coherent motion from random noise, Van der Grind et al (1983) demonstrated that motion detection performance is invariant throughout the temporal visual field provided stimuli are scaled using the cortical magnification factor of Drasdo (1977) to obtain equivalent cortical sizes and velocities. In contrast, D_{max}, the maximum displacement which allows a subject to report on the direction of apparent motion (Braddick 1974; Baker and Braddick 1982) and V_m, the highest velocity detectable as coherent motion, do not scale in accordance with the Rovamo and Virsu (1979) estimates, although D_{min}, the minimum displacement of random dots, increases with eccentricity in approximate proportion to M^{-1} (Baker and Braddick 1985). Interestingly, the apparent velocity of drifting gratings was made equivalent across the visual field, using factors which were found to be proportional to the square root of the macaque mean cortical receptive field area (Johnston and Wright 1986).

There are other visual functions, however, which do not become independent of retinal location by M - scaling spatial stimulus parameters using any of the conventional values of human M. Hyperacuity, as determined by vernier acuity or orientation detection paradigms (Westheimer 1982) and temporal order detection (Westheimer 1983) have been shown to decay faster than grating acuity with eccentricity and, when M - scaled, the superiority of the fovea over the periphery is retained. Similarly, for stereoacuity measurements described by using the outline of two squares as stimuli,

the peripheral retina is less sensitive than the fovea even when the optimum square separations are utilized (Fendick and Westheimer 1983).

Visual orientation discrimination has been shown to increase with scaled stimulus length up to a critical length for the particular eccentricity. Beyond this critical length the function plateaus, never attaining the sensitivity of the fovea (Spinelli et al 1984). Interestingly, Scobey (1982) proposed that orientation discrimination was related to cortical receptive field size. He scaled stimulus length by the average size of the receptive fields of single neurons in the striate cortex of monkey (Hubel and Wiesel 1974). In this way visual orientation discrimination was made independent of visual location out to an eccentricity of 20°; beyond this eccentricity, however, orientation discrimination decreased regardless of stimulus length (Scobey 1982). Hampton and Kertesz (1983) utilized the magnification factor of Rovamo and Virsu (1979) to scale the magnitude of the disparity and the length of the test stimulus for the measurement of the fusional vergence response to peripheral stimulation and evaluated the relative contributions of motor and non - motor components to the fusional response with eccentricity. This adjustment, however, failed to remove the variations in the size of the motor response with eccentricity. M - scaled critical flicker fusion frequency stimuli have also yielded different sensitivities across the temporal visual field, but have been equated by additionally adjusting the retinal illuminance, in inverse proportion to Ricco's area, a process termed F - scaling (Rovamo and Raninen 1984). The values used by Rovamo and Raninen (1984) for Ricco's area were pooled from Wilson's (1970) spatial summation data measured at an adaptation level of 674 asb, and from foveal and parafoveal values at 10 asb (Inui et al 1981) both of which were measured along the nasal visual field. Spatial summation, and by implication Ricco's area, varies both with eccentricity (Fankhauser and Schmidt 1958; Sloan 1961; Wilson 1970), and background luminance (Barlow 1958; Fankhauser and Schmidt 1958) and possibly meridionally (Obstfeld 1973). This type of calculation would therefore seem inappropriate. More recently, it has been suggested that MF - scaling ie. scaling in proportion to retinal illuminance as well as retinal ganglion cell density, is applicable only to cone and not to rod vision (Raninen and Rovamo 1986). These workers suggested that MF - scaling was inappropriate for rod vision firstly because estimates of scotopic Ricco's area increase with eccentricity faster than estimates of photopic Ricco's area and secondly the amount of luminous flux collected by ganglion cells in rod vision

cannot be calculated by simply multiplying retinal illuminance by the scotopic Ricco's area.

Levi et al (1985) suggested that the failure to produce isosensitivity profiles for position acuities using the scaling factors which had been successfully used for grating acuities, arises because resolution is limited by retinal processes, whereas position acuities are limited by cortical processes. These workers demonstrated that central and peripheral thresholds for position acuities (vernier, phase and stereopsis) could be equated by using an alternative value of M (Dow et al 1981; Tootell et al 1982; Van Essen et al 1984) which was derived from physiological and anatomical evidence on monkey studies, as opposed to conventional M - values based on human retinal ganglion cell and cone cell densities.

3.5 Aim of the investigation

The knowledge of the relationship between ganglion cell receptive field separation and the stimulus sizes necessary to produce isosensitivity profiles is important in providing further insight into the processing of perimetric stimuli.

It was envisaged that this relationship would be studied in the two types of static perimetry, namely, that which assesses the differential light threshold by varying stimulus luminance whilst maintaining a constant stimulus size and that in which both stimulus size and stimulus luminance are varied. The former approach to static threshold perimetry, in which stimulus luminance is variable, constitutes the conventional method of quantitatively determining the sensitivity profile across the visual field. The latter approach, in which stimulus size becomes larger as a function of eccentricity, compensates for the normal decay in sensitivity in the periphery and thus results in a clinically isosensitive profile across the visual field. This approach facilitates both single and multiple stimuli presentation of stimuli and enables suprathreshold gradient adapted strategies to be easily adopted in addition to threshold strategies (Figure 3.1). The magnitude of the increase in stimulus size with increasing distance from fixation is, however, determined empirically.

The particular configuration of the sensitivity profiles produced by both types of thresholding

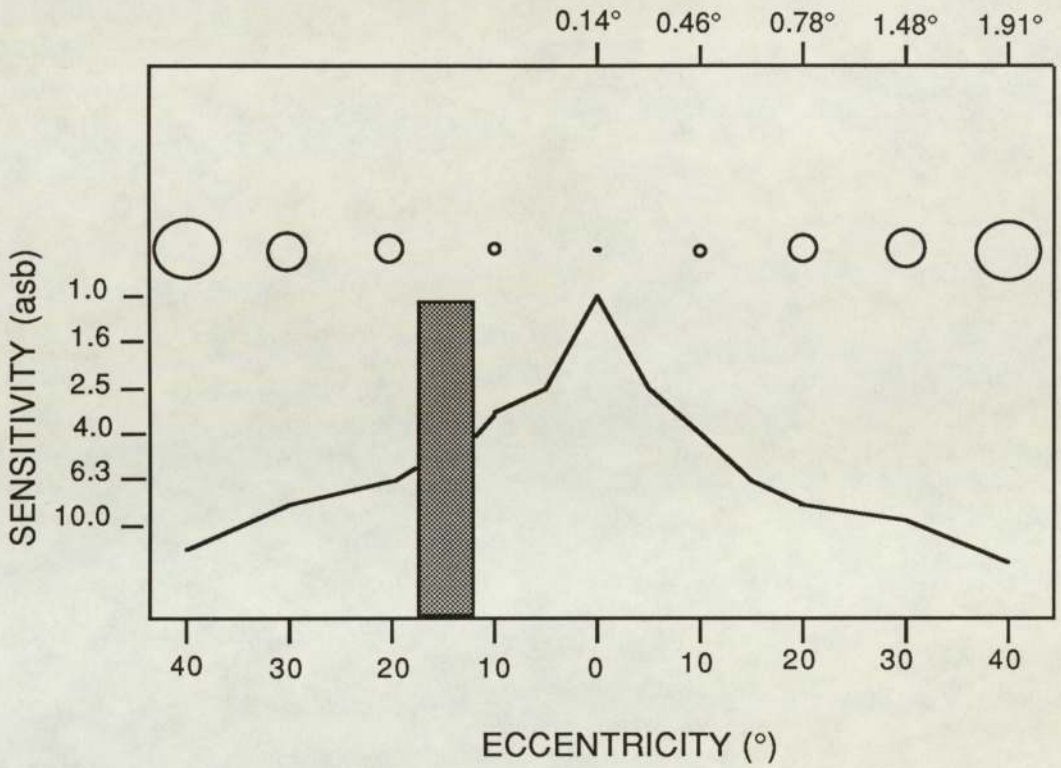


Fig. 3.1. Comparison of the two types of static perimetry: the profile of static perimetry with constant luminance and variable stimulus size (open circles) and the profile of static perimetry with constant stimulus size and variable stimulus luminance (solid line); the shaded area represents the blindspot (after Luddeke and Aulhorn 1977).

approach are a function of the interaction between the stimulus parameters afforded by the instrument and the individual patient.

The purpose of the investigation was to determine whether the M - scaling function using the conventional values of human M (Rovamo and Virsu 1979) could be successfully applied to the standard spot stimuli employed in the two types of static perimetry. This involved: firstly, M - scaling of the stimuli of a perimeter which normally records maximum sensitivity at the fovea; and secondly, investigation of the stimulus sizes employed by a standard clinical instrument, which produces a clinically isosensitive gradient, to determine whether the stimuli vary as a function of M with increasing eccentricity.

3.6 Experimental work

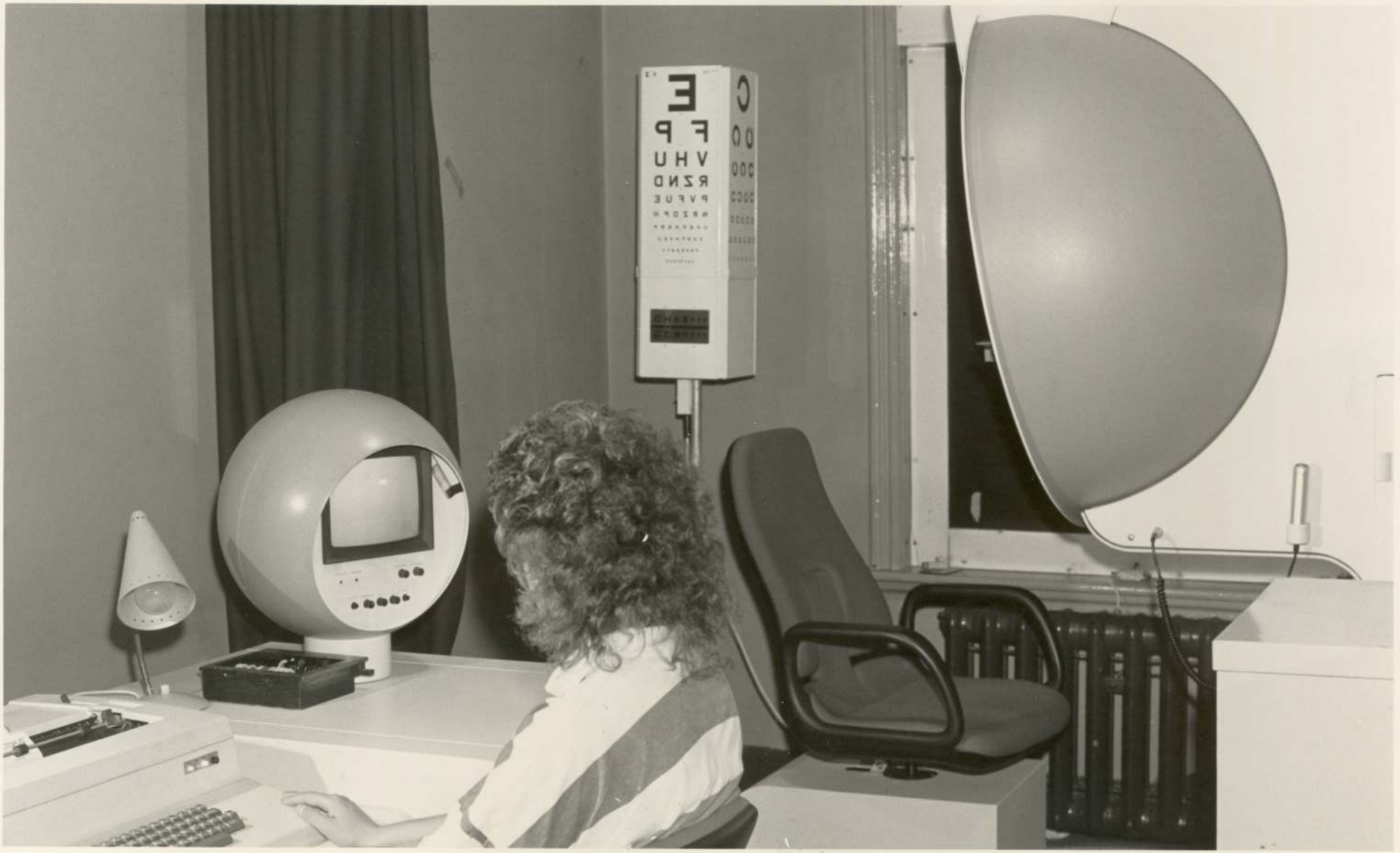
3.6.1 Static threshold automated perimetry: constant stimulus size, variable luminance

Hardware

The Octopus 201 is an automated projection perimeter consisting of a hemispheric bowl, projection system, microprocessor, double disc drive and keyboard (Plate 3.1). The perimeter bowl has a radius of 50 cm, and a luminance of 4 asb which is calibrated by the computer at the beginning of each examination. Stimulus size can be varied from one program to another (Goldmann equivalents 0 - V; 0.054°, 0.108°, 0.216°, 0.431°, 0.862° and 1.724° projected diameters respectively) and the stimuli may be presented at an almost infinite number of stimulus locations arranged on a square grid configuration. The stimulus duration is 100 ms and the inter - stimulus duration regulated according to the reaction time of the patient. The maximum stimulus luminance is 1000 asb, which permits a dynamic range of 0 dB (1000 asbs) to 51 dB (0.008 asbs), where a step of 1 dB corresponds to a stimulus luminance of 0.1 log unit. Fixation is monitored via an infra - red camera onto a television monitor.

Overleaf...

Plate 3.1 The Octopus 201 automated perimeter.



Software

The Octopus 201 employs both screening and threshold strategies, although the screening programs may only be executed with stimulus size III. The determination of threshold is carried out using a 4 - 2 - 1 double staircase thresholding strategy, in which the threshold is crossed first in steps of 4 dB and then in steps of 2 dB. The final 1 dB resolution of sensitivity is determined by interpolation. The starting value is selected from either the age - corrected standard data stored on the master disc or from previous data for that particular patient. The short - term fluctuation is measured in base programs such as Program 21 and 31, as the root mean square (R.M.S.) value of the differences between double measurements at 10 selected locations across the visual field. The R.M.S. value, in addition to the number of false - negative and false - positive responses, is printed out for each examination to provide an index of the reliability of that patient.

3.6.2 Materials and methods

The sample comprised 10 clinically normal, emmetropes (mean age 21.4 years, S.D. 1.35 years; 3 females, 7 males) who were experienced observers in perimetry and in general psychophysical techniques of measurement. Visual acuity was 6/5 or better in each eye. The differential light threshold for the visual field of the right eye was determined for each of the six stimulus sizes. Stimuli were presented at 15° intervals over the full field (Program 21) and at 6° intervals out to an eccentricity of 30° (Program 31). The head was steadied with the head clamps and chin bar of the instrument and fixation was constantly monitored with the video camera. Subjects were advised to rest at intervals throughout the examination and were advised if fixation was incorrect. Natural pupils were used throughout; the mean pupil size was 7.03 mm (S.D. 0.71 mm). The subjects attended for seven sessions within a maximum period of four weeks.

Each session consisted of a 10 minute adaptation period to the perimeter bowl luminance followed by two test programs separated by a short rest period. The order and combination of program and stimulus size were randomized. The first session for each subject was used as a familiarization period, the results of which were discarded prior to data analysis.

The equations for cortical representation proposed by Rovamo and Virsu (1979) (described in section 3.3) were used to derive the cortical representation (M_E) at each eccentricity examined along the four principal meridians. The diameter of the retinal stimulus (L_E) stimulating an equivalent cortical area to stimulus size 0 (projected diameter 0.054°) at the fovea (L_O) was then calculated by $L_E = M_O/M_E.L_O$ where $M_O = 7.99$ mm deg^{-1}. The value of differential light sensitivity corresponding to L_E, for each eccentricity, was obtained by graphical interpolation from the clinical data (Figures 3.3a; 3.3b) and plotted against peripheral angle.

The equations of Rovamo and Virsu (1979) were selected since these have previously been used in relation to the interaction of spatial summation with cortical magnification (Rovamo and Raninen 1984). The value of 0.054° was arbitrarily chosen to ensure that the M - scaled stimuli were kept within the stimulus range provided by the instrument.

3.6.3 Results

The group mean differential light sensitivity with increase in eccentricity as a function of stimulus size along the nasal - temporal meridian and the superior - inferior meridian of the visual field of the right eye is shown in Figures 3.2a and 3.2b respectively. The standard deviations are omitted for clarity; their magnitude increased with increase in eccentricity and decrease in stimulus size and were of the order of 2.5 dB, ranging from 0.32 dB to 6.82 dB.

The level of spatial summation, manifested by the steepening gradient, as a function of eccentricity, along the superior and inferior meridians is illustrated in Figures 3.3a and 3.3b respectively. Spatial summation increases with increase in eccentricity along both meridians. Similar results were obtained for the nasal and temporal meridians.

The interpolated sensitivity values with increase in peripheral angle for M - scaled stimuli, corresponding to stimulation of 0.146 mm^2 of striate cortex along the nasal - temporal and superior - inferior meridians are shown in Figures 3.4a and 3.4b respectively. Sensitivity increases with increase in eccentricity for all meridians.

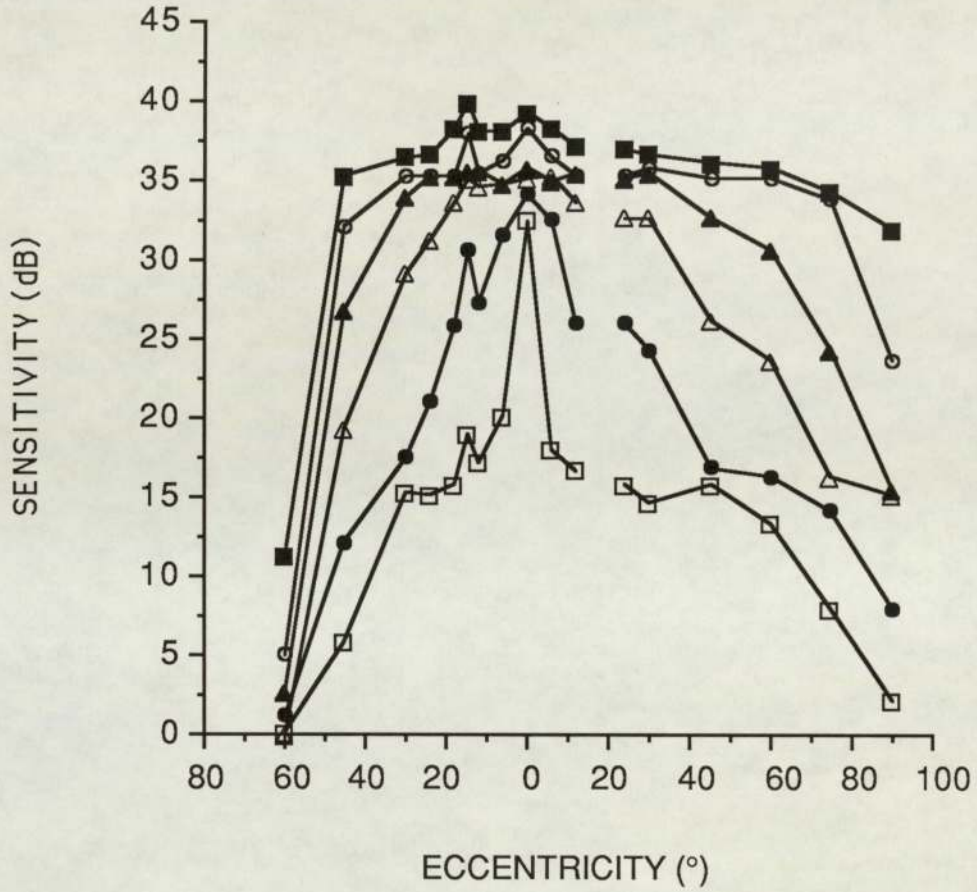


Fig 3.2a Group mean differential light sensitivity with eccentricity along the nasal (left) - temporal (right) meridian as a function of stimulus size (0.054° open squares, 0.108° filled circles, 0.216° open triangles, 0.431° filled triangles, 0.862° open circles, 1.724° filled squares) recorded with the Octopus 201 automated perimeter. The sensitivity values measured for locations falling within the blindspot are omitted for clarity.

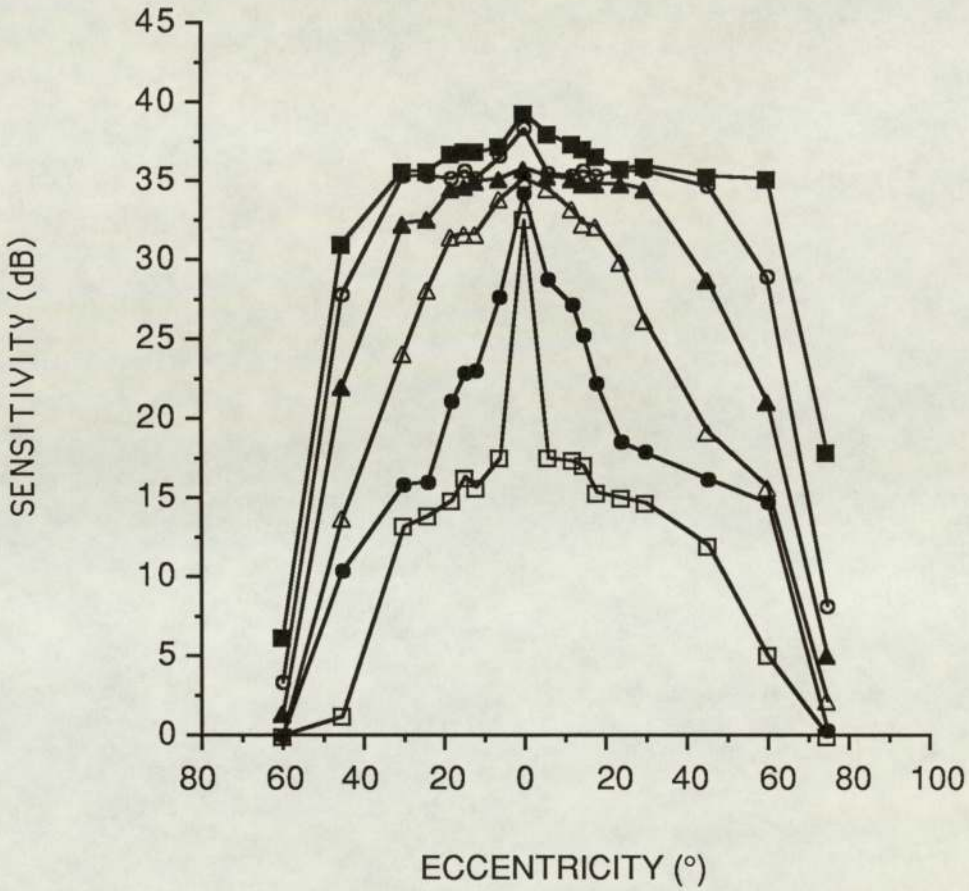


Fig. 3.2b Group mean differential light sensitivity with eccentricity along the superior (left) - inferior (right) meridian as a function of stimulus size (0.054° open squares, 0.108° filled circles, 0.216° open triangles, 0.431° filled triangles, 0.862° open circles, 1.724° filled squares) recorded with the Octopus 201 automated perimeter.

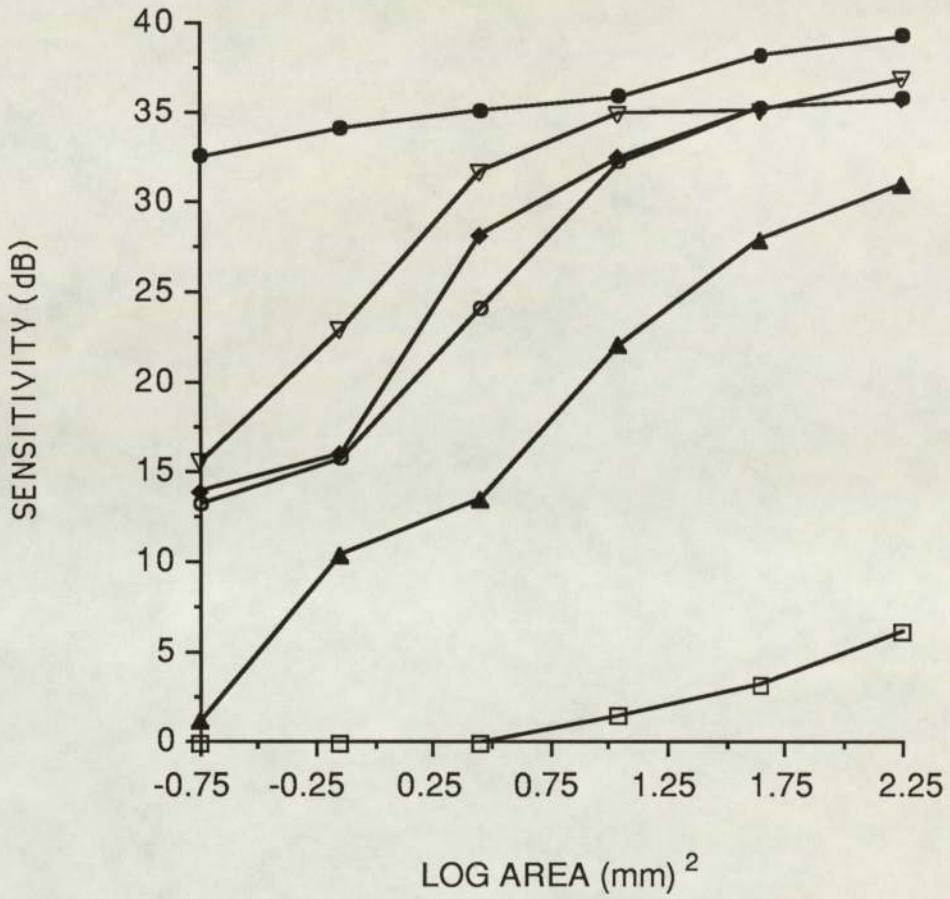


Fig. 3.3a Group mean differential light sensitivity against log stimulus area along the superior meridian of the visual field of the right eye as a function of eccentricity (0° filled circles; 12° open inverted triangles; 24° filled diamonds; 30° open circles; 45° filled triangles; 60° open squares) recorded with the Octopus 201 automated perimeter.

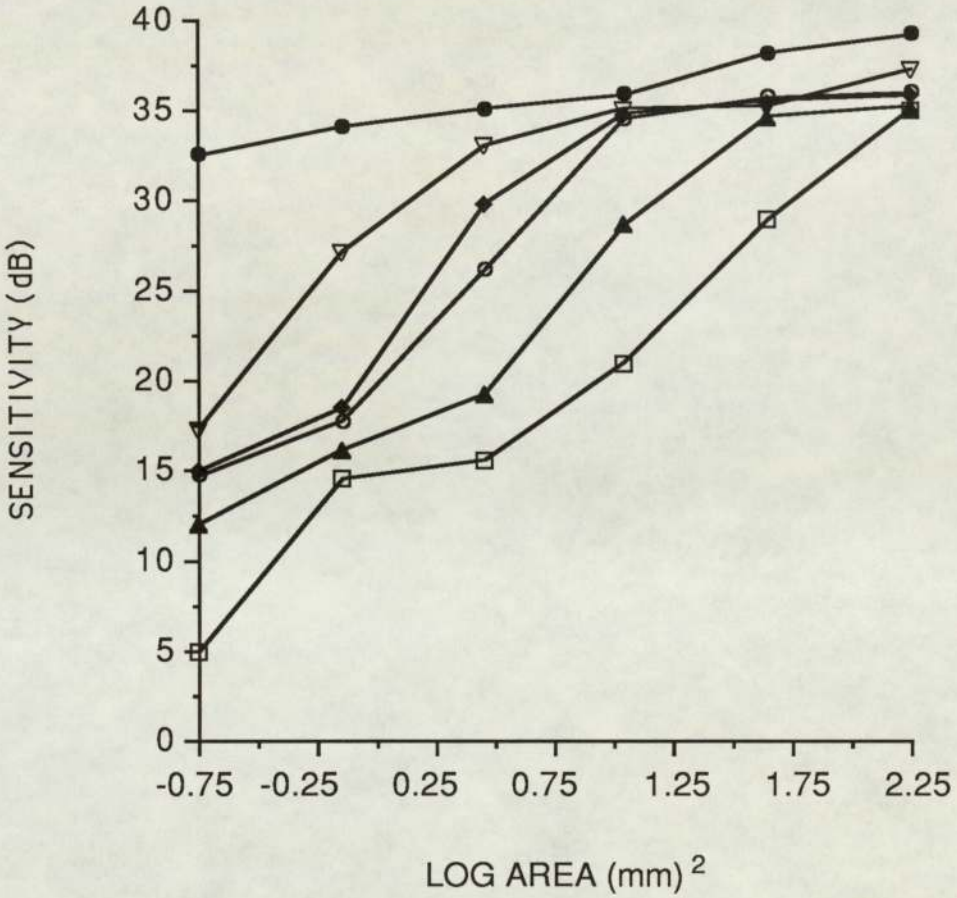


Fig. 3.3b Group mean differential light sensitivity against log stimulus area along the inferior meridian of the visual field of the right eye as a function of eccentricity (0° filled circles; 12° open inverted triangles; 24° filled diamonds; 30° open circles; 45° filled triangles; 60° open squares) recorded with the Octopus 201 automated perimeter.

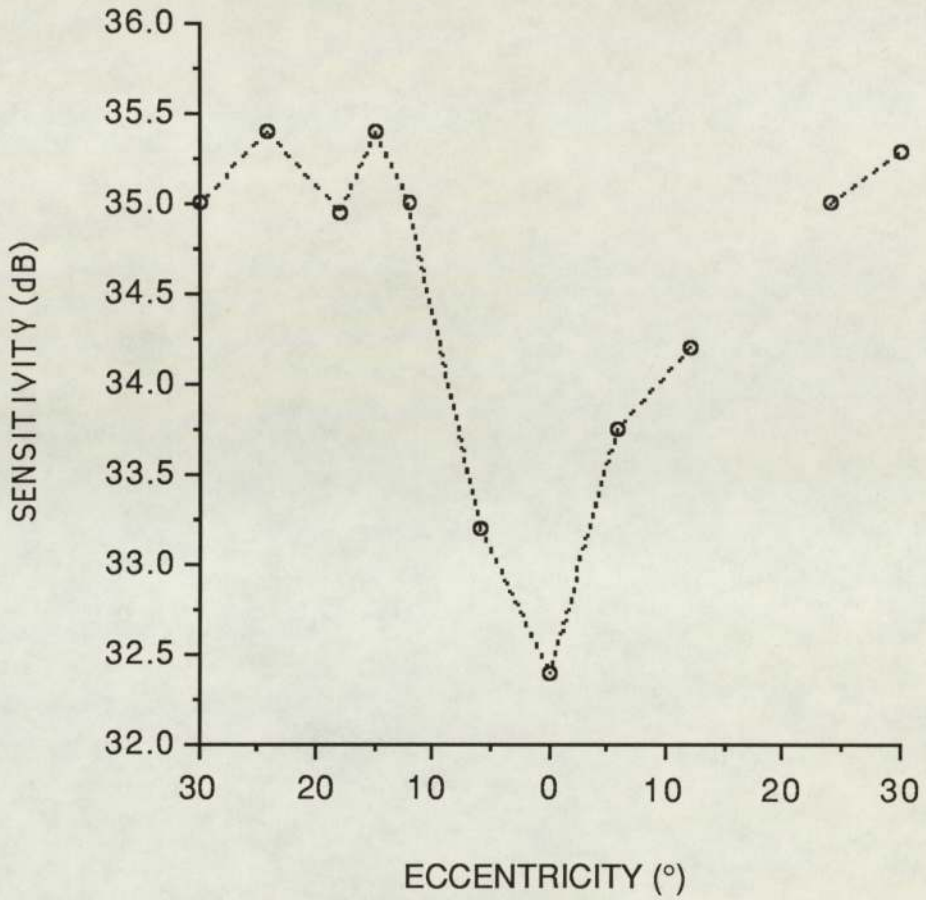


Fig 3.4a M - scaled values relative to the foveal value for stimulus size 0 (projected diameter 0.054°) stimulating an equal area of cortex (0.146 mm^2) with increase in eccentricity for the nasal (left) - temporal (right) meridian recorded with the Octopus 201 automated perimeter.

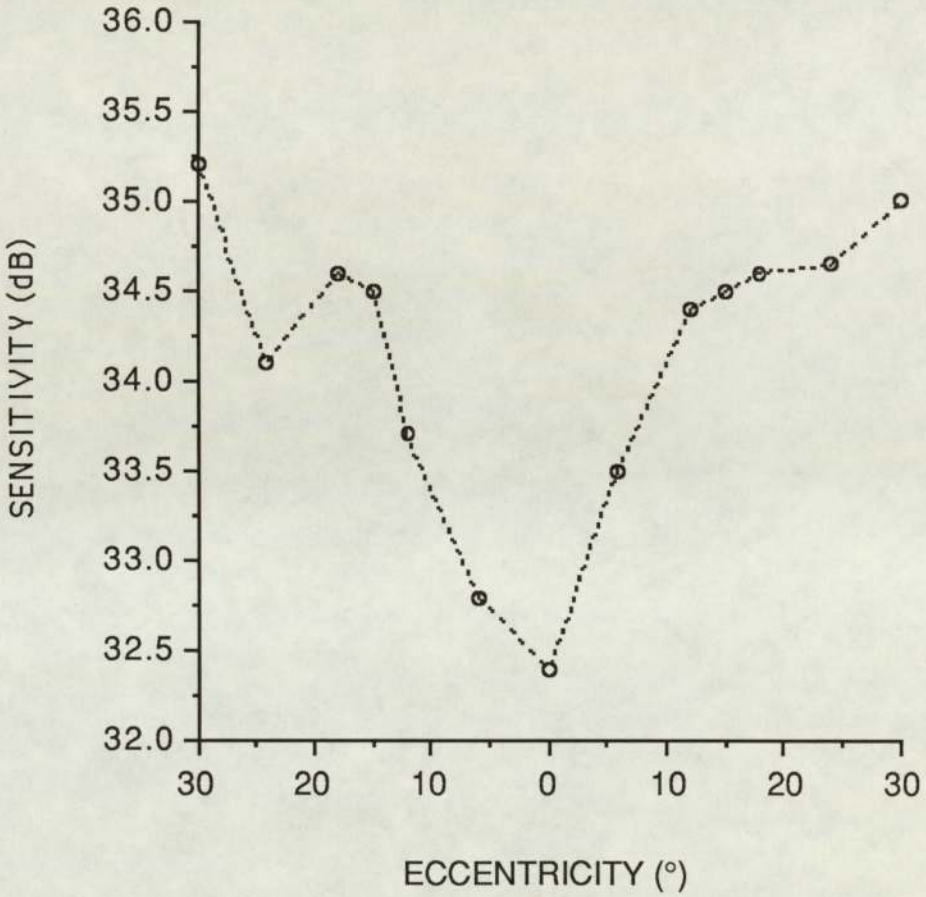


Fig. 3.4b M - scaled values relative to the foveal value for stimulus size 0 (projected diameter 0.054°) stimulating an equal area of cortex (0.146 mm^2) with increase in eccentricity for the superior (left) - inferior (right) meridian recorded with the Octopus 201 automated perimeter.

3.6.4 Discussion

The differential light sensitivity data are in agreement with previous manual perimetric investigations (Sloan 1961; Aulhorn and Harms 1972; Johnson et al 1978; Lie 1980). Sensitivity decreases monotonically with increase in eccentricity and with decrease in stimulus size for all six stimuli. The rate of change for both functions, however, reduces as stimulus size increases and is of least magnitude at the fovea. A clinically flat profile is found within the central 30° along the nasal - temporal meridian for stimulus size III (projected diameter 0.431°).

A region of enhanced sensitivity was found between 15° and 18° eccentricity nasally for all stimulus sizes with the exception of stimulus size III (0.431°). Such a peak has previously been reported for scotopic adaptation levels (Wolf and Zigler 1959; Wolf and Gardiner 1963) and corresponds to an area of maximum rod density (Osterberg 1935) and a region of increased ganglion cell density (Oppel 1967).

The increase in sensitivity with increase in stimulus size at the periphery is most likely to arise due to the greater capacity for spatial summation exhibited by the peripheral regions which in turn has been related to the increase in receptive field size with eccentricity (Glezer 1965; Levi and Klein 1987). Central saturation is likely to occur because the receptive fields within the central region are relatively small (Glezer 1965; Perry and Cowey 1985) therefore an increase in incident light over large stimulus areas results in a concomitant increase in sensitivity over a limited range only. The lack of sensitivity exhibited peripherally for the smaller stimulus sizes may arise as a direct consequence of reduced stimulus dynamic range. The differential threshold energy, calculated by log ΔL + log A, plotted against log A (Figures 3.5a; 3.5b) reveals, however, that the minima for each eccentricity are displaced further to the right as peripheral angle is increased. This demonstrates that the optimum areal distribution of energy necessary to evoke a response increases with eccentricity and indicates that factors other than spatial summation are involved

The various profiles may be influenced to a greater or lesser extent by factors other than neural processing. With increasing eccentricity, the apparent pupillary area is reduced, which decreases the

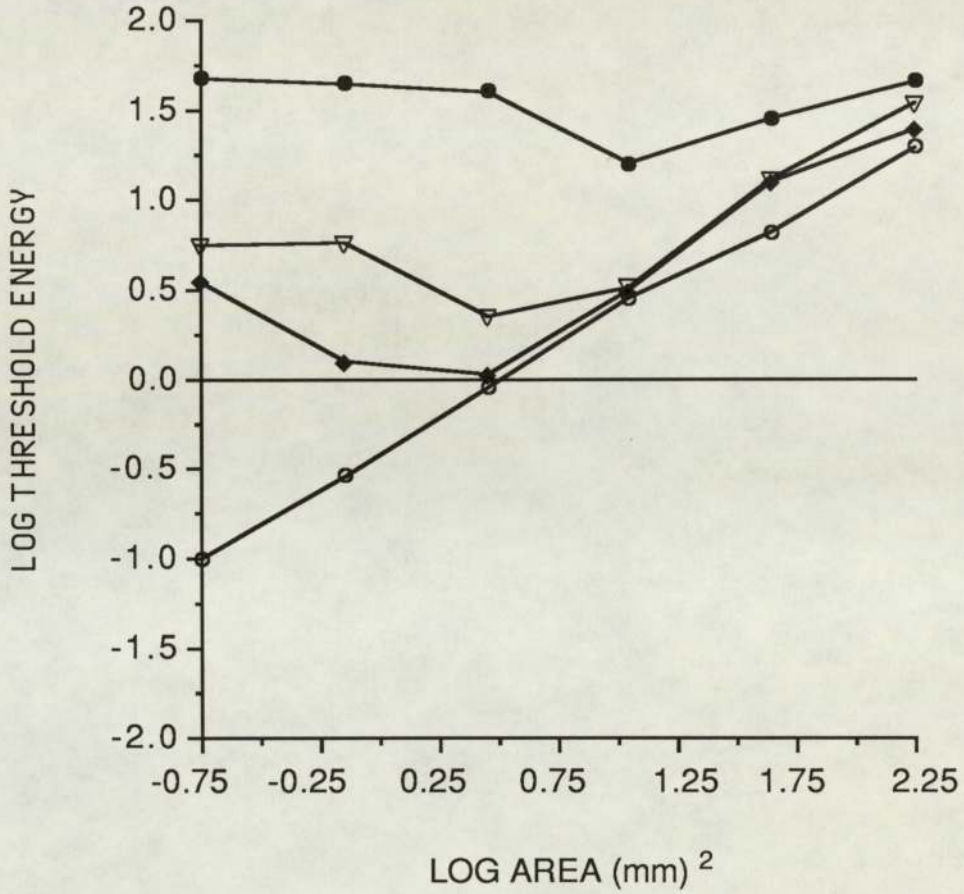


Fig 3.5a Log threshold energy against stimulus area for the nasal meridian as a function of eccentricity (0° filled circles, 12° open inverted triangles, 24° filled diamonds, 45° open circles) recorded with the Octopus 201 automated perimeter.

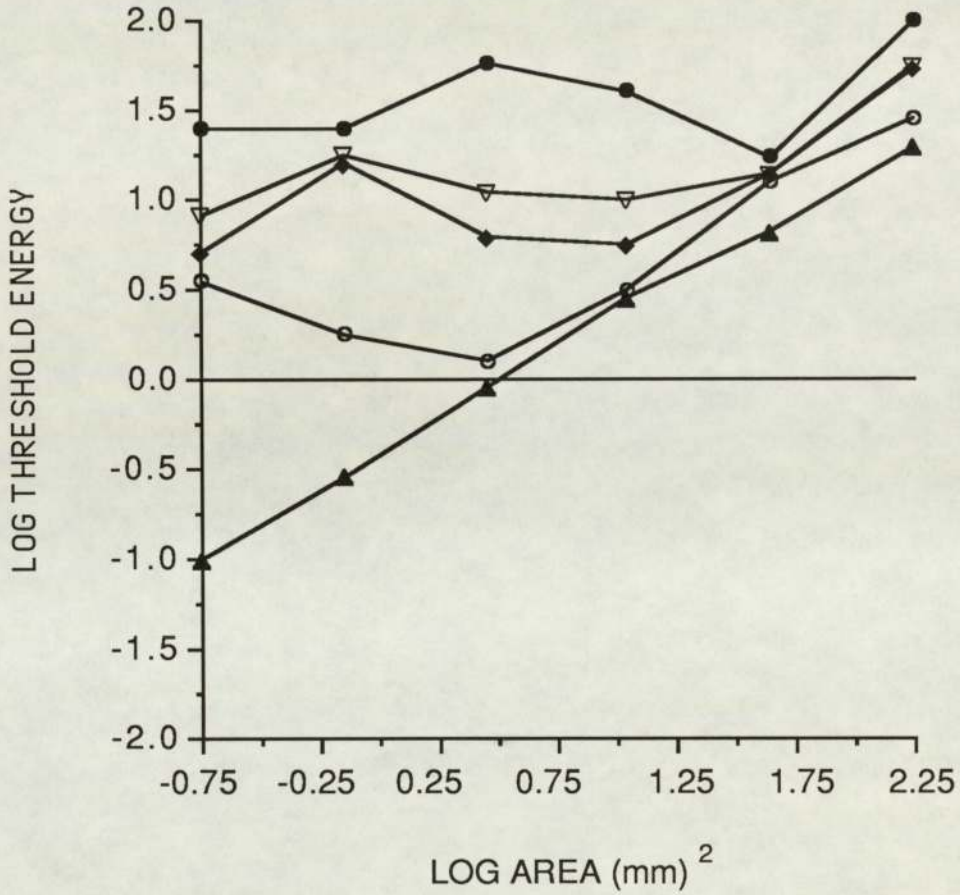


Fig 3.5b Log threshold energy against stimulus area for the temporal meridian as a function of eccentricity (0° filled circles, 12° open inverted triangles, 24° filled diamonds, 45° open circles, 60° filled triangles) recorded with the Octopus 201 automated perimeter.

effective retinal illumination, however, the reduced retinal image projection (Drasdo and Fowler 1974; Holden et al 1987) compensates for this effect, so that retinal illumination is constant out to an eccentricity of 80° (Bedell and Katz 1982; Koojiman 1983). Reductions in sensitivity for the smaller Goldmann stimuli arising from uncorrected errors of central refraction have been reported (Sloan 1961; Fankhauser and Enoch 1962) and it seems possible that the profiles for the smaller stimuli could be affected by off - axis effects. The mid - peripheral image quality of emmetropic observers, however, is believed to be more than adequate in relation to neural sampling despite the existence of oblique astigmatism (Jennings and Charman 1981a). In addition, short - and long - term fluctuations in perimetric sensitivity (described in section 1.5) may also influence the results.

Alternatively, the sensitivity distribution may reflect the increase in receptive field size with eccentricity and relate to the models which propose that spatial tuning may exist across the retina (Campbell and Robson 1968). Indeed, by correcting the width of a sine wave stimulus for cortical representation, the peripheral retina has been shown to exhibit a similar sensitivity to the fovea for all spatial frequencies although the peak sensitivity shifts to lower spatial frequencies (Koenderink et al 1978; Rovamo and Virsu 1979). The link between sine wave stimuli and spot stimuli must, however, be considered tenuous.

The M - scaled data for all four meridians exhibit an increase in sensitivity with increase in peripheral angle relative to the theoretical flat profile through the foveal point. The difference rises to approximately 3 dB at 30°. It is thus apparent that M - scaling stimulus area alone does not result in sensitivities which are independent of retinal location. The M - scaled data points at greater than 15° nasally and inferiorly exhibit scatter this may be attributable to variance in the data or may indicate that the M - scaling equations are not totally appropriate for clinical perimetry.

An interesting interpretation of the data can be seen if the eccentricities at which the standard Goldmann stimuli produce an isosensitivity profile relative to the foveal value for stimulus size 0 (0.054°) are determined by interpolation and then compared with the estimated M - scaled stimulus values at the same eccentricities (Figure 3.6). The discrepancy between the two curves increases with increase in eccentricity and further demonstrates the over - compensation of the M - scaling

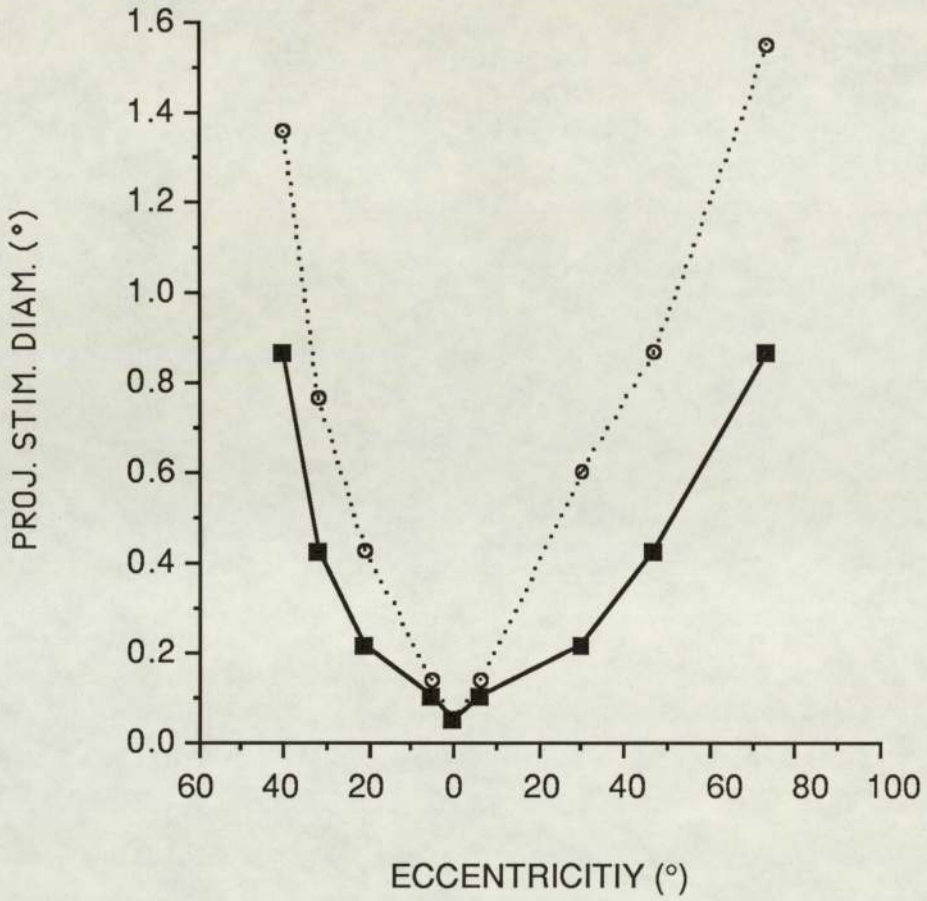


Fig 3.6 Stimulus size against eccentricity along the nasal (left) - temporal (right) meridian of the visual field of the right eye illustrating the eccentricities determined by interpolation at which standard Goldmann stimuli would produce a flat profile (filled squares) and the corresponding M - scaled values (open circles) recorded with the Octopus 201 automated perimeter.

equations. It would be expected that at higher background luminances this difference would diminish due to the decreasing spatial summation.

These observations, together with the finding that a clinically flat profile occurs within the central 30° along the 0 - 180° meridian for a 0.431° projected diameter stimulus (Figure 3.2a) are not entirely unexpected as the characteristics of the ganglion cells are not uniform across the retina. Dendritic field size increases with eccentricity (Perry et al 1984) and this compensates for the decrease in ganglion cell density. These two quantities may be expressed as the coverage factor, defined anatomically as dendritic field area (mm^2) x cell density (cells mm^{-2}) and physiologically as receptive field area (mm^2) x cell density (cells mm^{-2}). In cat, the coverage factor of ganglion cells has been demonstrated to be constant across the retina (Peichl and Wassle 1979). In macaca mulatta, however, the coverage factor of all types of ganglion cells has been shown to decrease with increasing peripheral angle (Perry et al 1984). This implies that the inverse relationship between dendritic field diameter and inter - ganglion cell separation changes with retinal location. It may be conjectured that this change in dendritic coverage factor contributes in part to the change in gradient of the M - scaled profile as the periphery is approached. Nevertheless, it has been reported that this constancy may not apply to receptive field coverage (Perry and Cowey 1985). Thus the difference between the two profiles is likely to arise in part as a result of spatial summation exhibited by the ganglion cells which increases with peripheral angle (Fankhauser and Schmidt 1958, 1960; Gougnard 1961; Sloan 1961; Hallett 1963; Verriest and Ortiz - Olmedo 1969; Wilson 1970; Dannheim and Drance 1971b; Scholtes and Bouman 1977) and decreases with increase in luminance levels (Barlow 1958; Fankhauser and Schmidt 1960; Meur 1965; Aulhorn and Harms 1967). Alternatively, it is possible that the current M - scaling equations misrepresent the visual field at the cortex. Indeed, Levi et al (1985) suggested that the fovea was underestimated at the cortex although this was only of significance when tasks such as position acuities were M - scaled. They conjectured that this disparity may arise because position acuity is primarily limited by cortical processing, whilst tasks such as resolution or threshold in perimetry are limited by retinal factors e.g., the blur function of the eye and the cone density (Westheimer 1982; Barlow 1979; 1981).

3.6.5 Static threshold perimetry: variable stimulus size, variable luminance

The Friedmann Visual Field Analyser II (F.V.F.A. II) was used as the instrument for investigation since it produces an isosensitivity profile out to an eccentricity of 25° in the normal eye, at a low photopic adaptation level of 1 asb and a presentation time of 0.25 s. The flat sensitivity gradient is achieved by employing stimuli which increase in diameter with increasing peripheral angle. In the design of the instrument, the aperture diameters necessary to produce a flat profile were determined experimentally, relative to a standard solid angle at fixation, using a front plate with variable sized apertures. The resultant values were then modified to allow for the effects of oblique viewing and a prototype front plate was produced with the estimated aperture diameters. These were subsequently modified following additional clinical trials.

3.6.6 Materials and methods

The sample consisted of 15 clinically normal, emmetropic observers (mean age 21.2 years, S.D. 1.25 years; 5 females, 10 males) who were experienced observers in perimetry and in psychophysical techniques of measurement in general. Visual acuity was 6/5 or better. The subjects were adapted to the screen luminance for 10 minutes and natural pupils were used throughout. The head was steadied with the head bar and chin rest of the instrument throughout the examination.

The instrument was used in the threshold mode: the thresholding procedure employed was that used by Barnes et al (1985), whereby stimuli were presented in 0.2 log unit steps from an infraliminal level until each individual stimulus had been correctly identified on two out of three presentations at a given intensity setting. The stimuli lying on, and within 1.5° of, the 4 principal meridians were used to create vertical and horizontal profiles.

The stimulus aperture diameters were measured using a Nikon Shadowgraph Projector at a magnification of 100 times and were each represented as the mean of four separate measurements made on one occasion by one observer. The observed elliptical areas of the circular stimulus diameters resulting from obliquity of viewing at 33 cm were calculated taking into account

eccentricity, front plate thickness and distance from the eye. The data for each stimulus aperture was then represented in terms of the diameter of the circle possessing the same area as that of the corresponding observed ellipse.

The M - scaling equations proposed by Rovamo and Virsu (1979) (described in section 3.3) were used to derive, along the four principal meridians, the cortical representation (M_E) in mm deg^{-1} at each aperture eccentricity using the same procedure as described in section 3.6.2. The derived aperture dimension at each eccentricity was then M - scaled to obtain the calculated dimension (L_E) which stimulated an equivalent area of cortex relative to the stimulus diameter of pattern H (L_H) for the appropriate meridian using the equation:

$$L_E = M_H/M_E \cdot L_H$$

The stimulus pattern H was selected since it was the central - most pattern to foveal fixation; the use of the macula threshold aperture does not produce an isosensitivity profile. The value, M_H, defines the cortical representation at this location.

3.6.7 Results

The group mean differential light sensitivity, the derived stimulus diameters and the corresponding calculated M - scaled dimensions for the nasal - temporal and superior - inferior meridians are illustrated in Figures 3.7a and 3.7b respectively. The variation of the standard deviation (S.D.) with eccentricity exhibits no definite trend although there would appear to be a slight increase in the S.D. in the mid - peripheral region which decreases as the peripheral angle approaches 25°. The S.D.s are of the order of 0.17 log units, ranging from 0.12 log units to 0.23 log units.

3.6.8 Discussion

The variation of the group mean differential sensitivity with increase in eccentricity along the four

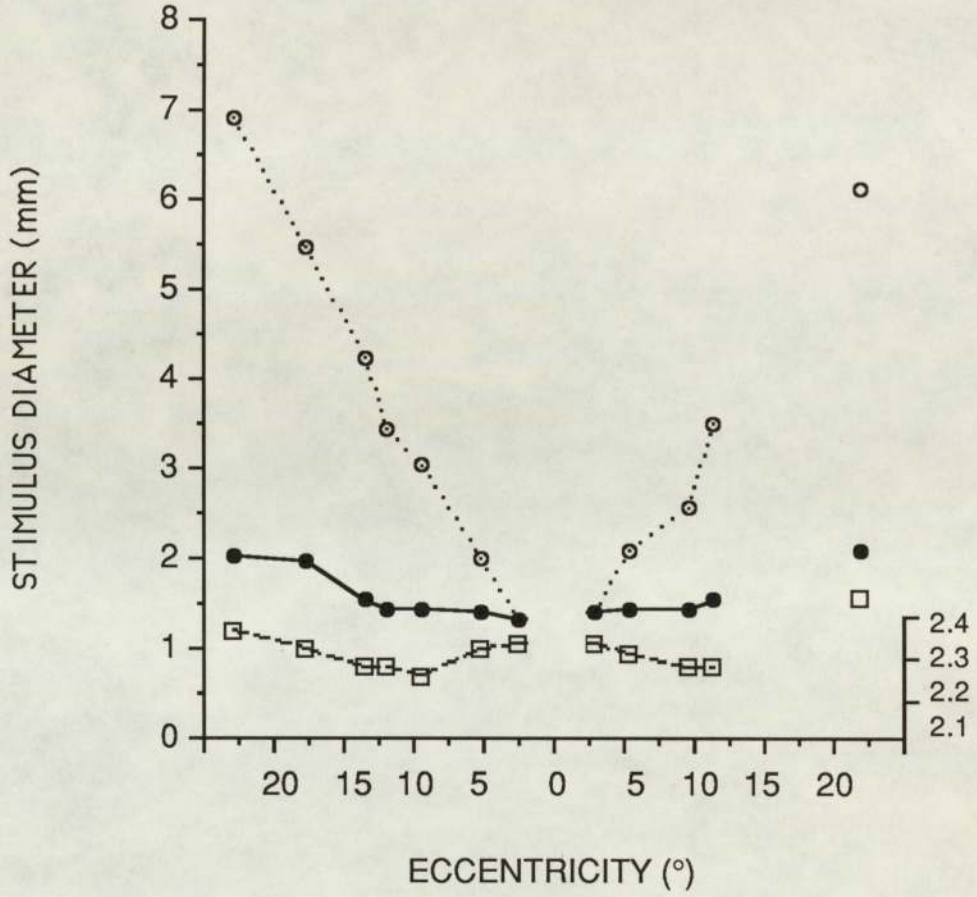


Fig 3.7a Equivalent (filled circles) and M - scaled (open circles) stimulus diameters (left hand axis) against eccentricity for the nasal (left) - temporal (right) meridian and group mean sensitivity (open squares) (right hand axis) in log units against eccentricity for the same meridian recorded with the Friedmann Visual Field Analyser II. The sensitivity values measured for locations falling within the blindspot are omitted for clarity.

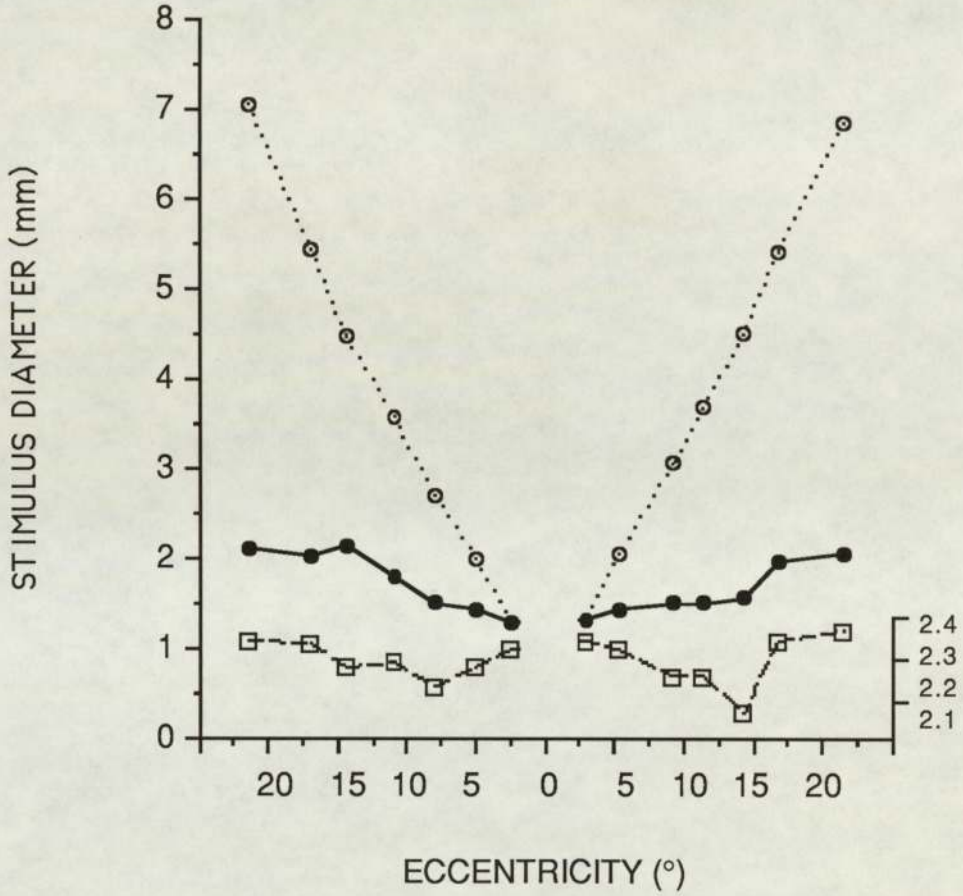


Fig 3.7b Equivalent (filled circles) and M - scaled (open circles) stimulus diameters (left hand axis) against eccentricity for the superior (left) - inferior (right) meridian and group mean sensitivity (open squares) (right hand axis) in log units against eccentricity for the same meridian recorded with the Friedmann Visual Field Analyser II. .

principal meridians does not describe an isosensitivity profile. Minor localized reductions in sensitivity occur between 7° and 17° of approximately 0.1 log units. This reduction appears to be similar to that reported by Henson et al (1984) and attributed to angioscotoma. A more likely explanation is that of incorrect stimulus aperture diameters in this region (Barnes et al 1985). The absence of any definite trend in the magnitude of the S.D.s with increase in eccentricity, is in disagreement with previous findings, where an increase in S.D. with increase in eccentricity was reported out to an eccentricity of 30° along the 45° meridian measured with the Perimetron, which employs a bowl luminance of 31.5 asb (Parrish et al 1984), and for the Octopus perimeter (section 3.6.3). Possible inter - subject variation in the shape of the gradient which has been shown with the V.F.A. I (Greve 1973) may, however, mask such a trend. It is also possible that the absence of any particular trend arises from the gradient compensation of the V.F.A. II.

The increase in the stimulus aperture diameters with increase in peripheral angle is non - linear. The apparent aperture diameters between 11° and 17° eccentricity in the superior field were found to be up to 0.7 mm larger than those for the same eccentricity in the inferior field.

The M - scaled diameters increase linearly with increase in peripheral angle. The difference between the actual and predicted stimulus aperture diameters necessary to evoke an apparent isosensitivity profile becomes greater with increase in eccentricity up to a factor of 3.5 times. The differences could possibly be attributed to increasing off - axis optical effects as described in section 3.6.4. The discrepancy is more likely to imply, however, that the sensitivity to perimetric spot stimuli across the visual field, at low photopic luminances does not depend upon the density of the retinal ganglion cells alone, and is in agreement with the findings for the Octopus automated perimeter.

3.7 The role of spatial summation in the cortical representation of the perimetric profile

It was apparent from the investigation of the cortical representation of the stimuli, in both of the types of visual field profile, that M - scaling, based on ganglion cell receptive field density alone, does not result in isosensitive profiles. The discrepancy between the M - scaled and experimentally determined isosensitive profiles was attributed to variations in ganglion cell physiological

characteristics across the retina most notably that of spatial summation. Spatial summation has been reported to increase in magnitude with increase in peripheral angle (Sloan 1961; Wilson 1970), with decrease in adaptation level (Barlow 1958; Fankhauser and Schmidt 1960) and with decrease in stimulus duration (Barlow 1958; Hallett 1963; Meur 1965). By utilization of a perimeter employing a higher bowl luminance and a longer stimulus duration, the role of spatial summation in the cortical representation of perimetric spot stimuli could be further investigated. The opportunity to test this hypothesis arose when a Humphrey Field Analyser 620 (H.F.A.) became available.

3.8 Experimental work

3.8.1 Static threshold automated perimetry: constant stimulus size, variable luminance, reduced spatial summation

Hardware

The Humphrey Field Analyser 620 (H.F.A.) is a single - unit automated projection perimeter which comprises a stimulus generation system, cathode ray tube unit, computer, double disc drive and a printer. The stimuli are projected on to a hemispheric bowl, whose radius is 33 cm and whose luminance is 31.5 asb. The stimulus is generated through a projection system using an incandescent lamp; the range of stimulus luminances is 0.08 - 10,000 asb. Stimulus duration is 200 ms. The instrument has the facility to vary stimulus size (Goldmann I - V equivalents: 0.108°, 0.216°, 0.431°, 0.862°, 1.724° projected diameters) and stimulus colour (red, blue, green and white). Fixation is assessed directly via a telescope and indirectly using the blindspot. The subjects blindspot is plotted at the beginning of the examination and thereafter, approximately 10% of the stimuli are presented in this region. The number of times a patient responds to stimulus presented within the plotted blindspot region is recorded. An additional assessment of reliability is obtained by the determination of false - negative and false - positive responses obtained by the same method as the Octopus.

Software

The H.F.A. permits the use of both screening and threshold strategies. In the current investigation only the threshold strategy was utilized. For thresholding, a 4 - 2 - 2 double staircase strategy is employed. The selection of the first stimulus luminance is based upon a starting value, for a specific stimulus location, developed from 4 primary points in each quadrant and derived from the immediately surrounding stimulus locations. If the measured threshold differs by more than 4 dBs from the nearest primary point, the thresholding procedure is continued until the threshold has been crossed four times. The order of stimulus presentation is controlled by computer and is completely randomized.

It can be estimated from the data of Barlow (1958) that the increased bowl luminance of the Humphrey perimeter will produce an approximate two - fold reduction in spatial summation compared with that of the Octopus. In addition, the longer stimulus duration of the Humphrey compared with that of the Octopus would also be expected to reduce spatial summation. It is not possible, however, to estimate the magnitude of the temporal influence on the degree of spatial summation due to the lack of appropriate data.

3.8.2 Materials and methods

The sample comprised 10 clinically normal, emmetropic subjects (mean age 22.92 years, S.D. 1.38 years; 6 males, 4 females) who were experienced observers in clinical perimetry and in psychophysical techniques in general and were free of ocular and systemic medication.

The differential light threshold for the visual field of the right eye was determined for each of the five stimuli at 6° intervals out to an eccentricity of 30° using Program 30 - 1 and at 12° intervals between 30° and 60° eccentricity using the Peripheral 30/60 - 1 Program. Each subject attended a total of five sessions, each session consisted of an adaptation period of 10 minutes followed by two programs separated by a ten minute rest period. The combination of stimulus size and program was randomized within any one session.

Fixation was constantly monitored using the instrument telescope and the head was steadied using chin and head rests. Subjects were again encouraged to rest at intervals during the examination and were advised if fixation was incorrect. Natural pupils were used; mean pupil diameter was 6.0 mm with a S.D. of 0.60 mm.

The equations of Rovamo and Virsu (1979) were used to calculate the stimulus diameters at the measured eccentricities necessary to produce an isosensitivity profile across the visual field using the same procedure as described in section 3.6.2.

3.8.3 Results

The group mean differential light sensitivity as a function of stimulus size with increase in peripheral angle for the visual field of the right eye is illustrated for the nasal - temporal (Figure 3.8a) and superior - inferior (Figure 3.8b) meridians. The magnitude of the accompanying S.D.s increases with decrease in stimulus size and with increase in peripheral angle and were of the order of 2 dB.

Group mean sensitivity against log stimulus size (which is representative of the level of spatial summation) as a function of eccentricity is shown for the superior (Figure 3.9a) and inferior (Figure 3.9b) meridians. Spatial summation increases with increase in eccentricity for both meridians. Similar results were found for the nasal and temporal meridians.

The sensitivity values of the M - scaled stimulus diameters, derived by interpolation for the visual field of the right eye, are illustrated for the nasal - temporal (Figure 3.10a) and superior - inferior (Figure 3.10b) meridians for both Drasdo's (1977) and Rovamo and Virsu's (1979) equations. Sensitivity is depressed paracentrally and then increases with increase in eccentricity for both equations.

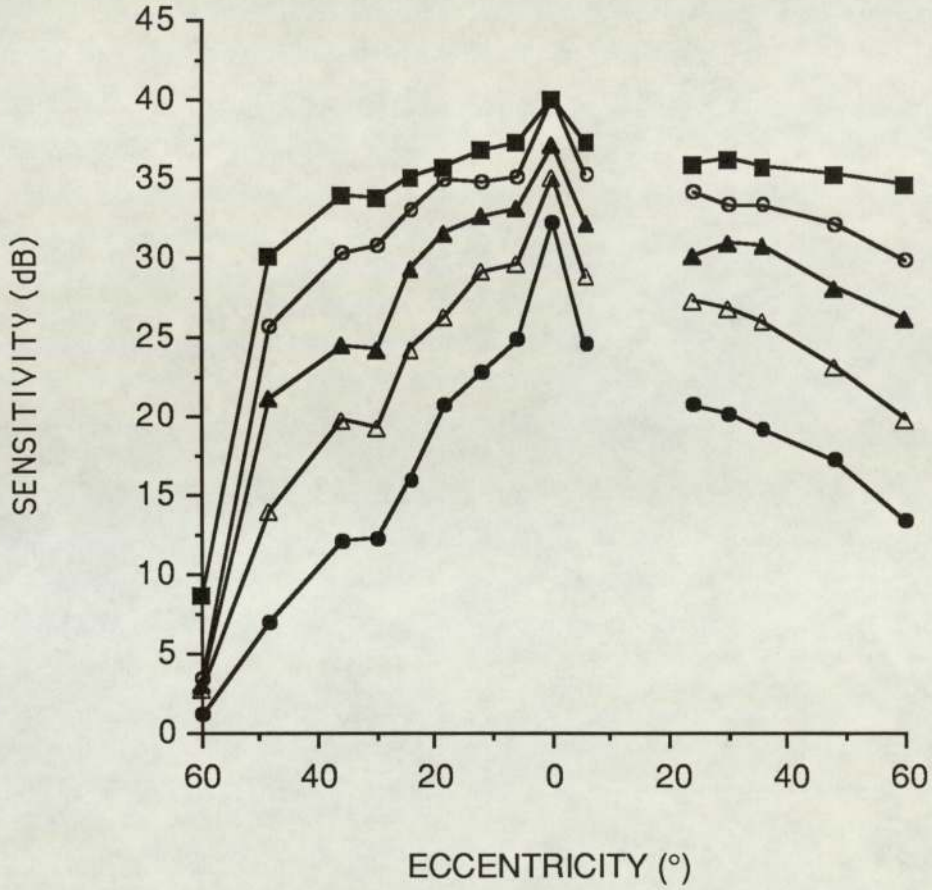


Fig 3.8a Group mean differential light sensitivity with eccentricity along the nasal (left) - temporal (right) meridian as a function of stimulus size (0.108° filled circles, 0.216° open triangles, 0.431° filled triangles, 0.862° open circles, 1.724° filled squares) recorded with the Humphrey Field Analyser 620. The sensitivity values measured for locations falling within the blindspot are omitted for clarity.

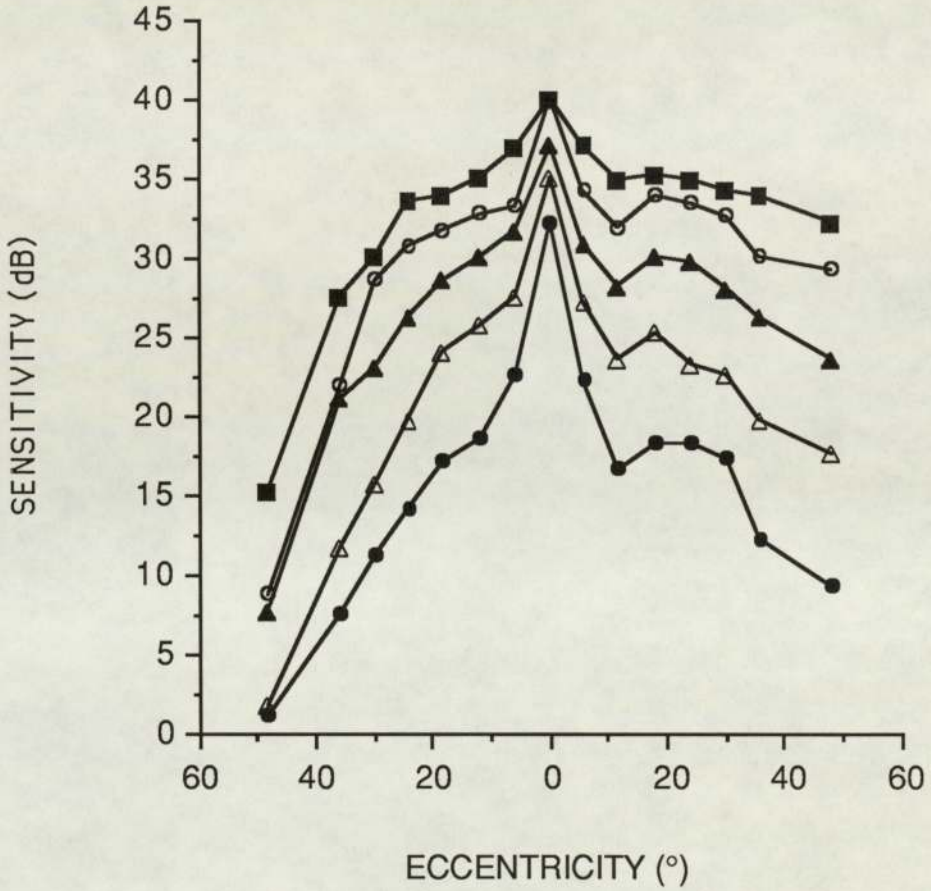


Fig 3.8b Group mean differential light sensitivity with eccentricity along the superior (left) - temporal (right) meridian as a function of stimulus size (0.108° filled circles, 0.216° open triangles, 0.431° filled triangles, 0.862° open circles, 1.724° filled squares) recorded with the Humphrey Field Analyser 620.

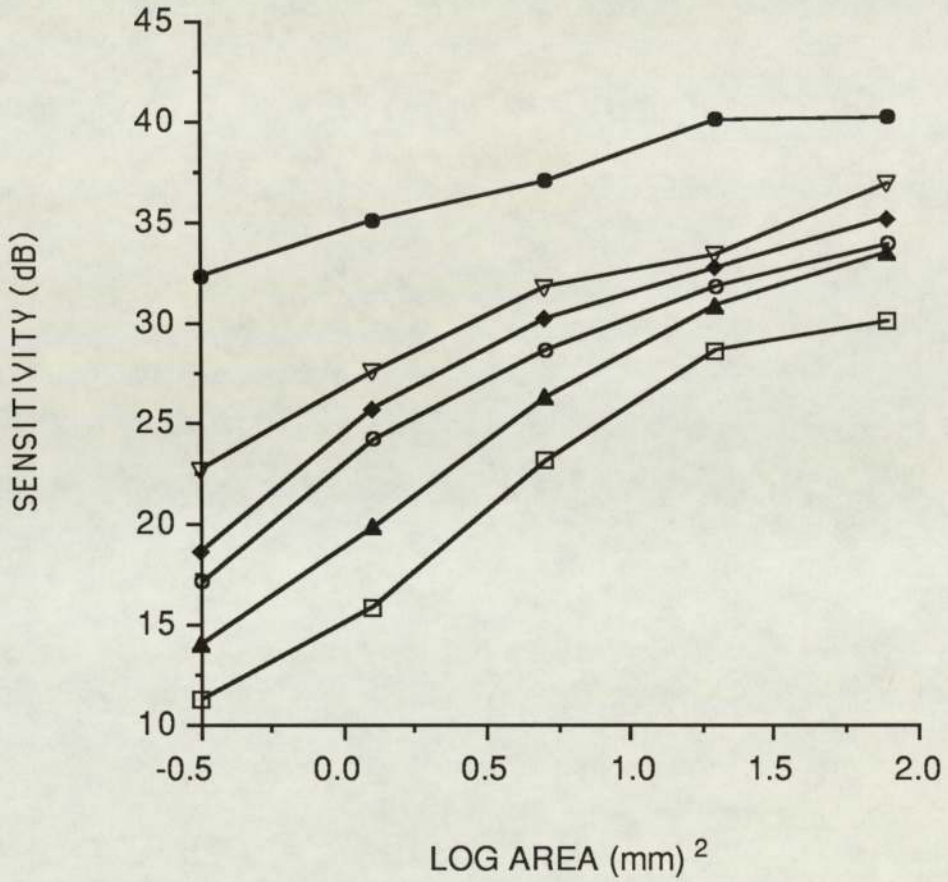


Fig. 3.9a Group mean differential light sensitivity against log stimulus area as a function of eccentricity for the superior meridian of the visual field of the right eye (0° filled circles, 6° open inverted triangles, 12° filled diamonds, 18° open circles, 24° filled triangles, 30° open squares) recorded with the Humphrey Field Analyser 620.

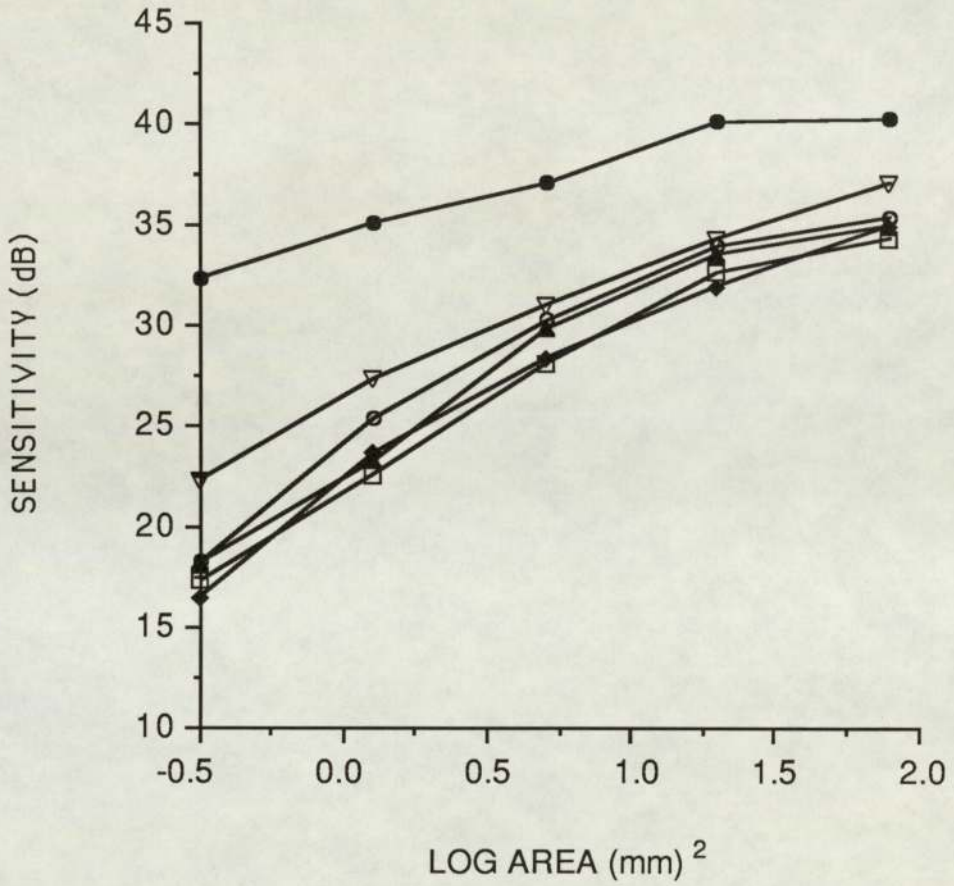


Fig. 3.9b Differential sensitivity against log stimulus area as a function of eccentricity for the inferior meridian (0° filled circles, 6° open inverted triangles, 12° filled diamonds, 18° open circles, 24° filled triangles, 30° open squares) recorded with the Humphrey Field Analyser 620.

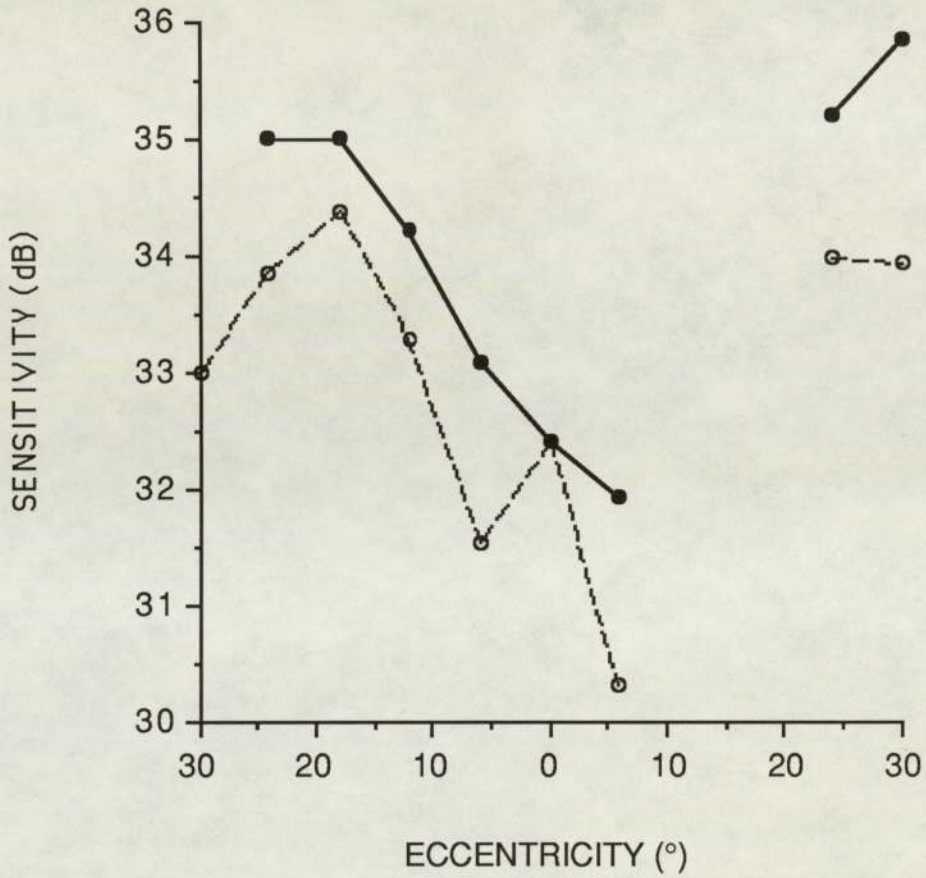


Fig. 3.10a M - scaled sensitivity values using the equations of Rovamo and Virsu (1979) (open circles) and Drasdo (1977) (filled circles) relative to the foveal value for the Goldmann stimulus size I stimulating an equal area of cortex along the nasal (left) - temporal (right) meridian recorded with the Humphrey Field Analyser 620. The sensitivity values measured for locations falling within the blindspot are omitted for clarity.

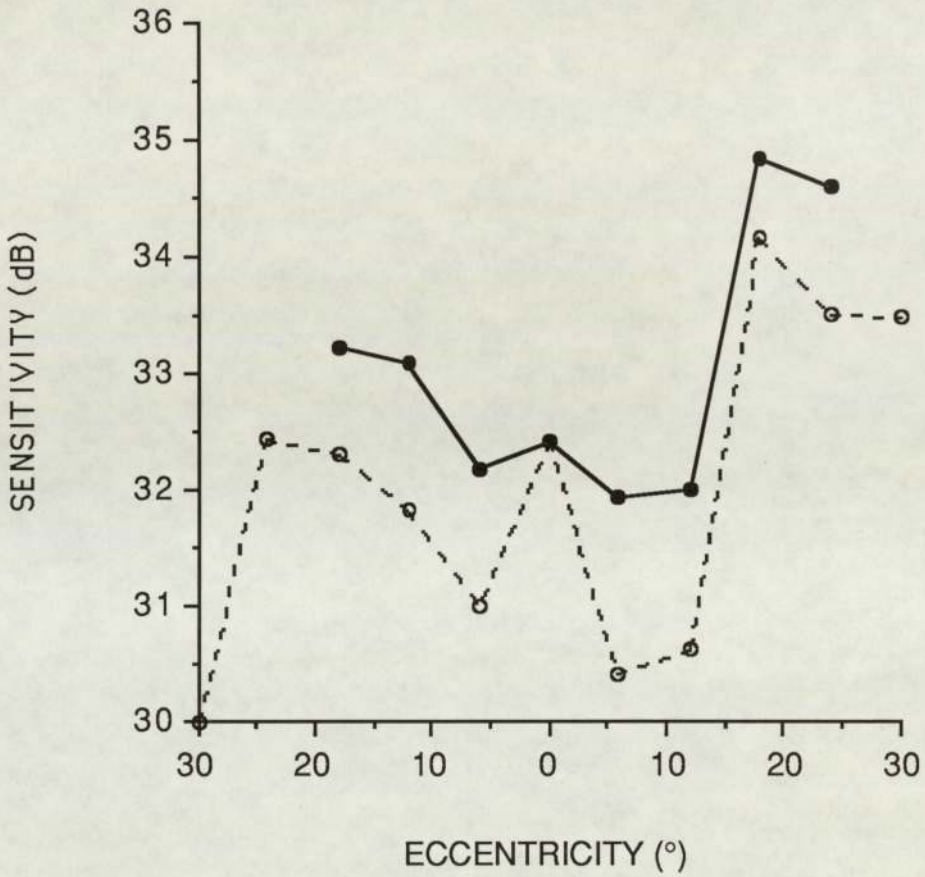


Fig. 3.10b M - scaled sensitivity values using the equations of Rovamo and Virsu (1979) (open circles) and Drasdo (1977) (filled circles) relative to the foveal value for the Goldmann stimulus size I stimulating an equal area of cortex along the superior (left) - inferior (right) meridian recorded for the Humphrey Field Analyser 620.

3.8.4 Discussion

The general relationship between differential light sensitivity as a function of eccentricity and stimulus size is in agreement with the results of section 3.6.3 recorded with the Octopus automated perimeter. There is no apparent difference in sensitivity between stimulus sizes IV and V at the fovea. This similarity, or saturation, of sensitivity at the fovea for stimulus sizes IV and V was not found at the lower adaptation level (4 asb) and shorter stimulus duration (100 ms) of the Octopus perimeter.

The increase in sensitivity with increase in stimulus size at the periphery is most likely to arise due to the greater capacity for spatial summation exhibited by the peripheral regions as described in section 3.6.4.

The various profiles may be influenced to a greater or lesser extent by factors other than neural processing as described in section 3.6.4.

For all meridians, M - scaling of perimetric sensitivity using the equations of Rovamo and Virsu (1979) does not result in an isosensitivity profile (Figures 3.10a; 3.10b). Sensitivity decreases within an eccentricity of 12° for the superior and inferior meridians and within an eccentricity of 6° for the nasal and temporal meridians. Sensitivity then increases along all meridians out to an eccentricity of 20° for the nasal and inferior meridians and out to an eccentricity of 25° for the temporal and superior meridians before decreasing again. This finding is in contrast to that reported for the Octopus perimeter in which the M - scaling of stimulus size also failed to produce an isosensitivity profile but exhibited an increase in sensitivity with increase in peripheral angle at all eccentricities for all four principal meridians (section 3.6.3).

An under - representation of the central regions would seem to be revealed under the condition of reduced spatial summation. To test this hypothesis, the sensitivity data was additionally M - scaled using the equations of Drasdo (1977) which are based upon a higher foveal representation namely 11.5 mm deg^{-1}. The M - scaled results for Drasdo's equations (Figures 3.10a and 3.10b) exhibit

minimal paracentral reduction in sensitivity compared with the M values of Rovamo and Virsu (1979). The disparity between the theoretical and obtained M - scaled profiles based upon 7.99 mm deg^{-1} can be further illustrated by determination of the eccentricities at which the five Goldmann stimulus sizes would produce equal sensitivities to that of the smallest stimulus at the fovea and by calculation of the corresponding M - scaled stimulus dimensions (Table 3.1). The stimulus diameters scaled according to the equations of Rovamo and Virsu (1979) are smaller than the actual stimulus diameters out to an eccentricity of 42.7° where the diameter becomes larger. Conversely, the stimulus diameters scaled according to the equations of Drasdo (1977) are larger than the actual stimulus diameters at all the eccentricities except 0°.

The implications from the data are that the foveal representation of 7.99 mm deg^{-1} is insufficient in the context of the processing of the spot stimuli used in clinical perimetry. This under - representation of the fovea at the lower photopic adaptation level is likely to have been masked by the increased spatial summation. It is likely that the further reduction of spatial summation facilitated by increasing the adaptation level to a greater extent will reveal a greater paracentral depression of sensitivity upon M - scaling the results. Indeed, Van Essen and Anderson (1986) have reported a greater foveal ganglion cell - cone ratio in the macaque fovea and therefore, by implication, a greater foveal enhancement at the cortex than previous workers; whilst evidence for two - stage magnification of the central field in macaque involving the retino - geniculate projections has been proposed (Perry and Cowey 1985).

3.9 Conclusions

The process of M - scaling applied to spatial stimulus parameters, alone, does not result in isosensitivity profiles using the various types of spot stimuli employed in conventional perimetry. An isosensitive profile may be obtained, however, using the standard Goldmann stimuli at given eccentricities or large constant size stimuli out to an eccentricity of 30°.

Meridian/ eccentricity (°)	Actual stimulus diameter (°)	Rovamo and Virsu (1979) scaled stimulus diameter (°)	Drasdo (1977) scaled stimulus diameter (°)
Superior			
0	0.108	0.108	0.108
2.05	0.216	0.201	0.246
5.00	0.431	0.336	0.443
15.9	0.862	0.881	1.264
26.3	1.724	1.536	2.12
Inferior			
0	0.108	0.108	0.108
2.35	0.216	0.215	0.276
4.70	0.431	0.322	0.443
12.4	0.862	0.681	0.992
31.2	1.724	1.687	2.332
42.7	1.724	2.465	5.370

Table 3.1 The eccentricities, determined by interpolation, at which the standard Goldmann stimuli employed by the Humphrey Field Analyser 620 would produce an isosensitivity profile and the corresponding M - scaled stimulus diameters scaled using the equations of Rovamo and Virsu (1979) and of Drasdo (1977).

3.9.1 Implications for M - scaling

For spot stimuli, the current human M - scaling equations do not account for the spatial summation characteristics of ganglion cells, and furthermore, under - represent the fovea at the cortex. These results support current findings in primates and also are consistent with reports that the retinal ganglion receptive field density at the fovea is far higher than had been previously anticipated. This latter finding would indicate that the estimated foveal representation in the human equations should be increased, since these are based upon retinal ganglion cell receptive field density.

3.9.2 Implications for perimetric design

Larger stimuli saturate the foveal regions at low photopic luminances and render them relatively insensitive to small variations in incident light; to optimize the examination performance it is preferable to employ smaller stimuli centrally and larger stimuli peripherally. The use of large stimuli peripherally increases the dynamic range which tends to be reduced in these regions. The design of such a program, based upon the coverage factor of retinal ganglion cells should result in easily interpreted isosensitive profiles and exhibit an equal ability to detect depression in sensitivity at all visual field locations. In perimetric terms this approach is highly desirable and could be used to facilitate multiple stimulus presentation and/or to permit maximum ease in identification and interpretation of abnormality. Implications at low photopic bowl luminances for perimetric program design incorporating varying stimulus sizes are far reaching.

4. TOPOGRAPHY OF THE PERIMETRIC PROFILE

4.1 Introduction

The data from section 3.6, in which the relationship between perimetric sensitivity and eccentricity as a function of stimulus size was investigated, presented some unexpected results; namely, the unique finding of an area of enhanced sensitivity with the Octopus 201 automated perimeter at an eccentricity of 15° along the horizontal meridian of the nasal visual field.

4.2 Psychophysical topographical studies

The variation in differential light sensitivity with eccentricity has been well documented in the normal eye, using manual static perimetry. Such studies, due to expediency, have been limited to the investigation of one or two meridians and the relationship with the remaining parts of the visual field has been inadequately defined. Nevertheless, asymmetry in static perimetric sensitivity recorded under various stimulus combinations has been reported between the nasal and temporal meridians (Kishto 1970; Aulhorn and Harms 1972; Harvey and Poppel 1972; Tate and Lynn 1977) and also between the superior and inferior meridians (Katz and Sommer 1986) of the visual field. Indeed, such findings are in accord with the topographical differences for other psychophysical functions which include: visual acuity (Millodot and Lamont 1974a), absolute thresholds (Abrahams et al 1983; Birch et al 1987), contrast sensitivity (Skrandies 1985a), critical flicker fusion (Skrandies 1985b) and for electrophysiological functions which include: visually evoked potential latencies (Eason et al 1967; Lehmann and Skrandies 1979; Barber and Galloway 1981).

4.3 Human anatomical topographical studies

Osterberg (1935) quantitatively investigated the distributions of human rod and cone densities across the retina. The data showed that rod density was highest within the region of 15° and 20° in the temporal retina (nasal visual field) extending in an arc around the horizontal, at this eccentricity,

whilst cone density was highest at the fovea. In studies of retinal cyto - architecture along the horizontal meridian Oppel (1967) reported some striking undulations in the distribution of both the retinal ganglion cells and the bipolar cells. These local undulations, which took the form of subsidiary peaks of ganglion cell density in the mid - peripheral retina, were not, however, reported by Van Buren (1963) who investigated the ganglion cell distribution across the whole retina. This latter worker demonstrated an ovoid pattern of ganglion cell density which was skewed nasally, and was of a similar configuration to the horizontal visual streak of ganglion cell density reported more recently by Stone and Johnston (1981).

4.4 Aim of the investigation

Several investigators have remarked upon the similarity between the topographical distribution of sensitivity across the visual field obtained manually under certain states of parametric adjustment and the variation in the underlying retinal architecture (Ten Doesschate 1949; Sloan 1950; Glaser 1967; Obstfeld 1973). In the extensive literature on visual fields only two contributions, namely, Wolf and Zigler (1959) and Wolf and Gardiner (1963) have reported local elevations in scotopic sensitivity at 15° nasally.

The aim of the study was therefore to determine whether the topographical distribution of sensitivity across the visual field and in particular, the local subsidiary peaks, related to the retinal cyto - architecture. A knowledge of such a relationship would provide further insight into the processing of perimetric spot stimuli.

4.5 Experimental work

4.5.1 Materials and methods

The sensitivity data, obtained by the methods of section 3.6, were further analysed along the oblique meridians. This data in conjunction with the data along the principal meridians illustrated in Figures 3.2a and 3.2b was further analysed using a 4 - way ANOVA to determine to what extent

eccentricity, meridian and stimulus size influenced the topography of the normal visual field.

4.5.2 Results

Group mean differential light sensitivity with increase in eccentricity as a function of stimulus size for the visual field of the right eye is illustrated for the (superio - temporal) - (inferio - nasal) meridian (Figure 4.1a) and the (superio - nasal) - (inferio - temporal) (Figure 4.1b) meridian. An area of enhanced sensitivity is present at 21.2° along the inferio - temporal meridian, with a peak of smaller amplitude at 21.2° along the superio - temporal meridian.

Eccentricity and stimulus size significantly affected sensitivity for both the cardinal and the oblique meridians at the $p<0.001$ level (Tables 4.1a; 4.1b). Similarly, meridian significantly affected sensitivity for the cardinal meridians at the $p<0.001$ level but affected sensitivity for the oblique meridians at the $p<0.01$ level only. The interaction terms between eccentricity and meridian; eccentricity and stimulus size; and eccentricity, meridian and stimulus size were significant at the $p<0.001$ level for both the cardinal and the oblique meridians.

Multiple two - tailed Student's t tests using Scheffe's correction (Tables 4.2a; 4.2b) revealed no conclusive trend in the difference between sensitivity for a given stimulus size at a given eccentricity along one cardinal meridian and that at the same eccentricity along another cardinal meridian. The differences in sensitivity between meridians at the given eccentricity vary with stimulus size in a random manner. The differences between meridians become more significant with increase in eccentricity, particularly, when eccentricity is greater than or equal to 45°. This arises because the retinal surface extends more peripherally in the nasal and superior directions (corresponding to the temporal and inferior fields respectively) than in the temporal and inferior directions. The temporal field exhibits reduced sensitivity relative to the nasal, superior and inferior meridians at 15° and 18° eccentricity at the $p<0.01$ level due to the presence of the blindspot.

Figures 4.2a and 4.2b illustrate the relationship between log ganglion cell receptive field density (calculated from the equations of Rovamo and Virsu (1979) and perimetric sensitivity for the nasal

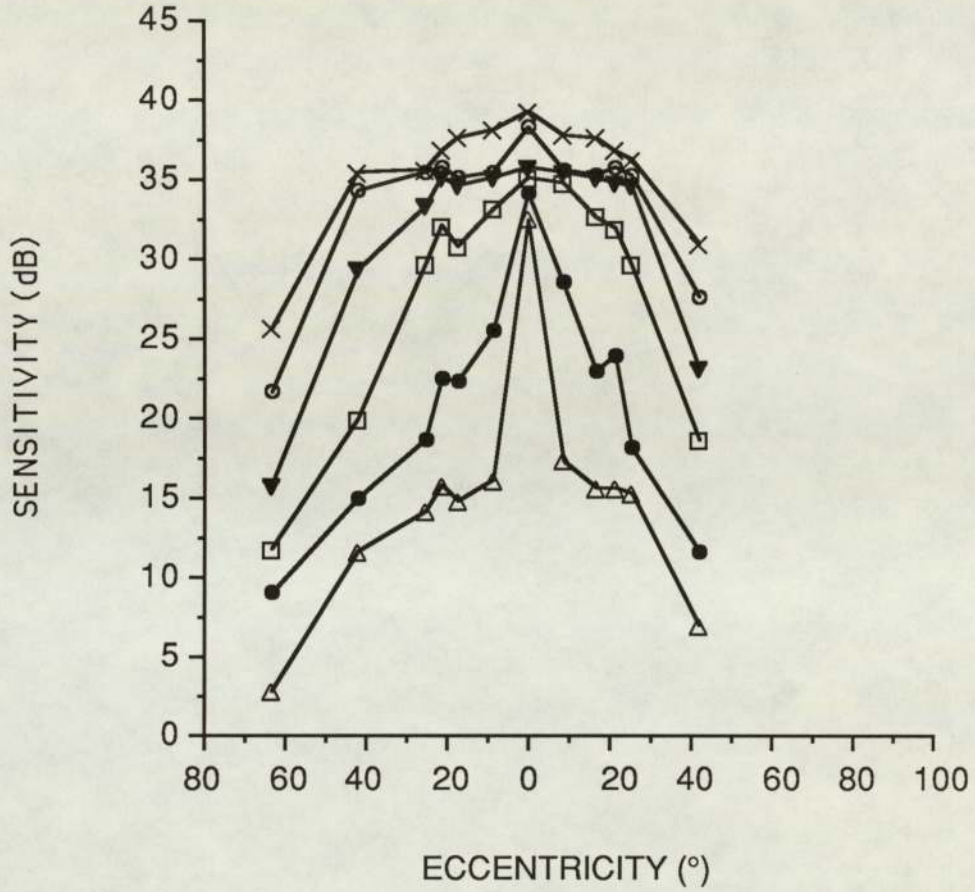


Fig. 4.1a Group mean differential light sensitivity with eccentricity along the superio - temporal (left) - inferio - nasal (right) meridian of the right eye as a function of stimulus size (0.054° open triangles, 0.108° filled circles, 0.216° open squares, 0.431° filled inverted triangles, 0.862° open circles, 1.724° crosses) recorded with the Octopus 201 automated perimeter.

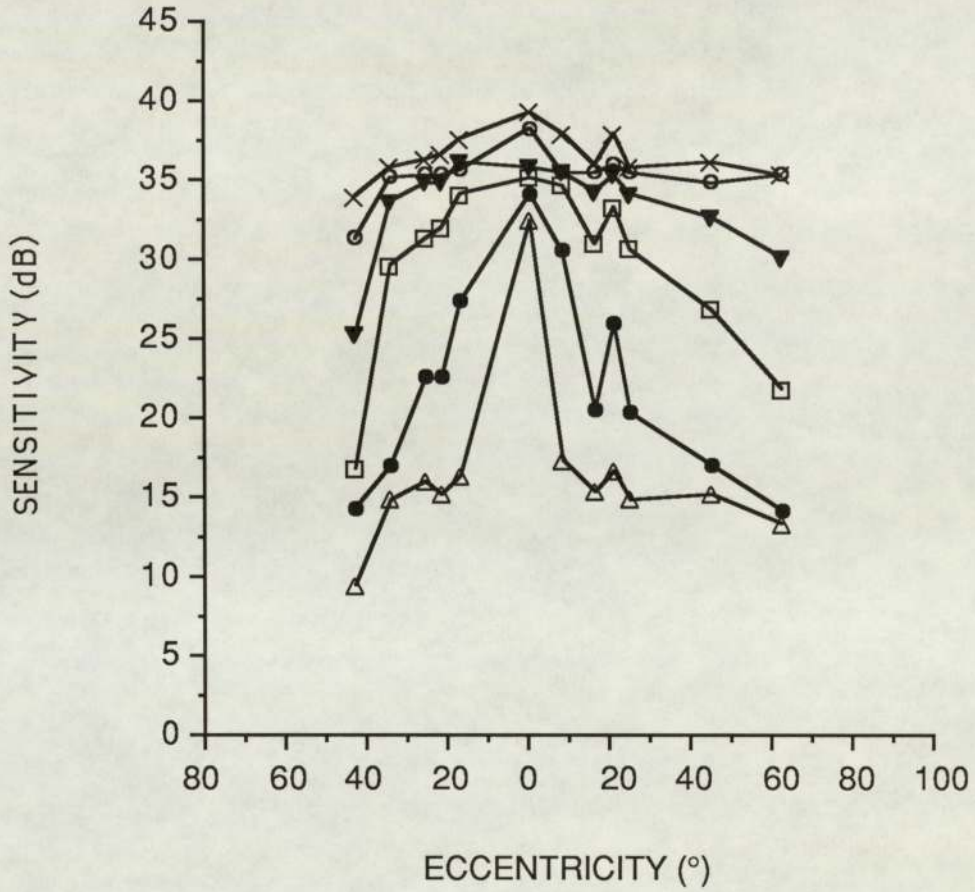


Fig. 4.1b Group mean differential light sensitivity with eccentricity along the superio - nasal (left) - inferio - temporal (right) meridian as a function of stimulus size (0.054° open triangles, 0.108° filled circles, 0.216° open squares, 0.431° filled inverted triangles, 0.862° open circles, 1.724° crosses) recorded with the Octopus 201 automated perimeter.

Source	SS	DF	MS	F	Significance Level
Eccentricity (A)	516.752	8	64.594	166.772	p<0.001
AS	27.887	72	0.387		
Meridian (B)	29.064	3	9.688	24.253	p<0.001
BS	10.785	27	0.400		
AB	392.714	24	16.363	45.500	p<0.001
ABS	77.680	216	0.359		
Stimulus size (C)	583.483	5	116.697	295.735	p<0.001
CS	17.757	45	0.395		
AC	84.187	40	2.105	8.898	p<0.001
ACS	85.15	360	0.237		
BC	4.045	15	0.270	1.488	NS
BCS	24.460	135	0.181		
ABC	62.412	120	0.520	2.455	p<0.001
ABCS	228.785	1080	0.2118		
Subjects (S)	14.839	9	1.649		p<0.001
TOTAL	2160.0	2159			

Table 4.1a Four - way analysis of variance with perimetric sensitivity as the dependent variable for the nasal - temporal and superior - inferior meridians of the visual field of the right eye.

Source	SS	DF	MS	F	Significance Level
Eccentricity (A)	251.925	5	50.385	192.632	p<0.001
AS	11.770	45	0.261		
Meridian (B)	4.829	3	1.610	4.673	p<0.01
BS	9.301	27	0.344		
AB	19.545	15	1.303	4.854	p<0.001
ABS	36.241	135	0.269		
Stimulus size (C)	846.319	5	169.264	586.839	p<0.001
CS	12.980	45	0.288		
AC	117.890	25	4.716	29.200	p<0.001
ACS	36.335	225	0.162		
BC	1.376	15	0.092	1.02	NS
BCS	12.140	135	0.090		
ABC	6.012	75	0.080	1.207	NS
ABCS	53.009	675	0.079		
Subjects (S)	20.328	9	2.259		p<0.001
TOTAL	1440.0	1439			

Table 4.1b Four - way analysis of variance with perimetric sensitivity as the dependent variable for the (superio - temporal) - (inferio - nasal) meridian and the (superio - nasal) - (inferio - temporal) meridian of the visual field of the right eye.

Temporal v Inferior Eccentricity (°)

Stimulus size	6	12	15	18	24	30	45	60
0	*	-	**	**	-	-	**	**
I	*	-	**	**	*	*	*	**
II	-	*	**	**	-	**	*	**
III	-	-	**	**	-	**	*	**
IV	-	-	**	**	-	**	-	**
V	-	*	**	**	-	-	-	**

Temporal v Nasal Eccentricity (°)

Stimulus size	6	12	15	18	24	30	45	60
0	-	-	**	**	-	-	*	**
I	-	-	**	**	**	-	-	*
II	-	-	**	**	**	**	**	**
III	-	-	**	**	-	*	*	**
IV	-	-	**	**	-	-	-	-
V	-	-	**	**	-	-	-	-

Nasal v Inferior Eccentricity (°)

Stimulus size	6	12	15	18	24	30	45	60
0	*	-	-	-	-	-	**	*
I	-	-	-	-	-	-	-	**
II	-	-	-	**	-	**	-	**
III	-	-	*	-	-	-	-	**
IV	-	-	-	-	-	**	-	**
V	-	-	*	-	-	-	-	**

Table 4.2a Level of significance (where * $p<0.05$; ** $p< 0.01$) attributed to the difference between perimetric sensitivity at a given eccentricity along the temporal and inferior meridians (top), temporal and nasal meridians (middle) and nasal and inferior meridians (bottom) derived with multiple two - tailed Student's t tests using Scheffe's correction.

Superior v Inferior Eccentricity (°)

Stimulus size	6	12	15	18	24	30	45	60
0	-	*	-	-	-	-	**	**
I	-	*	-	-	*	-	*	**
II	-	*	*	-	-	-	*	**
III	-	-	*	-	-	-	-	**
IV	-	-	-	-	-	-	*	**
V	*	-	-	-	-	-	-	**

Superior v Nasal Eccentricity (°)

Stimulus size	6	12	15	18	24	30	45	60
0	*	*	*	-	-	-	*	-
I	*	-	-	*	*	-	-	-
II	-	**	*	*	-	*	-	-
III	-	-	*	-	-	*	*	-
IV	-	-	-	-	-	-	-	-
V	*	*	*	-	-	-	-	-

Superior v Temporal Eccentricity (°)

Stimulus size	6	12	15	18	24	30	45	60
0	-	-	**	**	*	**	**	**
I	*	-	**	**	**	**	**	**
II	-	*	**	**	*	**	**	**
III	-	-	**	**	-	**	**	**
IV	-	-	**	**	-	-	*	**
V	*	-	**	**	-	-	-	**

Table 4.2b Level of significance (where * $p<0.05$; ** $p< 0.01$) attributed to the difference between perimetric sensitivity at a given eccentricity along the superior and inferior meridians (top), superior and nasal meridians (middle) and superior and temporal meridians (bottom) derived with multiple two - tailed Student's t tests using Scheffe's correction.

and inferior meridians. An approximately linear relationship is shown for stimulus size 0 which becomes non - linear for the larger stimulus sizes. Similar results were found along the temporal and superior meridians.

The relationship between log rod density and perimetric sensitivity is illustrated for the nasal (Figure 4.3a) and inferior (Figure 4.3b) meridians and that between log cone density and perimetric sensitivity illustrated for the nasal (Figure 4.4a) and inferior (Figure 4.4b) meridians. The rod and cone densities were derived by interpolation from the data of Osterberg (1935). An approximately linear relationship is demonstrated between log rod density and perimetric sensitivity for stimulus sizes 0 and I which becomes non - linear for the larger stimulus sizes. Similar results were found along the temporal and superior meridians. A non - linear relationship is, however, shown between the log cone density and perimetric sensitivity for both meridians for all stimulus sizes. The results for the superior and temporal meridians follow similar trends.

4.5.3 Discussion

Local relationship

The areas of enhanced sensitivity for the group mean data at 15° nasally and at 21.2° inferio - temporally could be construed as being artifactual since the thresholds at 15° nasally and 21.2° inferio - temporally were derived by Program 21 whilst the adjacent values at 12° and 18° and at 17° and 25.5° respectively were derived by Program 31. The argument does not hold, however, in relation to the superior and inferior meridians and this finding can thus be used as a control for the presence of enhanced sensitivity elsewhere.

The probability of the two subsidiary peaks of sensitivity occurring due to chance, with the proportion of cases in one category set at 0.3, was $p< 0.001$. The amplitude of the subsidiary peaks was stimulus size dependent being maximal for stimulus size I in both meridians, thereafter declining to a minimum value for stimulus size III nasally and stimulus size IV inferio - temporally before exhibiting an increased amplitude for the remaining stimulus sizes. Increased variance relative

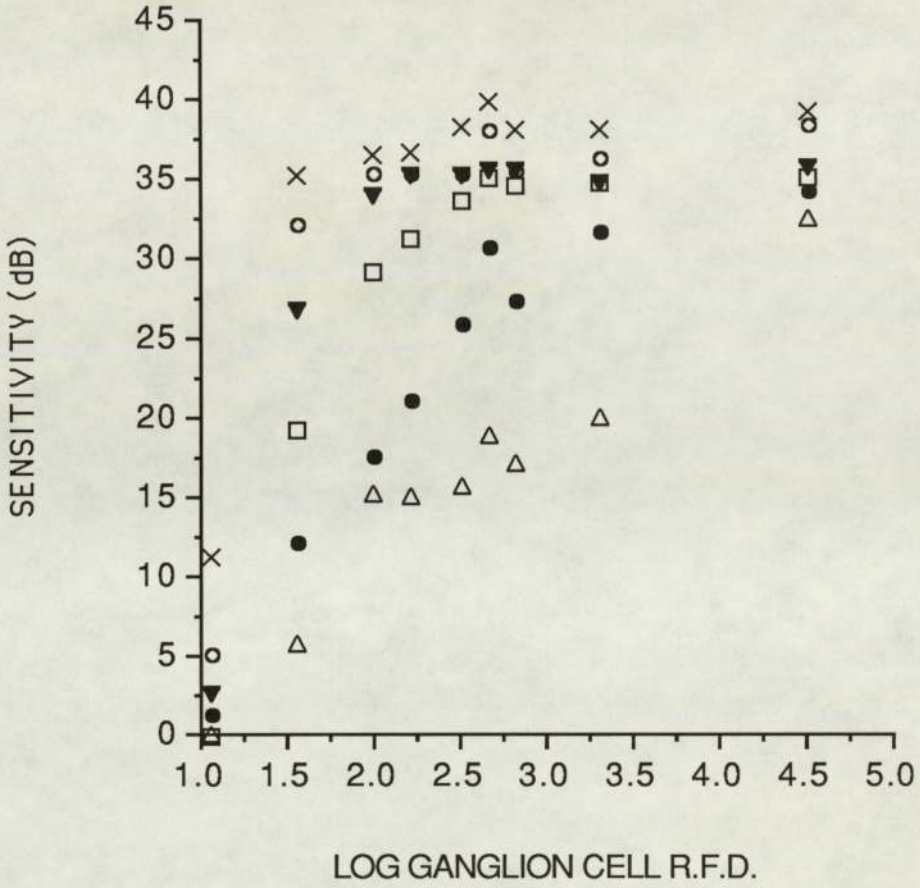


Fig. 4.2a Scattergram showing group mean differential light sensitivity with increase in stimulus size against log ganglion cell receptive field density for the nine sampled eccentricities of the nasal meridian of the visual field of the right eye (0.054° open triangles, 0.108° filled circles, 0.216° open squares, 0.431° filled inverted triangles, 0.862° open circles, 1.724° crosses) recorded with the Octopus 201 automated perimeter.

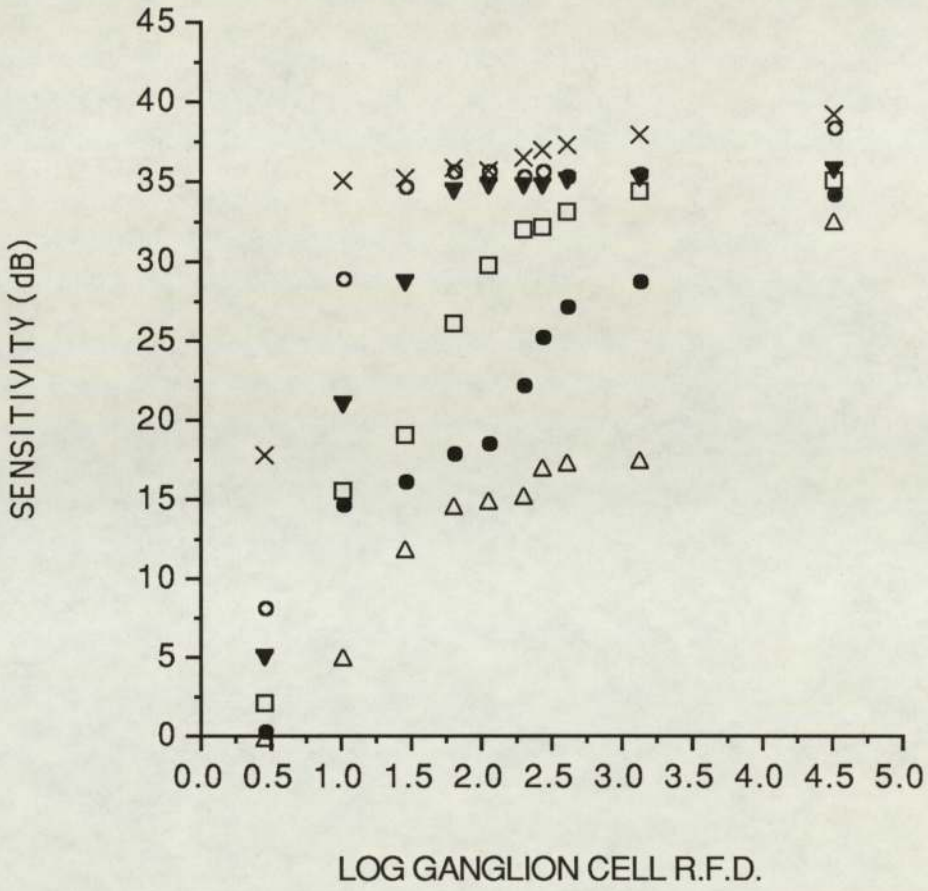


Fig. 4.2b Scattergram showing group mean differential light sensitivity with increase in stimulus size against log ganglion cell receptive field density for the ten sampled eccentricities of the inferior meridian of the visual field of the right eye (0.054° open triangles, 0.108° filled circles, 0.216° open squares, 0.431° filled inverted triangles, 0.862° open circles, 1.724° crosses) recorded with the Octopus 201 automated perimeter.

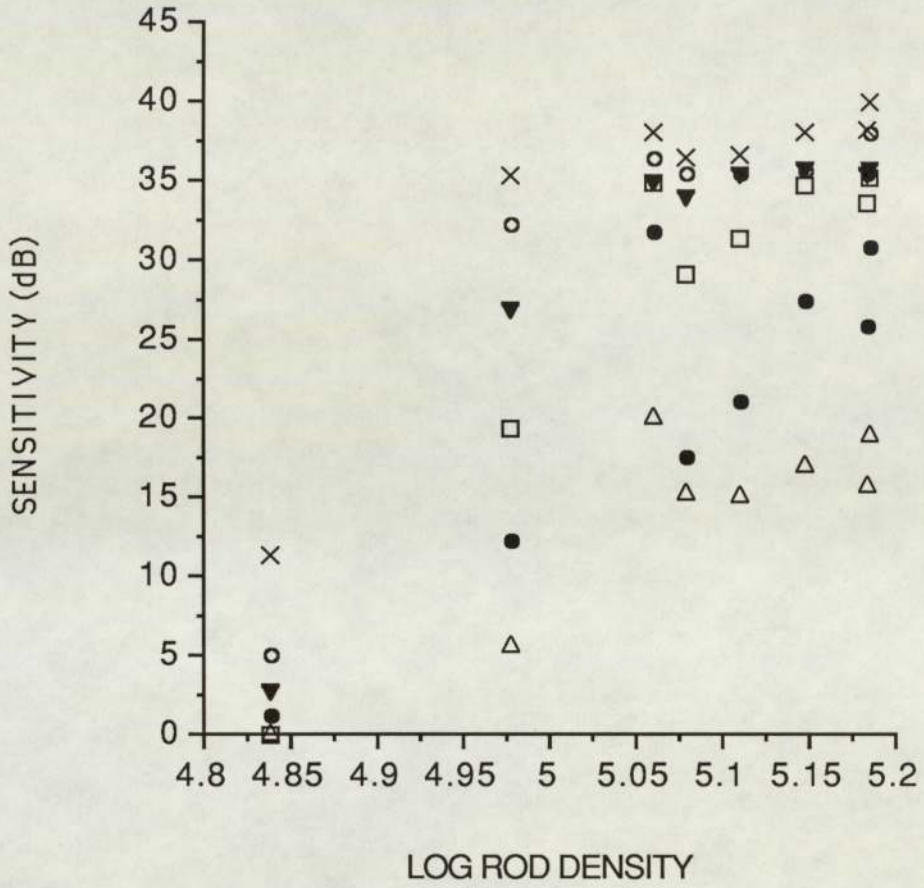


Fig. 4.3a Scattergram showing group mean differential light sensitivity with increase in stimulus size against log rod density for the eight sampled eccentricities of the nasal meridian of the visual field of the right eye (0.054° open triangles, 0.108° filled circles, 0.216° open squares, 0.431° filled inverted triangles, 0.862° open circles, 1.724° crosses) recorded with the Octopus 201 automated perimeter.

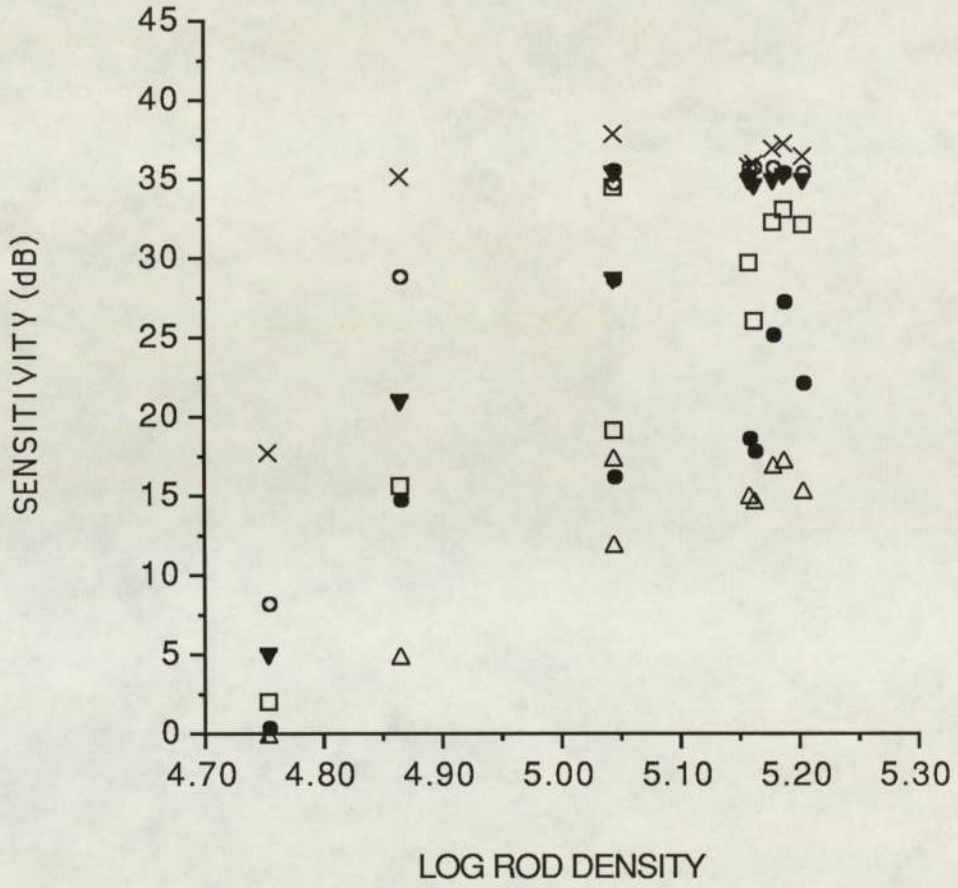


Fig. 4.3b Scattergram showing group mean differential light sensitivity with increase in stimulus size against log rod density for the nine sampled eccentricities of the inferior meridian of the visual field of the right eye (0.054° open triangles, 0.108° filled circles, 0.216° open squares, 0.431° filled inverted triangles, 0.862° open circles, 1.724° crosses) recorded with the Octopus 201 automated perimeter.

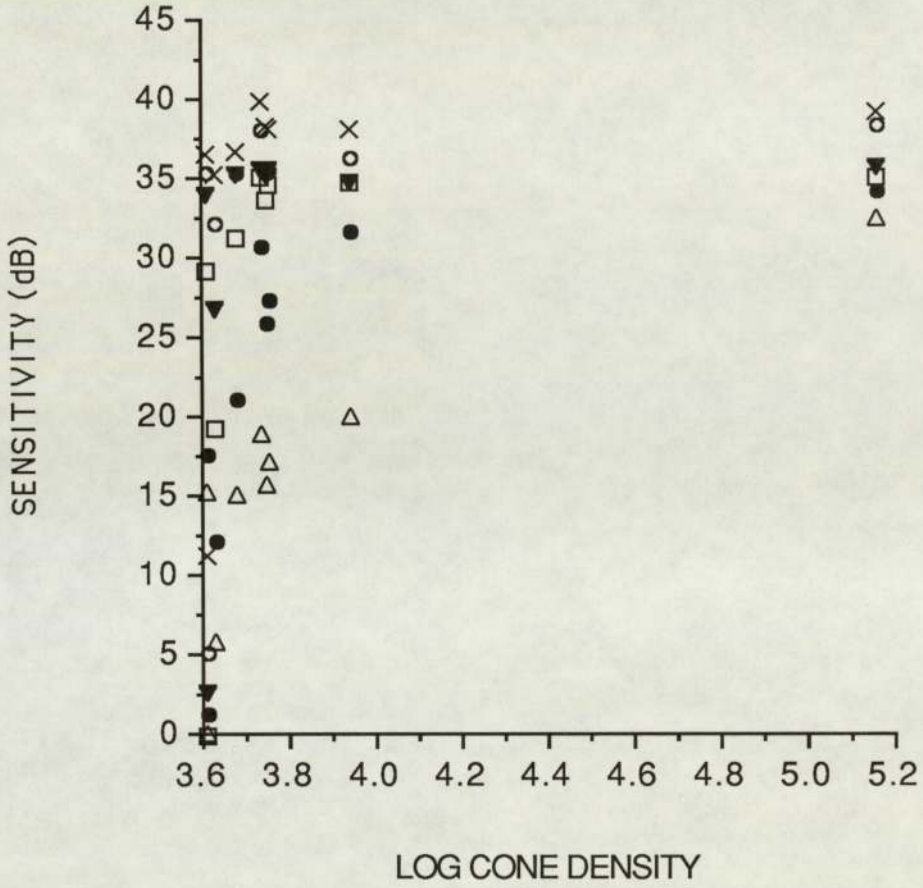


Fig. 4.4a Scattergram showing group mean differential light sensitivity with increase in stimulus size against log cone density for the eight sampled eccentricities of the nasal meridian of the visual field of the right eye (0.054° open triangles, 0.108° filled circles, 0.216° open squares, 0.431° filled inverted triangles, 0.862° open circles, 1.724° crosses) recorded with the Octopus 201 automated perimeter.

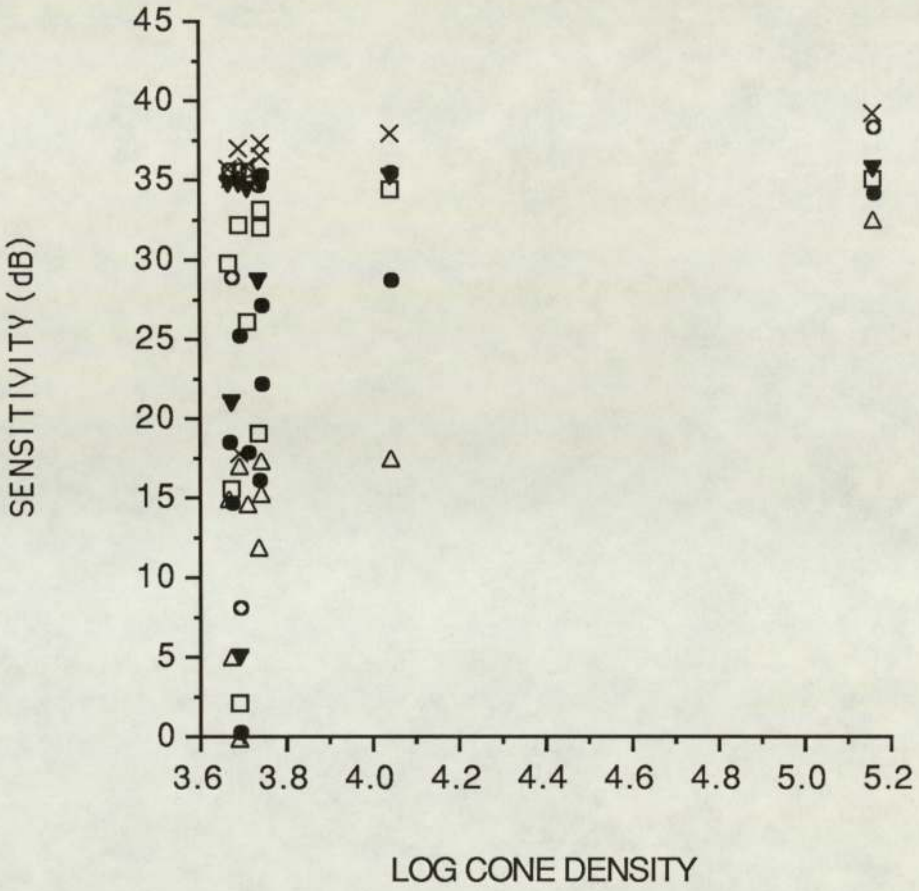


Fig. 4.4b Scattergram showing group mean differential light sensitivity with increase in stimulus size against log cone density for the ten sampled eccentricities of the inferior meridian of the visual field of the right eye (0.054° open triangles, 0.108° filled circles, 0.216° open squares, 0.431° filled inverted triangles, 0.862° open circles, 1.724° crosses) recorded with the Octopus 201 automated perimeter.

to the immediately adjacent locations is found at both locations for stimulus sizes I and V and additionally for stimulus size IV at the 15° nasal point. Nevertheless, inspection of the raw data confirmed the validity of the group mean as a representative measure of the underlying trend for the peaks of enhanced sensitivity. For stimulus size I, nine of the 10 individuals exhibited a 1 dB or greater increase in sensitivity between 12° and 15° and a decrease of similar magnitude between 15° and 18°. A similar result, using the same arbitrary criterion was also obtained for the stimulus size I peak at 21.2° along the inferio - temporal meridian. Statistically significant incidences of peaks were also obtained at 15° nasally for stimulus sizes 0 and V ($p<0.01$ and $p<0.05$ respectively).

A minor subsidiary peak was also found at 21.2° along the superio - temporal meridian. The maximum number of observers in which the peak was present for a given stimulus size was 4 out of 10. The peak was not statistically significant for any of the stimulus sizes using the above criteria.

The subsidiary peaks at 15° nasally and at 21.2° inferio - temporally were further investigated using stimulus sizes I and V, since the peaks of sensitivity were of highest amplitude for these sizes, using the SARGON Program of the Octopus 201 automated perimeter (described in section 1.6.3). The program was written to include stimulus locations around the 15° nasal region and the 21.2° inferio - temporal region of the left eye (Figure 4.5) and included two repetitions at the 15° nasal and 21.2° inferio - temporal locations. The sample comprised 7, clinically normal, emmetropic subjects (2 females, 5 males; mean age 22.81 years, S.D. 3.02 years) who were experienced observers in automated perimetry. Each subject attended one session and was adapted to the bowl luminance of the perimeter for 10 minutes prior to the examination. Natural pupils were used throughout. The head was steadied with the head clamps and chin bar of the instrument and fixation was constantly monitored with the video monitor.

The results are shown in Table 4.3 where a subsidiary peak of sensitivity was defined as, a stimulus location at which the sensitivity was higher than at least 50% of the adjacent stimulus locations, by a difference of greater than or equal to 1 dB. The results were inconclusive, and it became apparent that the peak of sensitivity was often displaced from the coordinates found in the original

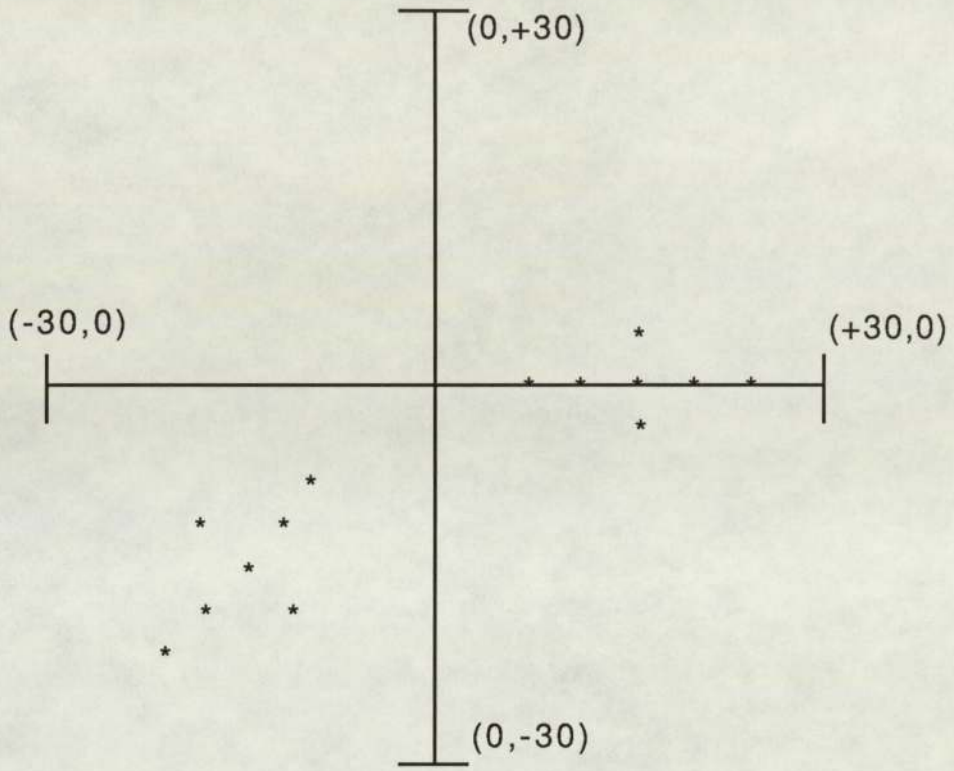


Fig. 4.5 Schematic representation of the SARGON Program stimulus grid of 3° resolution centred at the 15° nasal (15,0) and the 21.2° inferio - temporal (-15,-15) locations of the visual field left eye. Sensitivity at the (15,0) and (-15,-15) stimulus locations was measured twice during each examination.

	Stimulus size			
	I		V	
T.B.	(12,0)	(-15,-15)	(15,0)	(-15,-15)
	2/2	4/4,**3/4**	3/4	3/4
A.D.	_	(-12,-12)	(15,0)	(-15,-15)
		2/2	4/4	4/4
I.S.	_	(-15,-15)	(15,0)	_
		3/4	3/4	
N.H.	(15,0)	(-12,-12)	(15,0)	_
	3/4	2/4	3/4	
M.R.	(15,0)	(-12,-12)	(15,0)	(-12,-12)
	2/4	4/4	2/4	3/4
R.De.	(15,0)	(-12,-12)	_	_
	2/4,**3/4**	4/4,**3/4**		
R.Do.	(15,0)	(-12,-12)	(15,0)	_
	2/4	3/4	3/4	

Table 4.3 Stimulus coordinates, in parenthesis, of the subsidiary peaks of sensitivity at the 15° nasal (15,0) and 21.2° inferio - temporal (-15,-15) regions of the visual field of the left eye using the SARGON program. The number of adjacent locations where sensitivity was reduced compared to the peak of sensitivity, by 1 dB or more, are given as a fraction of the total number possible, which for the SARGON Program at (15,0) is 4. The results for repeated examinations are given in bold.

investigation. It was suggested that this finding may have arisen for two reasons: an inter - individual variation in the location of the subsidiary peaks of sensitivity or an error in the Octopus such that the coordinates of the given stimulus locations in the SARGON and the standard Programs such as 21 and 31 may not lie at exactly the same positions on the perimeter bowl.

It was decided to re - examine the 15° nasal region in both eyes using Program 61 which comprises a stimulus grid of 25 points each separated by 3° arranged in a 5 x 5 matrix, the centre of which is user - definable anywhere within the visual field. Sensitivity at each stimulus location is assessed three times during the examination and a measure of the local short - term fluctuation is also given. In this way, if the peak of enhanced sensitivity was displaced from the 15° nasal point it would still be recorded since the resolution of measurement within this program is relatively high. The program was centred in separate investigations using either the left or right eye on the 15° nasal point, on a further sample of 15, clinically normal, emmetropic subjects (3 females, 12 males; mean age 23.50 years, S.D. 2.85 years) who were experienced observers in automated perimetry. Sensitivity was measured with stimulus sizes I and V in all subjects, since, as already discussed, the peaks of sensitivity were of highest amplitude for these sizes. Sensitivity was additionally measured using stimulus sizes 0 and IV for 2 subjects. Each subject again attended one session and was adapted to the bowl luminance of the perimeter for 10 minutes prior to the examination, with the head being steadied and the fixation monitored as before. Natural pupils were used throughout.

The results from the 15 subjects assessed with Program 61 are illustrated for the right (Table 4.4a) and left (Table 4.4b) eyes. An area of enhanced sensitivity around the 15° nasal location was found in all of the 4 subjects examined for the right eye with stimulus sizes V and in 3 of the 4 subjects with stimulus size I. For the left eye, 8 of the 11 subjects exhibited a subsidiary peak of sensitivity with stimulus size I, and 9 of the 11 subjects with stimulus size V. The amplitude of these peaks in sensitivity is smaller, however, than that found for the subjects in the first study. An increased fluctuation of the threshold response was found to be present at the 15° nasally and 21.2° inferio - temporally locations compared with the adjacent locations for all stimuli, particularly stimulus size I. This is in agreement with the increase in S.D. of the group means at these locations but is not in accord with current perimetric theory which predicts an increase in fluctuation as sensitivity

	Stimulus size					
	0	I	II	III	IV	V
J.W.	(-15,0) 6/8,**6/8**	(-15,0) 6/8 (15,-3) 6/8,**4/8**	–	–	(-15,-3) 7/8	(-15,0) 7/8,**7/8**
R.De.	(-15,0) 4/8	(-18,-3) 7/8,**8/8**	–	–	(-15,0) 6/8	(-15,0) 8/8
R.Do.	–	–	–	–	–	(-12,0) 8/8
T.M.	–	(-12,0) 8/8 (-15,-3) 6/8,**8/8**	–	–	–	(-15,0) 8/8,**8/8**

Table 4.4a Stimulus coordinates, in parenthesis, of the subsidiary peaks of sensitivity at the 15° nasal region (15,0) of the visual field of the right eye. The number of adjacent locations where sensitivity was reduced compared to the peak of sensitivity, by 1 dB or more, are given as a fraction of the total number possible, which for program 61 is 8. The results for repeated examinations are given in bold.

	Stimulus size					
	0	I	II	III	IV	V
R.M.	–	(15,0) 6/8	–	–	–	(15,-3) 4/8
J.P.	–	(15,-3) 6/8	–	–	–	(15,-3) 8/8
R.B.	–	–	–	–	–	(18,0) 8/8
N.H.	–	–	–	–	–	(12,0) 8/8 (15,-3) 6/8
N.W.	–	–	–	–	–	(15,-3) 6/8
C.S.	–	(12,0) 6/8 (15,0) 5/8	–	–	–	(15,-3) 7/8
P.C.	–	(15,-3) 7/8	–	–	–	(15,0) 6/8
D.W.	–	(12,0) 6/8 (15,0) 5/8	–	–	–	(15,-3) 6/8
S.G.	–	(15,-3) 8/8,**7/8**	–	–	–	(15,0) 6/8
N.P.	–	(15,-3) 7/8	–	–	–	–
S.C.	–	(15,-3) 5/8	–	–	–	(15,-3) 6/8

Table 4.4b Stimulus coordinates, in parenthesis, of the subsidiary peaks of sensitivity at the 15° nasal region (-15,0) of the visual field of the left eye. The number of adjacent locations where sensitivity was reduced, compared to the peak of sensitivity by 1 dB or more, are given as a fraction of the total number possible, which for Program 61 is 8. The results for repeated examinations are given in bold.

decreases (Van den Berg et al 1985;Lewis et al 1986). It is possible that the peaks of enhanced sensitivity measured for stimulus size I may be a product of increased fluctuations in perimetric sensitivity, although this does not explain the presence of subsidiary peaks measured for the larger stimuli. Furthermore, it is unclear why sensitivity fluctuations should be increased at these locations in the visual field.

The presence of a peak of sensitivity at 21.2° inferio - temporally in the original investigation and in the data from the SARGON program, in addition to that at 15° nasally, tends to complicate the theory advocated by Wolf and Zigler (1959) and Wolf and Gardiner (1963) that the enhanced sensitivity at 15° nasally acts as a compensatory measure for the blindspot of the contralateral eye. Interestingly, areas of high rod density between eccentricities of 15° and 20° in the nasal visual field extending in an arc around the horizontal at this eccentricity have been reported (Osterberg 1935) and subsidiary peaks in ganglion cell density have also been demonstrated at these eccentricities (Oppel 1967). Good qualitative agreement is also present between the topography of differential sensitivity for the smaller stimuli (sizes 0 and I) and the horizontal visual streak of ganglion cell density proposed by Stone and Johnston (1981). The peaks in sensitivity may thus arise from regions of high ganglion cell density, however, the stimulus size dependency of the peaks, indicates that other factors such as spatial summation must be involved.

Interestingly, the resting position of accommodation and convergence in darkness is between 60 - 100 cms (Gilmartin et al 1984). The area of enhanced sensitivity at 15° nasally, when projected into space, will thus fall at a point approximately 10 cm from in front of the face, permitting inspection of near objects in darkness. This is further supported by the fact that binocular summation is enhanced in scotopic vision.

The clinical relevance of the subsidiary peaks of enhanced sensitivity is uncertain. The very specific spatial location of these areas necessitates accurate fixation and attention if the topography of the peaks is to be detected. The increased group mean variance associated with the enhanced sensitivity may also be due to inter - individual variation in the distribution of ganglion cell density.

Global relationship

The linear relationship between log ganglion cell receptive field density and perimetric sensitivity for the smaller stimulus sizes confirms the hypothesis that the format of the sensitivity profile depends to some extent upon the underlying retinal architecture. The absence of ganglion cells in the foveal pit necessitates the use of estimates of ganglion cell receptive field densities rather than ganglion cell densities. As described in section 3.3, it is generally accepted that the central foveal cones project to the ganglion cells immediately lateral to the foveal pit and therefore, the central foveal cone density provides a good estimate of the ganglion cell receptive field densities. It must be noted, however, that the relationship between sensitivity and the retinal elements is dependent upon the accuracy of the retinal counts. These counts are currently the best available. The finding that the relationship between log ganglion cell receptive field density and perimetric sensitivity becomes non - linear for stimuli larger than size 0 indicates that factors additional to ganglion cell density are involved. This may include a contribution due to spatial summation arising from the larger ganglion cell receptive fields at increasing eccentricities and supports the conclusion drawn in section 3.9 regarding the cortical representation of perimetric profiles. The finding of a linear relationship between log rod density and perimetric sensitivity for stimulus sizes 0 and I may indicate that rod - driven ganglion cells are dominant in the visual processing of perimetric spot stimuli at this adaptation level. This conclusion is further supported by the lack of correspondence found between log cone density and perimetric sensitivity. Indeed, it would be interesting to determine whether there is any relationship between perimetric sensitivity and the density of other retinal elements, such as amacrine cells and bipolar cells, however, accurate counts of these cells in the human retina are currently unavailable.

Interestingly, meridian as well as eccentricity and stimulus size were found to significantly affect perimetric sensitivity at the $p<0.001$ level (Table 4.1a). The finding of significant differences between sensitivity measured at a given eccentricity along a given meridian (for the cardinal meridians) using t tests (Tables 4.2a; 4.2b), further indicates that the decay in sensitivity with eccentricity is non - uniform across the visual field. A similar analysis along the oblique meridians was considered unnecessary since the overall trend had been established and the information gained

was believed to be of marginal importance and insufficient to justify the lengthy computational time. Indeed, the finding that sensitivity at 12° eccentricity along the superior meridian was significantly lower, for the smaller stimulus sizes, than that at 12° in the inferior meridian is in accord with the results for dark - adapted perimetric sensitivity of Abrahams et al (1983) and Birch et al (1987). Similarly, Katz and Sommer (1986) reported similar asymmetry using a size III stimulus under the parametric adjustment of the Humphrey Field Analyser. Birch et al (1987) suggested that the increased dark - adapted perimetric sensitivity of the inferior relative to the superior visual field, was related to the finding in other species, that rod outer segments are longer (Batelle and LaVail 1978) and rhodopsin content greater (Rapp et al 1985) in the superior retina. Moreover, Vilter (1954) found increased neuronal contiguity and greater ganglion cell numbers in the superior compared to the inferior retina in the region of the fovea.

4.6 The role of adaptation level on the topography of the perimetric profile

The findings of the previous section are confined to a parametric adjustment of a low photopic adaptation level of 4 asb and the use of polychromatic stimuli. It was conjectured that the relationship between the topography of the normal visual field and the underlying retinal architecture might alter with variation in adaptation level. This hypothesis was based on two facts. Firstly, the relative contribution of the retinal elements in visual processing is dependent upon adaptation level. Thus at low adaptation levels, the contribution from rods is greatest and at high adaptation levels the reverse is true (Davson 1980). It is generally accepted that rods are mainly responsible for vision below 0.1 asb, although there is some cone activity at luminances as low as 0.0014 asb (Bedwell 1982). There is no active division, however, between rod and cone functioning (Lythgoe 1940), indeed, except in rod - or cone - free regions of the retina, the rod and cone systems are believed to interact and combine into the same pathway (Granit 1943). The nature of this interaction is not, however, fully understood and constitutes the subject of numerous human psychophysical (Ikeda and Urakobo 1969; Drum 1982; Benimoff et al 1982) and animal electrophysiological (Steinberg 1969; Levine et al 1987) studies. The adaptation level of the retina also determines the level of spatial summation elicited by the retinal elements, indeed, adaptation level is believed to control the size of the retinal ganglion cell receptive fields (Barlow 1958).

Furthermore, numerous workers have suggested that perimetric assessment at certain adaptation levels provides extra diagnostic information (Jayle and Aubert 1958; Greve et al 1972; Hara 1979; Fellman and Lynn 1985; Drum et al 1986) although why this should be so remains unclear.

The purpose of the investigation was therefore to determine how the relationship between visual field topography and retinal architecture varies over the range of bowl luminances normally employed in automated perimeters.

4.7 Experimental work

The perimeter used for the investigation was the Dicon AP3000. This perimeter was selected since it provides the facility to vary adaptation level.

4.7.1 Dicon AP3000

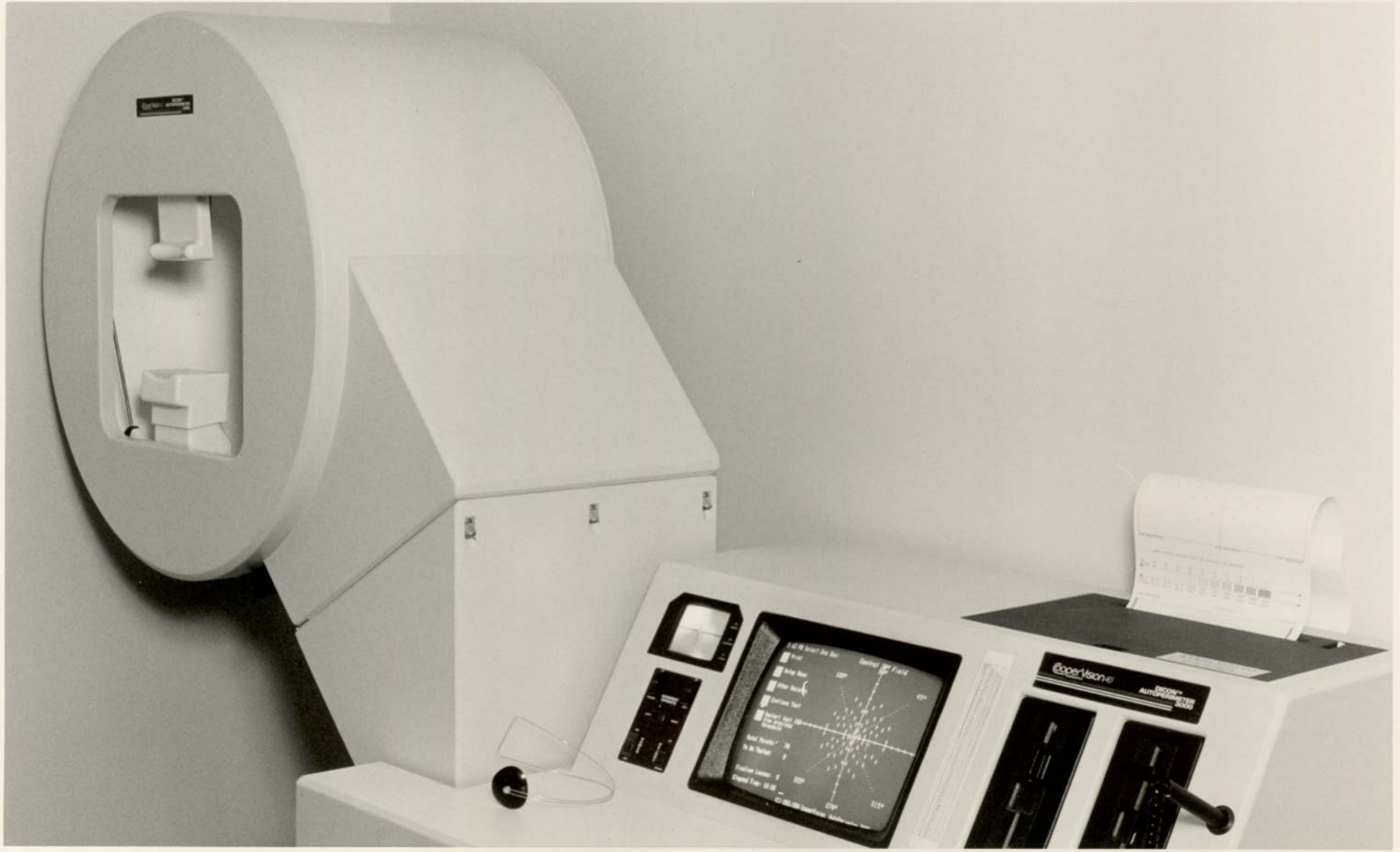
Hardware

The Dicon AP3000 consists of a hemispheric bowl, light emitting diodes (LED), microcomputer and twin disc drives (Plate 4.1). The 512 LEDs are arranged along radials from 5° to 355°, at eccentricity increments of 2.5° out to an eccentricity of 30°, and at 10° intervals at locations peripheral to this. Stimuli are located either side of the horizontal or vertical meridians, since this permits the detection of "steps" across these meridians (Mills 1985). The bowl radius is 33 cm; bowl luminance is adjustable to 0, 10, 31.5 and 45 asb. The LEDs are mounted in precision drilled holes and approximate to Goldmann stimulus size II (1.613 mm diameter). They have a peak emission of 570 nm and permit a range of luminance from 0 to 10,000 asb. To overcome variations in the light output each LED is calibrated during manufacture using a wide - angle lens and a photomultiplier tube. The LEDs are not covered with diffusing surfaces and have consequently been described as "black hole" stimuli (Heijl 1985).

An array of 21 stimuli are located at the expected location of the physiological blindspot. Prior to

Overleaf...

Plate 4.1 The Dicon AP3000 automated perimeter.


CooperVision
Dicon
AUTOPERIMETER
3000

each perimetric program, the blindspot is plotted using the maximum stimulus luminance at these locations. The Heijl - Krakau method of fixation monitoring is used, where a stimulus of maximum luminance is presented within the measured blindspot every 7 - 10 s. If the patient responds to this stimuli, all the measurements made within the 7 - 10 s prior to the fixation loss are repeated.

Software

The Dicon AP3000 provides suprathreshold, threshold related (hill of vision, two - zone screening) and threshold strategies. The threshold strategy, which consists of a heuristic semi - bracketing method with an infrathreshold approach to the end - point, was employed in the investigation. The threshold determination for a given location is completed before proceeding to the next stimulus location and has a resolution of 2 dB. The initial selection of the stimulus position is pseudo random although the sequence of stimulus presentations is not.

4.7.2 Materials and methods

The sample for the investigation comprised 10 clinically normal, emmetropic, males (mean age 20.4 years, S.D. 1.12 years), visual acuity was 6/5 or better. The subjects were experienced observers in automated perimetry and were free of ocular or systemic medication.

Perimetric sensitivity was determined at bowl luminances of 10 asb, 31.5 asb, and 45 asb along the horizontal and vertical meridians of the right eye. The Meridional Threshold Program was used to determine sensitivity along the 95°/85° meridians of the superior field and the 265°/275° meridians of the inferior field at eccentricities of 5°, 10°, 12.5°, 15°, 20°, 22.5°, 25°, 27.5°, 30°, 35°, 40° and 50°. Sensitivity was determined in the same way along the 185°/195° meridians of the nasal field and the 5°/355° meridians of the temporal field at eccentricities of 5°, 7.5°, 10°, 12.5°, 15°, 20°, 22.5°, 25°, 27.5°, 30°, 35°, 40°, 50°, 60°, 70° and 80°. The Macular Program was used to determine sensitivity at eccentricities of 0°, 1°, 2°, 4° along the horizontal meridian and at 0°, 1°, 3°, 5° along the vertical meridian. Prior to each session, the subject was adapted to the bowl luminance for 10

minutes. This was followed by 4 Meridional Threshold Programs along either the vertical or horizontal meridians at one of the three bowl luminances Since 8 meridians were measured in total, at each of the 3 bowl luminances, the subjects attended 6 sessions. In addition, sensitivity with the Macular programs was determined for each of the 3 bowl luminances on a separate session for both the vertical and horizontal meridians. The subjects thus attended a total of 7 sessions of 30 minutes duration each. The order of both bowl luminance and measured meridian were randomized.

Natural pupils were used throughout the examinations. Pupil size was measured at 5 minute intervals throughout the examination using the scaled axes of the video monitor of the perimeter, and were represented as the mean of these measurements.

The results were analysed using a 4 - way ANOVA to determine to what extent eccentricity, meridian and adaptation level influenced the topographical distribution of sensitivity across the visual field.

The values for ganglion cell receptive field density and rod and cone density were derived in the same manner as those of section 4.5.

4.7.3 Results

The group mean pupil sizes were 5.43 mm (0.84 mm) at 10 asb, 4.89 mm (0.65 mm) at 31.5 asb and 4.51 mm (0.56 mm) at 45 asb. Pupil size was not controlled in the study since it was envisaged that the data could be used as normative control data. Furthermore, the use of artificial pupils or ophthalmic drugs to modify pupil size would have introduced additional variables into the study (section 9.5) and thus altered retinal illumination.

The relationship between group mean perimetric sensitivity and eccentricity as a function of adaptation level is illustrated for the nasal - temporal (Figure 4.6a) and superior - inferior (Figure 4.6b) meridians. The results at each eccentricity are represented as the mean of the two measurements 5° either side of the particular meridian. The group mean S.D.s were of the order of 2

dB, ranging from 0.88 dB to 2.9 dB, they increase with increasing eccentricity and are independent of adaptation level.

Eccentricity, meridian and adaptation level all significantly affected sensitivity for the meridians assessed in the investigation at the $p<0.001$ level (Table 4.5). The interaction term between eccentricity and meridian was significant at the $p<0.001$ level and that between eccentricity, meridian and adaptation level was also significant at the $p<0.001$ level.

Figures 4.7a and 4.7b illustrate the relationship between log ganglion cell receptive field density and perimetric sensitivity for the nasal and inferior meridians respectively. The relationship is non - linear at all adaptation levels measured. Similar results were found along the temporal and superior meridians.

Figures 4.8a and 4.8b illustrate the relationship between log rod density and perimetric sensitivity for the nasal and inferior meridians. The relationship is non - linear at all adaptation levels and is similar for the temporal and superior meridians.

Figures 4.9a and 4.9b illustrate the relationship between log cone density and perimetric sensitivity for the nasal and inferior meridians. The relationship is non - linear at all adaptation levels and is similar for the temporal and superior meridians.

4.7.4 Discussion

Perimetric sensitivity measured with the LED stimuli of the Dicon decreases with eccentricity for all 3 bowl luminances. This is in agreement with the results of section 3.6 for projected stimuli.

Sensitivity increases as adaptation level decreases for all eccentricities along all meridians (Figures 4.5a; 4.5b; Table 4.5) which is in accord with previous findings obtained with manual perimetry (Fankhauser and Schmidt 1960; Aulhorn and Harms 1972). These findings conform to Weber's law which predicts that as adaptation level increases, threshold increases to maintain Weber's fraction

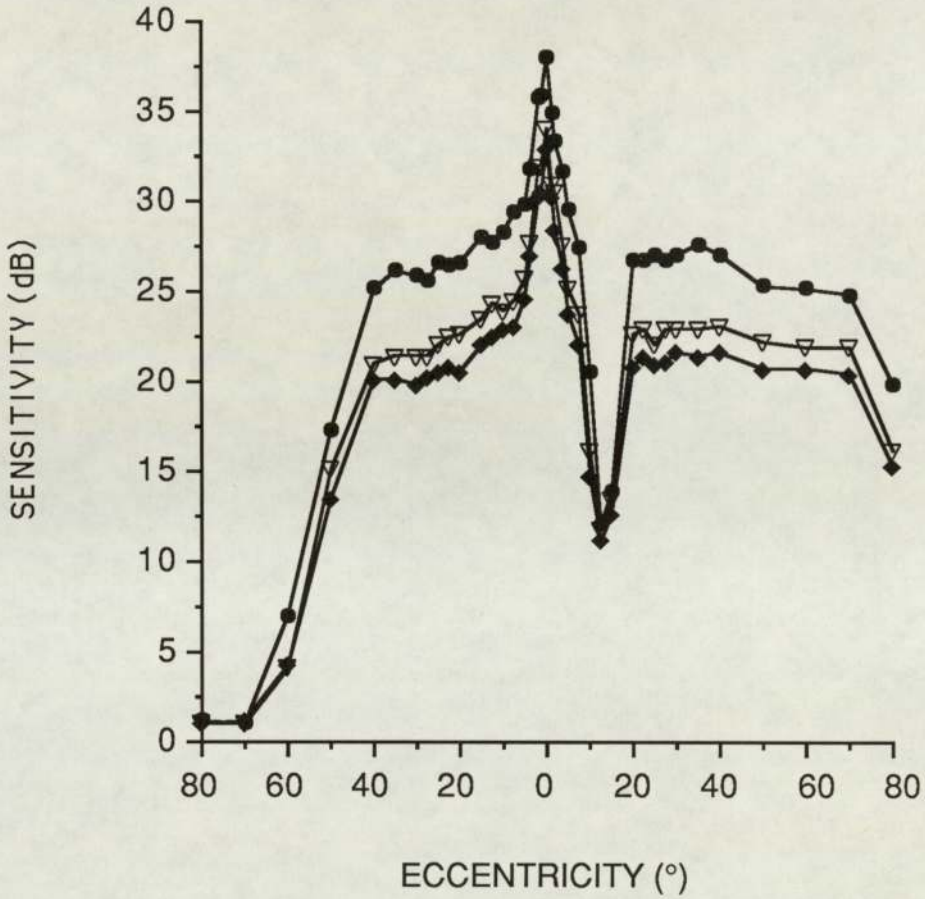


Fig. 4.6a Group mean perimetric sensitivity against eccentricity along the nasal (left) - temporal (right) meridian of the right eye as a function of adaptation level (10 asb filled circles, 31.5 asb open inverted triangles, 45 asb filled diamonds) recorded with the Dicon AP3000 autoperimeter.

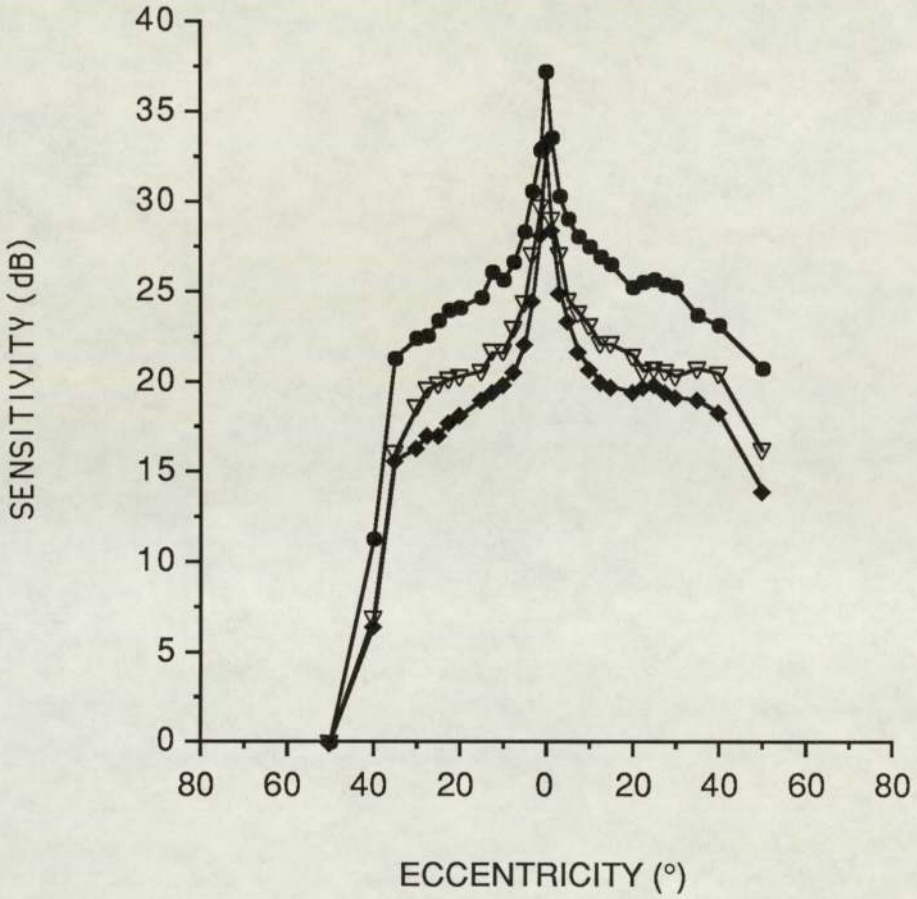


Fig. 4.6b Group mean perimetric sensitivity against eccentricity along the superior (left) - inferior (right) meridian as a function of adaptation level (10 asb filled circles, 31.5 asb open inverted triangles, 45 asb filled diamonds) recorded with the Dicon AP3000 autoperimeter.

Source	S.S.	D.F.	M.S	F	Significance Level
Eccentricity (A)	19172.6	7	2738.94	724.966	p<0.001
AS	238.081	63	3.779		
Meridian (B)	1012.49	3	337.496	71.701	p<0.001
BS	127.107	27	4.707		
AB	3934.3	21	187.348	82.825	p<0.001
ABS	427.52	189	2.262		
Adaptation level (C)	5256.62	2	2629.31	697.628	p<0.001
CS	67.850	18	3.769		
AC	62.065	14	4.361	1.734	NS
ACS	316.965	126	2.515		
BC	26.756	6	4.459	1.823	NS
BCS	132.181	54	2.447		
ABC	193.967	42	4.618	3.052	p<0.001
ABCS	571.722	378	1.513		
Subjects (S)	674.862	9	74.984	49.559	p<0.001
TOTAL	32216.3	959			

Table 4.5 Four - way analysis of variance with perimetric sensitivity as the dependent variable.

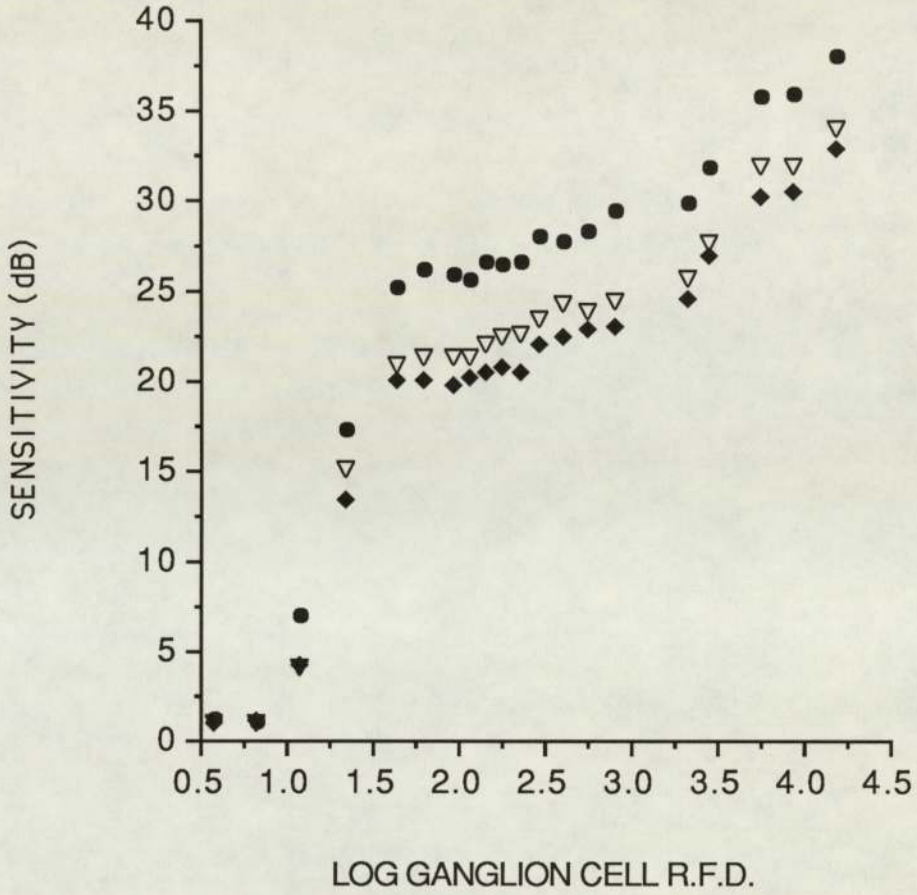


Fig. 4.7a Scattergram showing group mean differential light sensitivity with increase in adaptation level against log ganglion cell receptive field density for the twenty sampled eccentricities of the nasal meridian of the visual field of the right eye (10 asb filled circles, 31.5 asb open inverted triangles, 45 asb filled diamonds) recorded with the Dicon AP3000 autoperimeter.

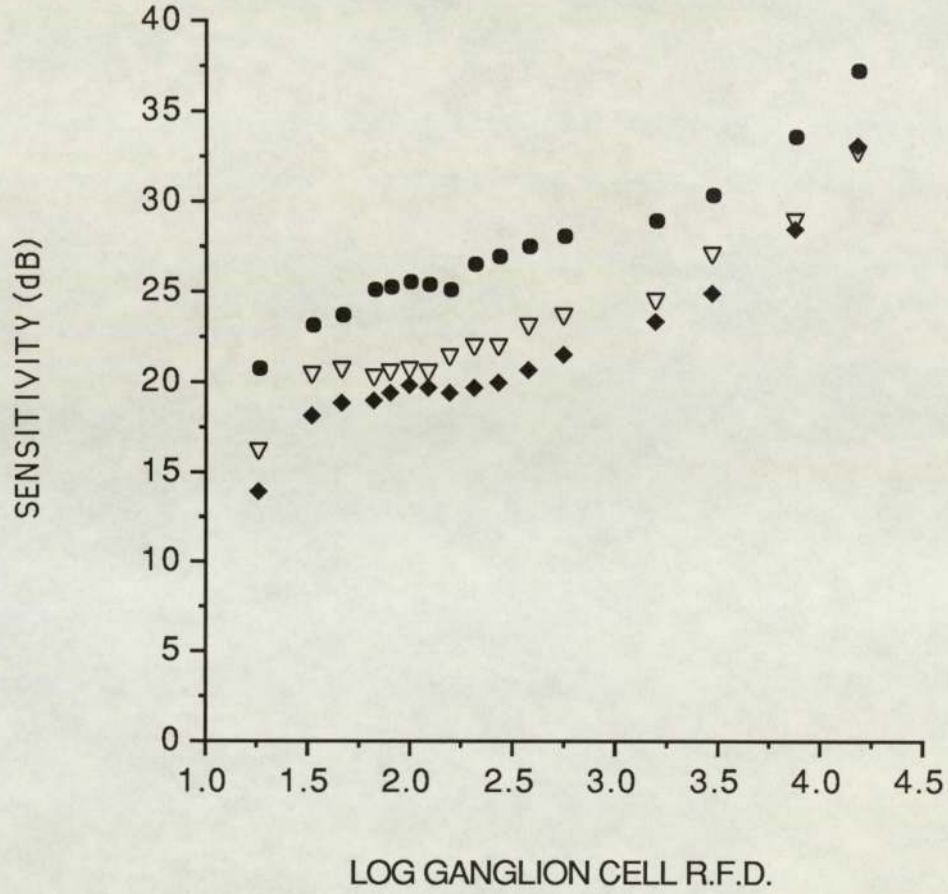


Fig. 4.7b Scattergram showing group mean differential light sensitivity with increase in adaptation level against log ganglion cell receptive field density for the sixteen sampled eccentricities of the inferior meridian of the visual field of the right eye (10 asb filled circles, 31.5 asb open inverted triangles, 45 asb filled diamonds) recorded with the Dicon AP3000 autoperimeter.

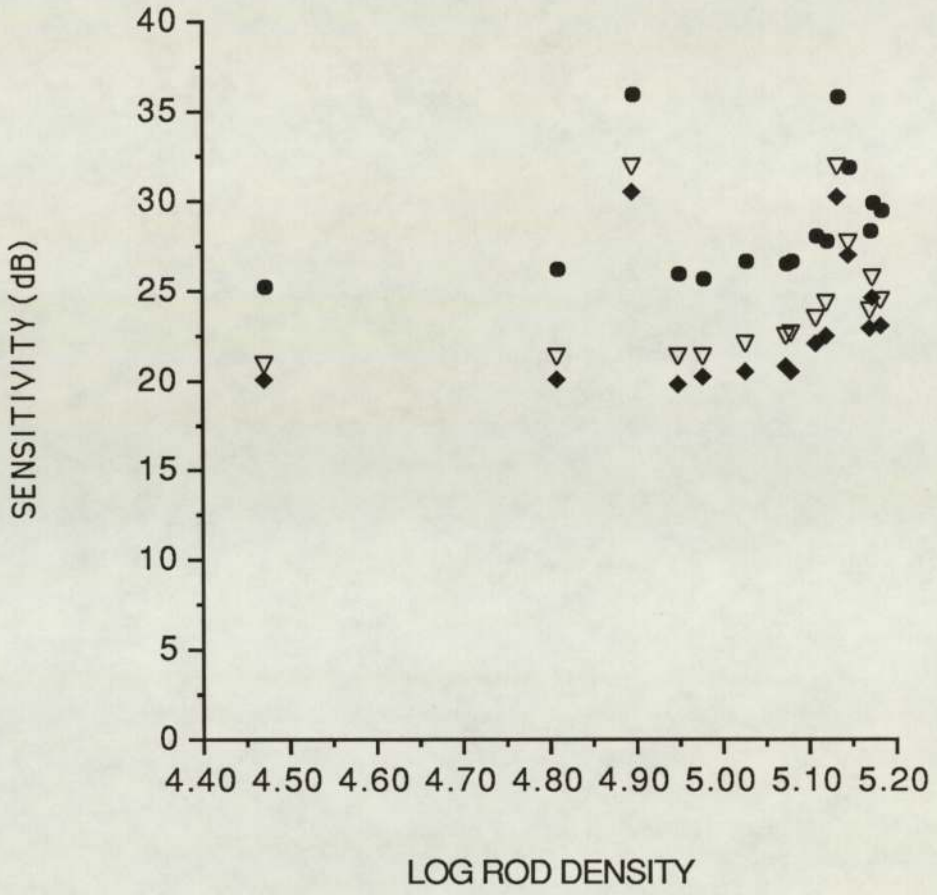


Fig. 4.8a Scattergram showing group mean differential light sensitivity with increase in adaptation level against log rod density for the fifteen sampled eccentricities of the nasal meridian of the visual field of the right eye (10 asb filled circles, 31.5 asb open inverted triangles, 45 asb filled diamonds) recorded with the Dicon AP3000 autoperimeter.

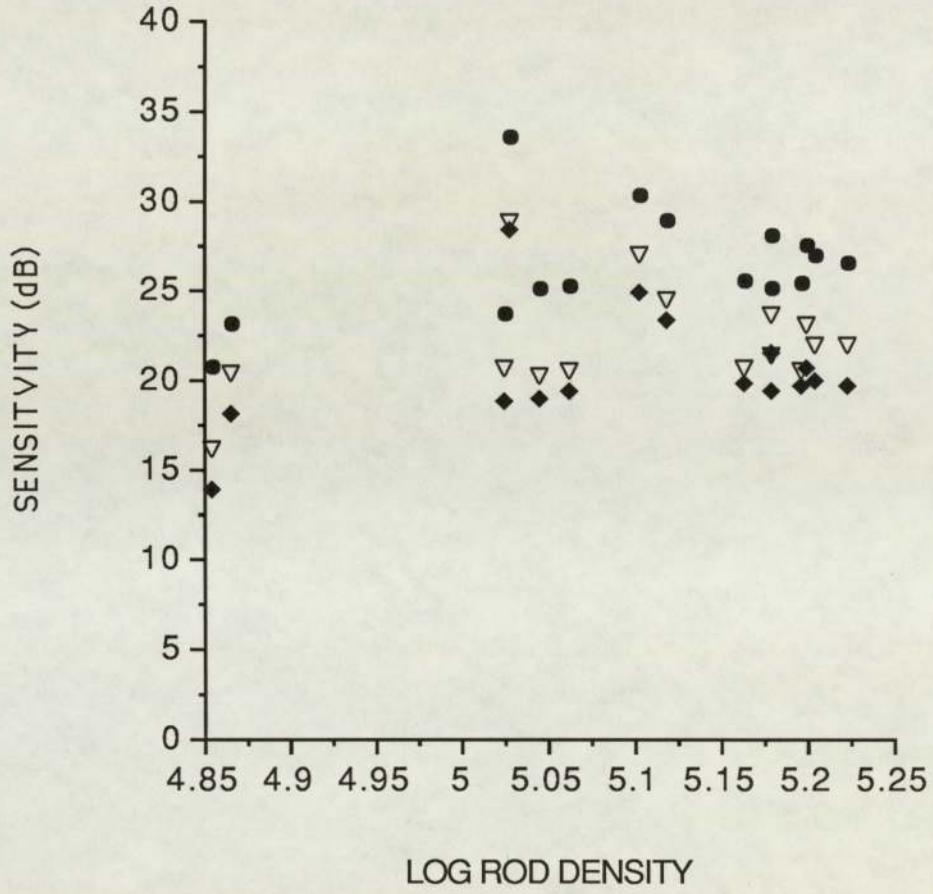


Fig. 4.8b Scattergram showing group mean differential light sensitivity with increase in adaptation level against log rod density for the fifteen sampled eccentricities of the inferior meridian of the visual field of the right eye (10 asb filled circles, 31.5 asb open inverted triangles, 45 asb filled diamonds) recorded with the Dicon AP3000 autoperimeter.

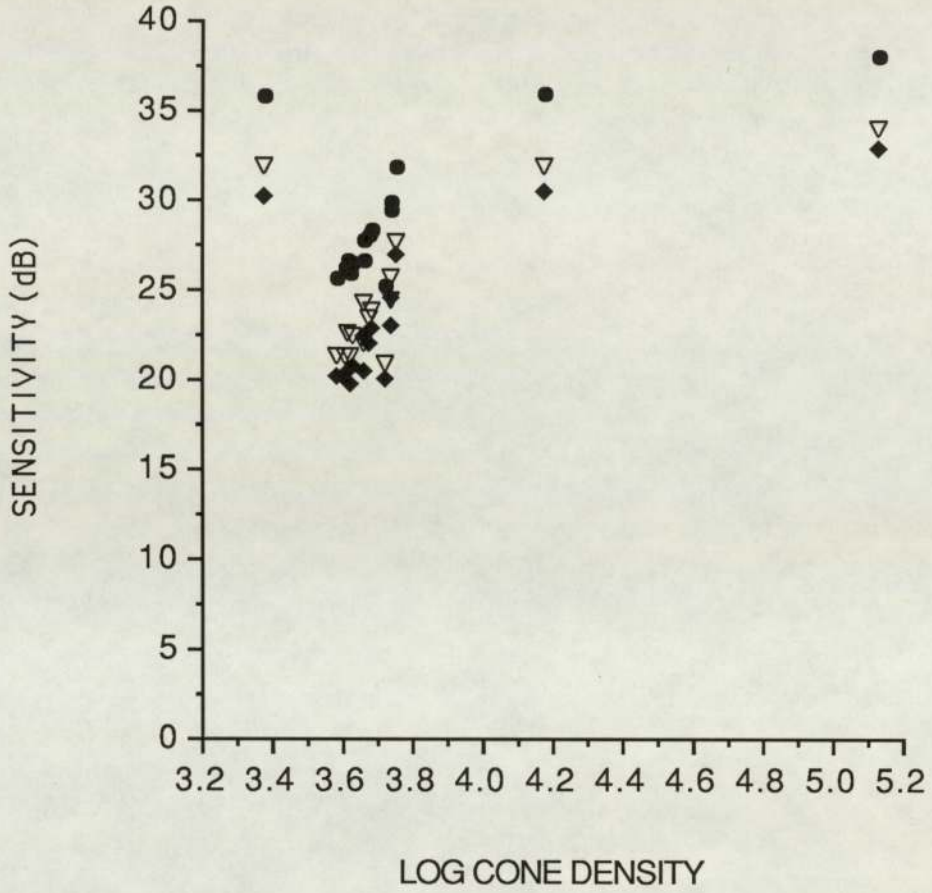


Fig. 4.9a Scattergram showing group mean differential light sensitivity with increase in adaptation level against log cone density for the fifteen sampled eccentricities of the nasal meridian of the visual field of the right eye (10 asb filled circles, 31.5 asb open inverted triangles, 45 asb filled diamonds) recorded with the Dicon AP3000 autoperimeter.

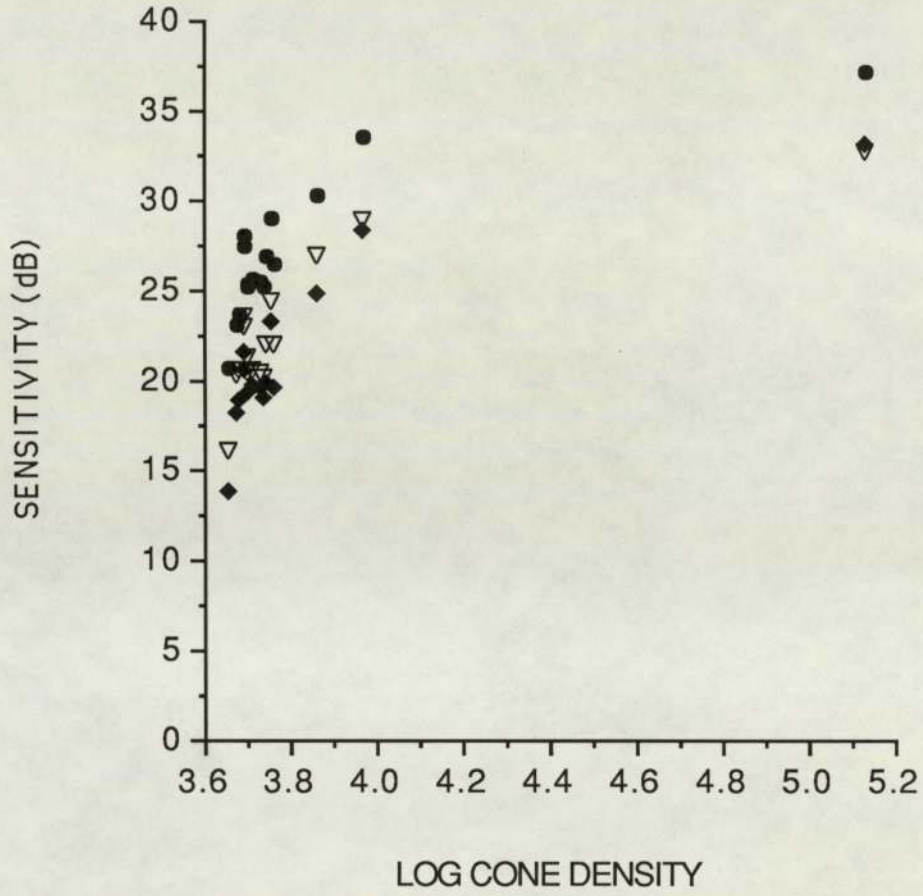


Fig. 4.9b Scattergram showing group mean differential light sensitivity with increase in adaptation level against log cone density for the fifteen sampled eccentricities of the inferior meridian of the visual field of the right eye (10 asb filled circles, 31.5 asb open inverted triangles, 45 asb filled diamonds) recorded with the Dicon AP3000 autoperimeter.

$\Delta L/L$. It is important to note that the Dicon does not measure a true increment threshold but the absolute threshold of the LED which may distort the results. In addition, it is unclear whether the unique characteristics of the Dicon "black hole" LED stimuli may change the format of the relationship between perimetric sensitivity and retinal elements. Indeed, Heijl (1985) suggested that the "black hole" effect of the Dicon may produce variations in local retinal adaptation.

Interestingly, the elevation in sensitivity at the 10 asb adaptation level, relative to the other adaptation levels, becomes greater with increasing eccentricity. This may be explained by the fact that at lower adaptation levels, spatial summation is increased (Barlow 1958) which will result in a concomitant increase in sensitivity for all but the smallest stimulus sizes (i.e. sizes 0 and I). Since the potential for spatial summation is greatest in the periphery the increase in sensitivity will be manifested in the more peripheral regions. Alternatively, the greater increase in sensitivity in the periphery with reduction in adaptation level may also relate to the distribution of the rods and cones on the retina, since rods function optimally at lower adaptation levels (Mandelbaum and Sloan 1947) and are most numerous in the peripheral retina (Osterberg 1935). In addition, sensitivity varied between meridians ($p<0.001$) and confirmed the findings relating to the Octopus data of section 4.5.2.

There is good correspondence between log ganglion cell receptive field density (log ganglion cell R.F.D.) and perimetric sensitivity measured with the LED stimuli whose diameter is equivalent to the Goldmann stimulus size II, although the relationship is non - linear. This finding is in agreement with the results of the previous section, where the relationship between log ganglion cell R.F.D. and perimetric sensitivity measured with the Octopus was linear for stimulus size 0 only. This tends to support the hypothesis that factors such as spatial summation were also involved.

The relationship between log rod density and perimetric sensitivity is non - linear along all meridians which would be expected on the basis of the results derived with projected stimuli (section 4.5.2) where the relationship was linear for stimulus sizes 0 and I only. Similarly, the non - linear relationship between log cone density and perimetric sensitivity measured for all meridians is in agreement with the results for projected stimuli. Variation in the adaptation level, between 10

asb and 45 asb, has no influence on the relationship.

The area of enhanced sensitivity at 15° nasally was not found at any of the adaptation levels employed in this study. This was not unexpected, since the subsidiary peaks in sensitivity were not present for stimulus size II of the Octopus which is the stimulus size equivalent to the Dicon LEDs. Furthermore, sensitivity was measured 5° either side of, rather than along, the horizontal meridian and was represented as the mean of the two measurement

4.8 Conclusions

Global variations in the topographical distribution of sensitivity across the visual field were demonstrated for the projected stimuli of the Octopus. Furthermore, the shape of the visual field profile, measured with the LED stimuli of the Dicon, was found to vary significantly with adaptation level. There is no systematic trend, however, in the relationship between sensitivity measured in one region of the field compared to another, in terms of stimulus size and adaptation level.

The global variations in the topographical distribution in sensitivity over the visual field measured with projected and LED stimuli demonstrates a good correlation with variations in ganglion cell receptive field density over the retina. The relationship is linear for small stimulus sizes becoming non - linear with stimuli of projected diameter larger than 0.054° (size 0). This finding implies that factors such as spatial summation are important in the visual processing of perimetric spot stimuli. The good relationship between log rod density and perimetric sensitivity measured with stimulus sizes 0, and I suggests that rod - driven ganglion cells are dominant in the visual processing at the adaptation levels employed in the investigation. This conclusion is further supported by the finding of a poor relationship between log cone density and perimetric sensitivity measured with both projected and LED stimuli. Adaptation level, over the ranges normally employed in clinical perimetry, does not influence the relationship between the topography of the normal visual field and variations in the retinal architecture.

Local variations in sensitivity, in particular the subsidiary peaks of sensitivity at 15° nasally and 21.2° inferio - temporally measured under the parametric adjustment of the Octopus, may arise due to undulations in ganglion cell density. The investigation reports the presence of these areas rather than defines their parameters which is the subject of on - going investigations.

These findings in conjunction with those of sections 3.6 and 3.8 suggest that the topography of the normal perimetric differential light threshold appears to be significantly influenced by retinal configuration and processing, in particular, the combination of retinal ganglion cell density and their spatial summation characteristics.

5. STIMULUS INVESTIGATIVE RANGE IN RETINITIS PIGMENTOSA

5.1 Introduction

Retinitis pigmentosa (R.P.) may be defined as "a set of progressive hereditary disorders that diffusely and primarily affect photoreceptor and pigment epithelial function" (Marmor et al 1983). The vast literature regarding all the characteristics of R.P. has been compiled in several reviews which include: Krill (1972), Merin and Auerbach (1976), Landers et al (1977), Allard (1983), Bird (1981; 1983) and Marmor et al (1983). The signs and symptoms of typical R.P. comprise nightblindness, annular scotoma and/or peripheral field contractions, mid - peripheral intraretinal bone - spicule - like pigmentation and narrowed retinal arterioles (Merin and Auerbach 1976; Massof and Finkelstein 1979b). R.P. is believed to be inherited in three ways: autosomal dominant, autosomal recessive, and sex - linked recessive; however, the homogeneity of the genetic groups has never been demonstrated. Cases of R.P. without known affected relatives are termed either simplex or multiplex (Jay 1981; Boughman 1982). The simplex category comprises families where only one sufferer has been identified over three generations. Multiplex describes the situation where the siblings may be affected but where there is no gene penetrance over three generations. Krill (1972) recommended that autosomal recessive R.P. should be subdivided into early and late onset groups. Berson et al (1968) and Berson et al (1969) suggested that autosomal dominant R.P. may be divided into two groups on the basis of gene penetrance (either full or reduced) and stated that the temporal characteristics of the electroretinogram (E.R.G.) differed between the two groups. Further subdivision of both autosomal recessive and autosomal dominant R.P. has been suggested by Massof and Finkelstein (1979a; 1981) based upon differences in the relationship between rod and cone sensitivity, whereas other workers have proposed subgroups on the basis of E.R.G. data (Marmor 1979; Arden et al 1983) and D.N.A. probes (Wright et al 1983). Interestingly, Pearlman and Saxton (1979) reported that subjects with different genetic forms of R.P. performed similarly in a series of psychophysical tests which included visual acuity, dark adaptation and kinetic Goldmann visual fields.

5.2. Psychophysical function in R.P.

Visual acuity in patients with R.P. tends to remain relatively less affected compared with peripheral visual function until later in the course of the disease (Marmor 1980; Farber et al 1985). Indeed, impairment of absolute foveal thresholds, measured for a 500 nm and a 655 nm test flash, have been reported in R.P. patients with relatively good visual acuity, which suggests the presence of foveal changes despite the retention of good visual acuity (Alexander et al 1986). When visual acuity is reduced, it is unclear whether the attenuation results from primary damage to the photoreceptors or from secondary degenerative phenomenon such as cystoid macular oedema (Marmor 1980).

Contrast sensitivity has been reported to be depressed in patients with R.P. (genetic typing was not stated), the degree of depression being related to the stage of the disease rather than the visual acuity, size of the visual field, or the age of the patient (Hyvarinen et al 1981). Similarly, Lindberg et al (1981) reported that contrast sensitivity was depressed in patients with R.P. (mixed genetic types), the magnitude of this effect being greatest at high spatial frequencies. In addition, Lindberg et al (1981) found that those patients with autosomal recessive and sex - linked R.P. exhibited a higher sensitivity at low spatial frequencies than either patients with simplex or autosomal dominant R.P., although the reason for this finding could not be explained.

When assessed with critical flicker fusion frequency tests, sensitivity was found to be depressed at some temporal frequencies in observers with R.P. compared to normal subjects (Tyler et al 1984). Scotopic sensitivity losses have been reported to occur across a broad range of temporal frequencies in the periphery of a group of sex - linked R.P. patients (Ernst et al 1981) whereas, photopic sensitivity losses occur predominantly at the high temporal frequencies in simplex and multiplex R.P. (Tyler et al 1984). These latter workers attempted to reproduce such losses in sensitivity, in a group of normal observers, by reducing either the stimulus luminance or the signal - to - noise ratio of the visual system, however, their attempts were unsuccessful.

Colour vision is also affected in R.P; the effect being well documented in the literature (Ohta 1957; Cox 1961; Verriest 1963; Kurata 1967; Adams et al 1972). The presence of blue defects on the Farnsworth Munsell 100 - hue test and protanomalous - like changes on the Nagel anomaloscope have been reported in patients with R.P. by several investigators (Cox 1961; Verriest 1963; Grutzner 1972; Merin and Auerbach 1976; Massof et al 1979; Young and Fishman 1980). Moreover, it was shown that the results from these standard colour vision tests were dependent upon the visual acuity, genetic typing and the presence or absence of foveal lesions (Fishman et al 1981). When the visual acuity was better than 20/30, patients with autosomal dominant disease performed better in colour vision tests than patients with either autosomal recessive, sex - linked or simplex R.P. (Fishman et al 1981).

Pronounced abnormalities in the increment threshold curves for the blue and green cone mechanisms were demonstrated at 10° from the fovea, and in some cases at the fovea in a group comprising all genetic types of R.P. (Sandberg and Berson 1977). The thresholds determined by the blue cone mechanism were more elevated than those determined by the green, and the latter were more elevated at low adaptation levels than at either intermediate or high adaptation levels. Sandberg and Berson (1977) suggested that these findings were indicative of a reduction in the summation pools for blue and green cone mechanisms in R.P. Young and Fishman (1980) demonstrated that the foveal Rayleigh colour matches, in a group comprising all genetic types of R.P., differed from those of normal observers. The results were interpreted as demonstrating that the effective optical density of red and/or green cones was reduced, or alternatively, that the peak of the extinction spectrum of the visual pigments was shifted towards shorter wavelengths (Young and Fishman 1982). More recently, Alexander et al (1986) reported that patients with R.P. exhibited foveal threshold elevations compared to normals for a 500 nm and a 655 nm test flash. The duration of the test flash was 500 ms and stimulus size varied in diameter from 7' to 1.7°. The threshold elevations were not believed to result from abnormalities in spatial summation, a significant correlation was, however, demonstrated between foveal cone thresholds and the mid - point of the patient's Rayleigh matches. Interestingly, the directional sensitivity of individual cones (the Stiles - Crawford effect) has been reported to be greater in R.P. than in normals (Birch and Sandberg 1982; Birch et al 1982). These

workers suggested that the findings resulted from morphological abnormalities increasing the optical bandwidths of individual cones rather than from increased disarray among cones with normal bandwidths.

The E.R.G., a record of a transient retinal action potential resulting from light striking the retina, has historically been reported to be completely absent or of very low amplitude in R.P. (Karpe 1945; Bjork and Karpe 1951). With the advent of selective electronic filtering techniques and microprocessor technology, however, E.R.G.s of small amplitude have been recorded in patients with R.P. (Henkes et al 1956; Armington et al 1961). Typically, the scotopic b wave in R.P. patients is severely diminished or non - recordable (Allard 1983) and is believed to reflect a widespread rod disease preceding cone involvement and correlates with late reduction of good central visual acuity and early reduction in dark adaptation thresholds (Moses 1965). Indeed, it has been suggested that there is a good relationship between E.R.G. sensitivity and the functioning regions of the retina in all genetic types of R.P. (Armington et al 1961; Berson et al 1985). Similarly, Marmor (1979) reported a good correlation between the photopic and scotopic b wave amplitudes, visual acuity and age but not with the dark adaptation thresholds of a group comprising all genetic types of R.P. Conversely, Arden and Fojas (1962) reported that there was no correlation between the size of the kinetic visual fields and the E.R.G. sensitivity, although the genetic types were not given in this paper.

Several investigators have demonstrated that the E.R.G. responses of the various genetic types of R.P. differ (Berson et al 1968; Berson and Kanters 1970; Arden et al 1983). Patients with autosomal recessive R.P. exhibit a reduction in the amplitude and an increase in the latency of both the rod and cone responses of the E.R.G. (Berson and Kanters 1970) whereas, patients with autosomal dominant R.P. exhibit a reduction in rod function only (Berson et al 1968). Indeed, Arden et al (1983) demonstrated, in a series of patients with autosomal dominant R.P., that over half had no rod b wave; they subdivided the whole group of patients into those in whom the scotopic E.R.G. was smaller than expected from visual field losses and those in whom the reverse applied.

Classically, the visual field in R.P. is characterized by a ring scotomata corresponding to the regions of the retina that initially degenerate. The ring scotomata originates as a group of separate scotomatas 20° to 25° from fixation which eventually coalesce to form a complete annulus. The outer margin of the annulus expands rapidly peripherally, while the inner margin contracts slowly towards fixation leaving a small island of intact central field in the late stages of the disease (Harrington 1981). The area of field loss has been shown to be greater in the superior than inferior visual field when measured by a kinetic Goldmann stimulus IV_{4e}, in patients with autosomal dominant R.P. (Lyness et al 1985). Similarly, Birch et al (1987) reported that patients with R.P. (mixed genetic typing) exhibited increased dark - adapted perimetric sensitivity in the inferior compared to the superior field, however, normal subjects also manifested this asymmetry.

It has been suggested, however, that visual field losses do not occur during the early stages of R.P., despite depression of the E.R.G., vitreous degeneration and symptoms of night - blindness (Choy et al 1987) and it is only in the second stage of the disease that visual field losses occur (Massof et al 1984). Several workers, from their experimental findings, have estimated the rate of field loss per year exhibited by patients with R.P. The values vary due to differences in visual field technique and the genetic types examined. Berson et al (1985) reported that R.P. patients, on average, lost 4.6% of the visual field area (assessed kinetically with a Goldmann V_{4e} stimulus) per year and 2.4 % of the remaining visual field diameter per year, whilst Lyness et al (1985) found that for every year of field loss there was a decline in field area by a factor of 1.09. Pearlman and Saxton (1979) reported that the rate of loss in Goldmann kinetic field area in the autosomal recessive form is initially greater than the rate for either the autosomal dominant or for the sex - linked type. The rate of field loss of the autosomal recessive form, however, was found to plateau with the duration of the disease. It should be noted, however, when analysing the change in visual fields with time, that R.P. patients exhibit greater variability in response than normals when assessed by manual kinetic and static Goldmann perimetry (Ross et al 1984).

Two colour static perimetry in the dark - adapted eye has been employed to permit assessment of the relative sensitivity of the rod and cone mechanisms in a particular region of the retina (Massof and Finkelstein 1979a; Ernst et al 1983; Lyness et al 1985). Disturbance of rod function is identified by a threshold elevation for the green stimuli and of cone function by a threshold elevation for the red stimuli. This system of measurement has permitted further subdivision of both simplex and autosomal dominant R.P. patients (Massof and Finkelstein 1979a). Indeed, it has been suggested that the subtypes defined in this way by dark - adapted perimetry may represent different underlying disease mechanisms (Massof 1985). Similarly, Birch et al (1987) measured dark - adapted visual fields using red and blue filters to separate the rod and cone responses and reported that rod perimetric thresholds (obtained with the blue filter) were significantly correlated to rod E.R.G. thresholds. The dark - adapted fields were measured using an Octopus 201 perimeter, modified by masking the background beam and disabling the fixation monitoring system.

Light - and dark - adapted visual field analysis using static automated perimetry has been advocated as a means of assessing the level of visual disability of patients with R.P. and also as a method of defining subtypes (Jacobson et al 1986). These workers used a modified Humphrey Field Analyser, which permitted perimetric examination at both 31.5 asb and 0 asb.

The perception of the eccentricity of a suprathreshold light flash (III_{4e}) with a Goldmann perimeter has been reported to be abnormal in a sample of three patients with early R.P. (mixed genetic typing) compared to four normal observers (Temme et al 1985). In the R.P. subjects, the perceptual magnification of the central field had doubled with respect to the whole field despite the absence of field constriction measured kinetically with a II_{4e} stimulus.

Taylor (1987) reported that the V_{4e} kinetic isopter recorded with the Topcon SBP20 bowl perimeter in the apparently unaffected members of a family with autosomal dominant R.P., was normal when the stimulus was moved from "non seeing" to "seeing" but was reduced when the stimulus was moved in the reverse direction. In normal subjects, the kinetic visual field is smaller when the stimulus is moved from "non seeing" to "seeing areas"; this is a consequence of the patients

reaction time, between when the appearance of the stimulus is first noted and when the subject responds to the examiner. Interestingly, Taylor (1987) found that when the subjects returned on subsequent occasions for testing, their anomalous field findings were reproducible. It was also noted that these subjects were developing early signs of R.P. such as abnormalities in dark adaptation, indicating that this abnormal sensitivity to the direction of stimulus motion may be an early sign of R.P.

5.4. Anatomical and physiological characteristics of R.P. (morphology)

Histologically, retinal changes in R.P. occur both in rods and cones, but initially in rods near the equator, until only a tiny central island of visual field remains (Marmor 1980). Coincident with this loss of receptor cells, pigment epithelium cells demonstrate proliferative as well as degenerative changes, and in conjunction with macrophages, migrate into the retinal stroma and to vascular layers adjacent to the veins. These cells then degenerate, permitting free pigment granules to accumulate around the retinal blood vessels (Allard 1983). Symmetrical development of pigmentation is a characteristic of R.P., differentiating it from chorioretinitis (Biro 1959). The retinal vessels exhibit thickening of their walls with diminution in the calibre of the lumen, which is manifested by an apparent reduction in the size of the vessels. The optic nerve changes are relatively inconsistent, and depend upon the severity of the vessel damage and upon the extent of the degenerative changes present in the ganglion cells and nerve fibres (Allard 1983).

In an ultrastructural study of the donor eyes from a 74 year old man with moderately advanced, simplex R.P. and from a 51 year old man with far advanced simplex R.P. it was reported that the only photoreceptors present were the remnants of cones at the fovea (Mizuno and Nishada 1967). Degeneration of the photoreceptors was found to coincide with attenuation of the basement membrane and infoldings of the pigment epithelium; the gaps in this being replaced with vacuolated tissue and melanin granules. Similarly, Kolb and Gouras (1974), in an ultrastructural study of the donor eye from a 68 year old patient with autosomal dominant R.P., demonstrated that the only remaining photoreceptors present were foveal cones. The outer segments of these cones were shorter

and wider than normal and their discs were disoriented. Foveal pigment epithelial cells contained excessive quantities of lipofuscin. Kolb and Gouras (1974) interpreted this finding as implying that either the outer segment material was being phagotized and digested by the pigment epithelium, or that there was a disturbance in the pigment epithelial cells themselves which led to eventual death of the photoreceptors. Szamier et al (1979), in an ultrastructural study from a postmortem donor eye of a 24 year old male with sex - linked R.P., demonstrated abnormalities in all the remaining rod and cone photoreceptors. Interestingly, the patient had full visual fields measured with a Goldmann V_{4e} stimulus three weeks prior to his death despite the fact that the cones were reduced in density and had no organized outer segments. In a 79 year old female carrier of sex - linked R.P. who had no visual symptoms, areas of apparently normal appearing photoreceptors were found in the mid - and far - peripheral retina adjacent to areas of photoreceptor degeneration (Szamier and Berson 1985). In the areas of photoreceptor cell degeneration, remaining rods and cones were few in number and had shortened and distorted outer segments. Remaining cones also had autophagic vacuoles in the perinuclear cytoplasm. Rods, cones and pigment epithelium in the central retina appeared normal. The major difference between the female carrier and the affected male in these two studies, was that the carrier had only patches of photoreceptor cell degeneration with adjacent pigment epithelial cell abnormalities, whereas the affected male had generalized photoreceptor epithelial cell disease. Interestingly, the choriocapillaris was comparable in both degenerated and non - degenerated regions in the carrier, lending support to the hypothesis that choroidal vascular changes are not primarily involved in the pathogenesis of this disease (Szamier and Berson 1985).

5.5 Pathophysiology of R.P.

Investigation of the mechanisms underlying R.P. has been limited by two factors, namely, that postmortem tissue from human R.P. patients is relatively rare and that the extent of retinal atrophy in most of the donor eyes is usually too far advanced (Bird 1983). Consequently, the current understanding of the mechanism which produces the reduction in both rod and cone sensitivity in R.P. is based upon psychophysical evidence.

From this psychophysical evidence it has been advocated that spatial summation is abnormal in R.P. (Sandberg and Berson 1977), although this finding was not substantiated by Alexander et al (1986). Alternatively, it has been suggested that the reduction in rod and cone sensitivity in subjects with R.P. may arise from a reduction in the number of retinal photoreceptors, as illustrated by the ultrastructural studies of Mizuno and Nishada (1967), Kolb and Gouras (1974) and Szamier et al (1979). Indeed, Sandberg and Berson (1983) proposed that the reduction in cone density may account for the reduced foveal thresholds observed in patients with R.P. A third explanation attributes a major component of the sensitivity loss to the decrease in the quantum catching ability of the photoreceptors. Fundus reflectometry studies (which assess the level of retinal pigment) have indicated that the quantity of rhodopsin is reduced in the mid - periphery of patients with autosomal dominant (Highman and Weale 1973; Ripps et al 1978; Kemp et al 1983) and sex - linked (Highman and Weale 1973; Perlman and Auerbach 1981) R.P. These reductions have been linearly correlated with the elevation of the dark - adapted threshold found in the same retinal areas (Ripps et al 1978). Furthermore, the elevation in cone thresholds has been interpreted as arising, in part, from a reduction in cone optical density (Young and Fishman 1982; Alexander et al 1986). Alternatively, the tilting and misalignment of the photoreceptors, described in section 5.4 (Kolb and Gouras 1974; Szamier et al 1979; Szamier and Berson 1985) may decrease the effective intensity of the stimulus (Greenstein et al 1984). Indeed, the abnormal foveal Stiles - Crawford effects reported by Birch and Sandberg (1982) and Birch et al (1982) are consistent with morphological changes in the cone photoreceptors.

Two explanations of early rod and cone sensitivity loss in R.P. were investigated by Greenstein et al (1984) and Greenstein and Hood (1986). These workers used a probe - flash paradigm, in which the observer was required to detect the presence of a small brief light, the probe, presented upon a second light, the 500 ms flash. The predicted probe - flash functions for the two hypotheses (decrease in quantum catching ability and decreased responsiveness) were modelled in terms of response - intensity functions which related the size of the response to the intensity of the flash of light. The experimental results of the R.P. patients (of mixed genetic types) were compared to the predicted models and it was suggested that the loss of foveal sensitivity in R.P. may be due to a

decreased responsiveness of the retinal elements, rather than a decrease in quantum catching ability of the functioning photoreceptors, coupled with a complex adaptation model.

5.6 Aim of the investigation

Empirical evidence has indicated that certain states of parametric adjustment, provided by a given instrument, can provide diagnostic information, additional to that obtained from the conventional perimetric examination.

Dubois - Poulsen (1952) and Dubois - Poulsen and Magis (1957), using Goldmann kinetic perimetry, demonstrated abnormalities of spatial summation in certain disorders which they termed photometric dysharmony. These workers considered that photometric dysharmony resulted from oedema of the retina or optic nerve. This finding was not substantiated by Sloan (1961) and Sloan and Brown (1962) who, using static Goldmann perimetry, reported that photometric dysharmony resulted when the cone receptor mechanism was impaired. Wilson (1967) demonstrated, at an adaptation level of 674 asb, abnormalities of both spatial and temporal summation in post - geniculate lesions and abnormalities of spatial summation, alone, in pre - geniculate lesions.

Perimetry performed at certain adaptation levels is also believed to provide additional diagnostic information. Greve et al (1977) demonstrated, using the Friedmann Visual Field Analyser I, that examination by means of comparative mesopic and scotopic perimetry aided the differential diagnosis of maculopathies and central neuropathies. Paige (1985) using the Humphrey Field Analyser suggested that the detection of early visual field defects was enhanced at a high adaptation level of 315 asb in suspected and in confirmed glaucoma, and in neuro - ophthalmological lesions. Conversely, several workers have demonstrated that scotopic sensitivity tends to be more severely affected than photopic sensitivity in glaucoma and have suggested that scotopic perimetry is a potentially more sensitive test for early glaucoma detection than perimetry at photopic levels (Fellman and Lynn 1985; Drum et al 1986; Starita et al 1987).

Recently, using automated perimetry, (Flanagan et al 1984b) suggested that the perimetric response in R.P. is atypical for a range of stimulus combinations and strategies.

The aims of the experiment were to investigate the hypothesis of Flanagan et al (1984b) and to determine whether this data could be used to provide additional diagnostic information in R.P.

5.7 Experimental work

Since none of the currently available automated perimeters permit variation of all the stimulus parameters required by the experimental protocol, several perimeters were employed, whose combined characteristics fulfilled the experimental criterion. The Octopus 201 automated perimeter was used in the study to investigate the interaction between perimetric sensitivity and eccentricity as a function of stimulus size. The Tubinger manual static perimeter permitted investigation of the interaction between spatial and temporal variations in stimulus presentation. Since the Tubinger perimeter is manual and not automated, threshold assessments were made only along meridional cuts as full field assessment was too time - consuming. The manual Goldmann perimeter was also employed since this is the standard against which other perimeters have traditionally been compared.

The R.P. patients were selected from the records of the Retina Department of the Birmingham and Midland Eye Hospital (B.M.E.H.). The minimum criterion for patient selection was the retention of some peripheral visual field. Those patients with reduced central visual acuity were rejected since good fixation is necessary for accurate field assessment.

A list of 40 potential patients was made. A signed letter was sent to each patient detailing the reasons for the study and the experimental procedures. The patients were advised that they were required to visit the B.M.E.H. on three occasions. Thirty positive replies were returned, of whom, ten were rejected due to problems in travelling to and from the Department, and a further three were subsequently rejected because their visual fields had deteriorated to such an extent that they did not fulfil the original patient selection criteria.

5.7.1 Materials and methods

Ten of the 17 R.P. patients who exhibited varying degrees of visual field loss were selected for the preliminary study. The age of the sample ranged from 22 to 50 years (mean age 41.9 years; S.D. 9.3 years) and comprised 9 males and 1 female. The genetic typing included 5 autosomal recessive, 2 simplex, 2 autosomal dominant and 1 unknown. Details of scotopic and photopic E.R.G. results and dark adaptation were available for each patient. The eye to be examined was selected on the premise of clearest media and largest peripheral island of vision. All patients were familiar with automated perimetric techniques.

The patients each attended 3 sessions. The first session consisted of kinetic perimetry with the Goldmann bowl perimeter (bowl luminance 31.5 asb; stimulus sizes III and V; intensity 4e). The second and third sessions comprised full field examination to a 15° resolution using Program 21 of the Octopus (bowl luminance 4 asb; stimulus sizes III and V; stimulus duration 100 ms) and static cuts along an arc and a meridian using the Tubinger (bowl luminance 10 asb; stimulus sizes III and V; stimulus duration 100 ms and 500 ms). The sequence of perimetry over the latter 2 sessions, of stimulus size within an examination and, in the case of the Tubinger, stimulus duration, were all randomized. The examinations for a given patient were all undertaken within a maximum period of 28 days.

Kinetic perimetry with the Goldmann perimeter was performed by one examiner to minimize inter - examiner variation (Berry et al 1966; Ross et al 1984) and to ensure standardization of technique. The meridian and the arc, for Tubinger perimetry, were selected from the Goldmann results to cut through a region of high sensitivity in the peripheral field. Threshold was determined manually, in 1 dB intervals from an infrathreshold direction, using an ascending method of limits and was recorded as the mean of 3 determinations at each eccentricity. The Tubinger examinations were undertaken by a second clinician who had been informed of the most appropriate location for the investigation of each patient.

Prior to each examination, patients were adapted to the bowl luminance of the perimeter for 10 minutes. For perimetry out to an eccentricity of 30°, patients wore the distance refractive correction together with the near correction, if necessary, for the particular working distance. Fixation was strictly monitored and natural pupils were used throughout. For Octopus perimetry, patients were instructed to ignore the light flashes which filled the central bowl (Fankhauser and Haeberlin 1980) and to ignore reflections in the fixation tube.

A qualitative comparative analysis of the field plots from the Octopus (numerical printout and gray scale) and Goldmann perimeters was carried out using the level 4 analysis of Flanagan et al (1984a). For a given patient, the field measured with a given stimulus combination was compared, in terms of type, shape, area, depth and location of field loss, to the field for a second stimulus combination which was designated as the reference field. The level of compatibility between the comparison field and the reference field was ranked on a 5 point scale where scores I+, I and I- represented levels of compatible fields and scores II and III represented levels of incompatible fields. The process was repeated for all stimulus combinations with each instrument in turn providing the reference field. Plate 5.1. illustrates an example of the scoring system employed to analyse the results of the investigation.

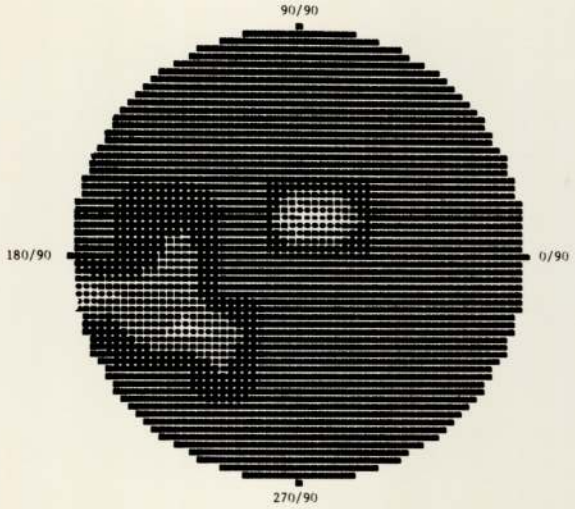
5.7.2 Results

Tables 5.1a - 5.1d demonstrate the degree of compatibility between the selected reference field and the comparison fields for the Octopus and Goldmann fields. Seven of the 10 kinetic stimulus size III_{4e} Goldmann fields exhibited a high degree of compatibility (Score I) with the static stimulus III field of the Octopus. The results also show that all 10 individuals exhibited less field loss (Score I-) with Octopus stimulus size V in terms of area and depth. Eight individuals showed less areal field loss with the kinetic V_{4e} Goldmann due to the suprathreshold nature of the stimulus (Table 5.1a).

When compared to Octopus stimulus size V as the reference (Table 5.1b), 7 of the Goldmann III_{4e} fields exhibited more loss in terms of area, whilst all 10 Octopus size III plots also exhibited more

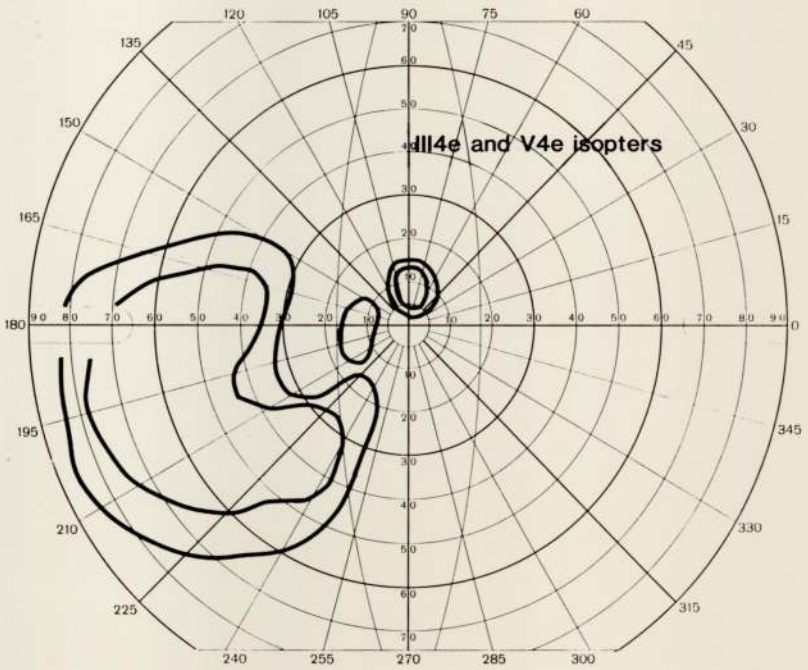
Overleaf...

Plate 5.1 The qualitative scoring procedure used to compare the field plots in the investigation illustrated for the left eye of a 42 year old male with R.P. Top left: gray scale printout of Octopus Program 21 (stimulus size III) as reference field. Bottom left: gray scale printout of comparative field from Octopus Program 21 (stimulus size V) scored as I- (less field loss). Right: comparative fields from Goldmann III_{4e} and V_{4e} kinetic isopters. $III4_e$ isopter scored as I (similar field loss); V_{4e} scored as I- (less field loss).



FLUCTUATIONS (R.M.S.): 1.1 DB LUM. INTERVAL: 4

FLUCTUATIONS (R.M.S.): 1.9 DB LUM. INTERVAL: 4



loss in terms of both area and depth. The trend from Tables 5.1a - 5.1d demonstrates that the Octopus stimulus size V yielded the greatest range of sensitivity. Within the limited numbers of the sample, the kinetic Goldmann III_{4e}, by virtue of performance against Octopus stimulus size V, appeared to give a slightly greater areal investigative range than that of Octopus stimulus size III. The Goldmann V_{4e} produced the lowest range. The effect of the stimulus combinations is illustrated diagrammatically in Figure 5.1

Tables 5.2a - 5.2d illustrate the degree of compatibility between the selected reference field and the comparison fields for the Tubinger fields. Only 9 patients were included in this analysis, since 1 patient failed to return for the third session which in his case comprised measurement of the Tubinger fields. These tables demonstrate that the Tubinger stimulus size V at 100 ms produced less field loss in 8 of the 9 cases examined when compared to stimulus size III at 100 ms as the reference field, thus obeying conventional perimetric theory. In contrast, stimulus size III at 500 ms showed a similar result to the reference (stimulus size III at 100 ms) in 6 cases. These findings demonstrate that for the sample under study, increase in stimulus size, rather than increase in stimulus duration from was more efficient in extending the dynamic range

Table 5.3 illustrates the number of stimulus locations exhibiting a spatial summation coefficient > 1, as a fraction of the total number of locations at which an assessment of k was possible for the sample of R.P. patients together with control data derived from the normal subjects in the experiment described in section 3.6. The spatial summation coefficient was calculated from the sensitivity data derived with Octopus Program 21 for stimulus sizes III and V using Gougnard's (1961) formula:

$$k = \frac{\log I(2) - \log I(1)}{\log A(1) - \log A(2)}$$

where I represents the stimulus luminance and A represents the area of stimulus size (1) and stimulus size (2).

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Octopus III)				
	I+ More	I Similar	I- Less	II Different field loss	III Normal
OCTOPUS V	–	–	10	–	–
GOLDMANN III_{4e}	1	7	2	–	–
GOLDMANN V_{4e}	–	2	8	–	–

Table 5.1a The degree of compatibility between the reference field of the Octopus stimulus size III and the comparison fields of the Octopus stimulus size V and the Goldmann stimulus sizes III_{4e} and V_{4e}.

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Octopus V)				
	I+ More	I Similar	I- Less	II Different field loss	III Normal
OCTOPUS III	10	–	–	–	–
GOLDMANN III_{4e}	7	2	1	–	–
GOLDMANN V_{4e}	1	3	6	–	–

Table 5.1b The degree of compatibility between the reference field of the Octopus stimulus size V and the comparison fields of the Octopus stimulus size III and the Goldmann stimulus sizes III_{4e} and V_{4e}.

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Goldmann III_{4e})				
	I+ More	I Similar	I- Less	II Different field loss	III Normal
OCTOPUS III	2	7	1	–	–
OCTOPUS V	1	2	7	–	–
GOLDMANN V_{4e}	–	–	10	–	–

Table 5.1c The degree of compatibility between the reference field of the Goldmann stimulus size $III4_e$ and the comparison fields of the Octopus stimulus sizes III and V and the Goldmann stimulus size V_{4e}.

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Goldmann V_{4e})				
	I+ More	I Similar	I- Less	II Different field loss	III Normal
OCTOPUS III	8	2	–	–	–
OCTOPUS V	6	3	1	–	–
GOLDMANN III_{4e}	10	–	–	–	–

Table 5.1d The degree of compatibility between the reference field of the Goldmann stimulus size V_{4e} and the comparison fields of the Octopus stimulus sizes III and V and the Goldmann stimulus size III_{4e}.

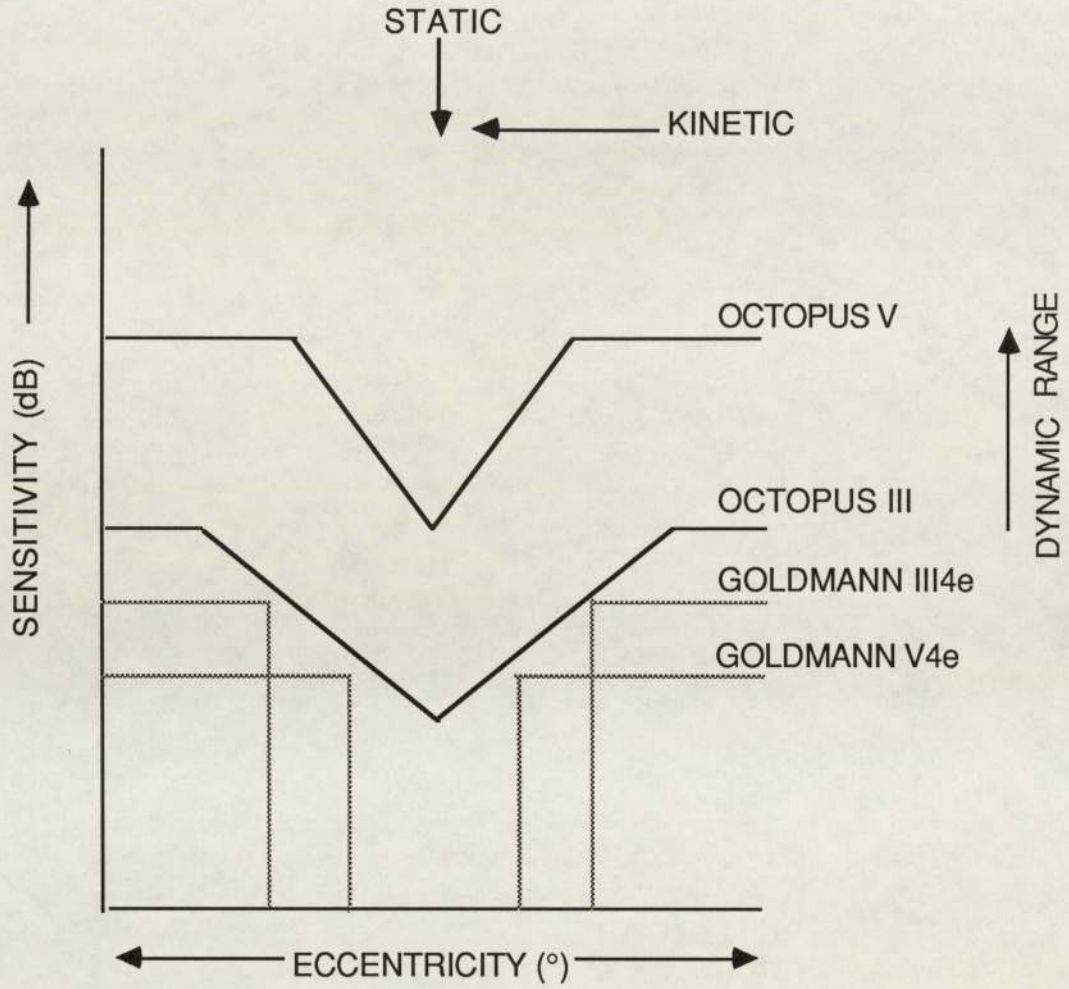


Fig. 5.1 Schematic representation of the investigative range of the static threshold Octopus (stimulus sizes III and V) and kinetic Goldmann (stimulus sizes III and V; intensity 4e) stimulus combinations in the detection of reduced perimetric sensitivity.

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Tubinger III: 100)				
	I+ More	I Similar	I- Less	II Different field loss	III Normal
TUBINGER V: 100	_	1	8	_	_
TUBINGER III: 500	2	6	1	_	_
TUBINGER V: 500	_	2	7	_	_

Table 5.2a The degree of compatibility between the reference field of the Tubinger stimulus size III: 100 ms and the comparison fields of the Tubinger stimulus size III: 500 ms and the Tubinger stimulus size V: 100 ms and 500 ms.

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Tubinger III: 500)				
	I+ More	I Similar	I- Less	II Different field loss	III Normal
TUBINGER III: 100	1	6	2	_	_
TUBINGER V: 100	_	2	7	_	_
TUBINGER V: 500	_	2	7	_	_

Table 5.2b The degree of compatibility between the reference field of the Tubinger stimulus size III: 500 ms and the comparison fields of the Tubinger stimulus size III: 100 ms and the Tubinger stimulus size V: 100 ms and 500 ms.

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Tubinger V: 100)				
	I+ More	I Similar	I- Less	II Different field loss	III Normal
TUBINGER III: 100	8	1	_	_	_
TUBINGER V: 500	7	2	_	_	_
TUBINGER V: 500	4	5	_	_	_

Table 5.2c The degree of compatibility between the reference field of the Tubinger stimulus size V:100 ms and the comparison fields of the Tubinger stimulus size V: 500 ms and the Tubinger stimulus size III: 100 ms and 500 ms.

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Tubinger V: 500)				
	I+ More	I Similar	I- Less	II Different field loss	III Normal
TUBINGER III: 100	7	2	_	_	_
TUBINGER III: 500	7	2	_	_	_
TUBINGER V: 100	_	5	4		

Table 5.2d The degree of compatibility between the reference field of the Tubinger stimulus size V: 500 ms and the comparison fields of the Tubinger stimulus size V: 100 ms and the Tubinger stimulus size III: 100 ms and 500 ms.

	Number of stimulus locations having a value of k>1 as a fraction of the total number of stimulus locations at which an assessment of k was possible.		
Subject	R.P.		Normals
P.W.	20/35	J.W.	36/76
D.W.	34/69	T.T.	36/76
B.F.	0/10	P.C.	7/76
D.H.	16/40	N.C.	13/76
P.S.	27/62	M.P.	16/76
D.G.	2/12	R.D.	20/76
P.C.	28/64	M.D.	18/76
B.C.	10/19	M.B.	47/76
D.W.	10/20	P.W.	28/76
G.J.	11/40	K.W.	22/76

Table 5.3 The number of stimulus locations where the coefficient of spatial summation derived from the equation of Gougnard (1961) is greater than 1, recorded as a fraction of the total number of stimulus locations where an assessment of k was possible, for 10 R.P. patients. The control data was based upon all 76 data points measured in each of 10 normal subjects with Program 21, using the experimental procedures described in section 3.6. Sensitivity for both groups was recorded with the Octopus 201 automated perimeter.

5.7.3 Discussion

Tables 5.1a - 5.1d indicate that the combination of static threshold presentation with stimulus size III at a bowl luminance of 4 asb together with a 15° spatial resolution yields a similar level of areal field loss to that of the kinetic stimulus size III_{4e} at a bowl luminance of 31.5 asb, for the sample of subjects investigated. Interestingly, Fellman and Lynn (1985) reported that perimetry at the lower bowl luminance of 4 asb of the Octopus compared to that of 31.5 asb of the Humphrey Field Analyser yielded earlier and deeper field loss in glaucoma, although Heijl (1985) considered that automated perimetry at low bowl luminances offered no diagnostic advantage over the conventional 31.5 asb. The finding that field area is greater with stimulus size V of the Octopus compared to size III for all of the sample is in accord with normal perimetric theory (Fankhauser 1979) whereby a larger stimulus extends the dynamic range by virtue of spatial summation. Indeed, Wilensky et al (1987) using automated perimetry suggested that stimulus size V should be employed to monitor visual field changes in regions considered to be absolute scotomatas when measured with stimulus size III.

The results regarding the spatial and temporal characteristics of the sample may be influenced by extraneous stray light associated with the use of large stimuli (Fankhauser and Haeberlin 1980). Indeed, Wilson (1968) measured the thresholds for the detection of light scattered from stimuli presented in densely impaired regions of the field. From these investigations Wilson (1968) proposed various arbitrary limitations on the maximum stimulus luminance in order to avoid light scatter. These restrictions were only valid for a parametric adjustment of a bowl luminance of 236 asb and a stimulus duration of 1 s. Indeed, Weale and Wheeler (1977) concluded, from their study on stray light with the Tubinger perimeter, that both instrument design and observer and patient variability excluded the possibility of applying any but the crudest correction to perimetric measurement.

Interestingly, Table 5.2c illustrates that, when compared to stimulus size V at 100 ms, 4 of the 9

patients showed more field loss with the same stimulus at a presentation time of 500 ms, i.e., extending the stimulus duration reduces perimetric sensitivity. Such a finding is contrary to conventional perimetric theory, whereby the dynamic range can be extended by increasing the presentation time provided the latter remains within the critical stimulus duration (Aulhorn and Harms 1972; Greve 1973). Estimates of the length of the critical stimulus duration vary (see section 1.3.2) because of different experimental techniques, and lie between 60 ms and 500 ms. Abnormalities in the temporal responses of patients with R.P. would be expected if the temporal summation of the rod and cone systems (which are believed to degenerate at different rates in R.P.) were dissimilar, however, temporal summation has been reported to be of the same magnitude in both the rod and cone systems (Brown and Black 1976; Montellese et al 1979; Skottun et al 1982).

The results of Table 5.3 suggest that spatial summation is enhanced across the islands of residual vision in the R.P. patients compared to that in normal subjects. The coefficient of spatial summation in normal subjects has been reported to lie within the range of 0.3 to 1.0 regardless of eccentricity (Dubois - Poulsen 1952; Dubois - Poulsen and Magis 1957; Gougnard 1961; Sloan 1961) although the magnitude is dependent upon stimulus size, duration and eccentricity. The normal subjects would thus appear to exhibit higher spatial summation than previously quoted. This may have arisen as a result of light scatter from the larger stimulus (Fankhauser and Haeberlin 1980) or because of the short - and long - term fluctuations (Bebie et al 1976b; Flammer, Drance and Schulzer 1984; Flammer, Drance, Fankhauser and Augustiny 1984) which are inherent in any perimetric examination and which confound quantitative analysis. Furthermore, the calculation of spatial summation coefficients using the sensitivity values from only two stimulus sizes may introduce errors into the analysis which ideally should include values from at least 6 different stimulus sizes (Wilson 1970). The normal subjects (described in section 3.6) were not age - matched with respect to the R.P. patients. Evidence pertaining to the effect of age on spatial summation is equivocal. Dannheim and Drance (1971b) considered in studies with manual perimetry that the age of the observer had no effect on spatial summation and this finding has recently been confirmed with the Octopus 201 automated perimeter by Zulauf et al (In press). Owsley and Sekuler (1982), however, reported that spatial summation decreased with age. It would therefore seem

prudent to treat the conclusion from this analysis with caution.

Interestingly, it has been reported that spatial summation is normal in R.P. at the fovea (Alexander et al 1986) and out to an eccentricity of 15° along the nasal meridian (Sloan and Brown 1962) but is abnormal in subjects with progressive cone degeneration (Sloan and Brown 1962). The latter workers concluded that anomalies of spatial summation could be associated with impairment of the inhibitory mechanisms of the cone receptor system. This conclusion is based upon the assumption that the rods and cones do not interact, however, there is extensive psychophysical evidence to suggest that the 2 systems do interact (Latch and Lennie 1977; Temme and Frumkes 1977; Buck et al 1979; Drum 1982; Benimoff et al 1982; D'Zmura and Lennie 1986), furthermore, mediation through gap junctions has also been demonstrated between vertebrate photoreceptors (Cohen 1969; Raviola and Gilula 1975). The recent finding of abnormal rod - cone interactions in autosomal dominant R.P. (Alexander and Fishman 1985; Arden et al 1987) may, however, lend support to the hypothesis of Sloan and Brown (1962).

Many patients in the study demonstrated greater areal field retention inferiorly than superiorly. This finding is in agreement with the clinical findings of Lyness et al (1985) and Birch et al (1987) and the observation of Biro (1959) that the primarily site of pigmentation in R.P. is in the inferior nasal region of the retina (corresponding to the closure line of the optic cup). Indeed, in the more advanced cases of field loss, the peripheral field was usually retained in the inferior temporal quadrant (Plate 5.1). It can be speculated that this retention arises either because the superior nasal quadrant of the retina is more resistent to damage due to the underlying architecture or because less light falls upon the superior retina by virtue of the eyelids. This latter hypothesis is commensurate with the theory from animal studies that light acts as a catalyst to the pigmentary changes in R.P. Various studies on animals with retinal degeneration, which include, R.C.S. albino rats (Dowling and Sidman 1962), vitamin A depleted rod dominated rats (Noell et al 1971) and vitamin A depleted 13 - lined ground squirrel (Berson 1973) have suggested that light exposure results in further photoreceptor destruction once the photoreceptor - pigment epithelial cell complex has become abnormal. Such findings led to the proposal that light deprivation may act as a therapeutic measure

for patients with early R.P. (Berson 1971) Whatever the reason for the pattern of field loss, the end product is advantageous to the patient in that the inferior temporal vision provides some aid towards mobility.

Interestingly, those patients who demonstrated either increased spatial summation or who exhibited a decreased sensitivity to long duration stimuli were not confined to any one genetic group. This is contrary to previous findings which suggest that the different genetic groups (Massof and Finkelstein 1979a; Massof 1985) perform differently in different psychophysical tests.

It was noted during kinetic Goldmann perimetry that if a moving "seen" stimulus was made momentarily stationary it often became "non seen". The patients responded to the static stimulus again, only if it was made brighter and larger or if it was moved.

5.8 Further experimental work

An additional study on a separate sample of R.P. patients was undertaken to investigate the stato - kinetic dissociation, recorded empirically in the first sample, whereby a "seen" kinetic stimulus becomes "non seen" when made stationary. This investigation was undertaken using a manual Goldmann perimeter which could be used in both the static and kinetic mode.

It was also hypothesized that a greater field retention would result at higher bowl luminances since in R.P. the rods are believed to degenerate before the cones. Although, as described in section 5.4, ultrastructural studies have demonstrated a reduction in number and distortion both of rods and cones in R.P. (Kolb and Gouras 1974; Szamier et al 1979; Szamier and Berson 1985). It was therefore decided to carry out a preliminary pilot study to investigate this hypothesis. The Dicon AP3000 (described in section 4.7.1) was utilized since this instrument permits variation in bowl luminance in discrete steps from 0 to 45 asb.

The patients were selected in the same manner as the preliminary sample and were advised that they

would be required to attend the B.M.E.H. on 2 occasions and on one occasion at Aston University.

5.8.1 Materials and methods

The sample comprised 7 patients with R.P., 5 males and 2 females, age range from 39 to 66 years (mean age 48.8 years; S.D. 8.8 years). The genetic typing included 3 autosomal dominant, 1 sex - linked and 3 unknown.

Each patient attended for 2 sessions at the B.M.E.H. In the first session the patients were examined with the Octopus Program 21 (stimulus sizes III and V) using the same procedures as for the first sample. In the second session both static and kinetic perimetry were undertaken using the Goldmann perimeter using stimulus sizes III and V. The kinetic examination was carried out as for the first sample at intensity 4e. The static investigation was undertaken along an arc in the middle of the region of preserved field (based upon the Octopus examination); stimulus presentation time was 1 s and threshold was determined by a descending method of limits. In cases where the stimulus could not be seen at the maximum intensity (V_{4e}) the presentation time was increased to between 3 s and 5 s. The order of examination for a given instrument was randomized.

Five of the seven patients from the second sample were selected to investigate the influence of adaptation level on apparent field retention. The remaining 2 patients from the sample were unable to attend for the extra session at Aston University. The sample consisted of 4 males and 1 female, whose ages ranged from 39 to 57 years (mean age 46.4 years; S.D. 7.1 years) and whose genetic typing comprised 2 autosomal dominant, 1 sex - linked and 2 unknown. The patients were examined with the Dicon AP3000 autoperimeter at bowl luminances of 10 asb, 31.5 asb and 45 asb across their peripheral islands of vision (the location of which had been determined at the previous sessions). For each patient a ZETA program was written which permitted measurement of sensitivity along an arc and meridian which passed through the patients islands of peripheral vision. Prior to the first examination, patients underwent 10 minutes adaptation to the bowl luminance. As for the other perimetric investigations, patients wore the distance refractive correction together with

the appropriate near correction, if necessary, for measurements out to an eccentricity of 30°. The head was steadied with the head clamps and chin bar of the instrument and fixation was monitored via the video monitor during the examination. Patients were advised to rest at intervals throughout the examination and were also advised if fixation was incorrect. The order of bowl luminances examined were randomized throughout the sample.

5.8.2 Results

The kinetic Goldmann isopters and the static Octopus fields were analysed as for the first sample. The results are summarized in Tables 5.4a - 5.4d and further support the original conclusion from the initial sample.

All 7 of the patients from the second sample exhibited stato - kinetic dissociation (S.K.D.) manifesting an increased sensitivity in response to kinetic compared to static stimuli under the same parametric adjustment and further support the results from the original sample. The dissociation appeared to be of greatest magnitude with stimulus size V. Three cases illustrating S.K.D. are illustrated in Plates 5.2, 5.3 and 5.4.

In 4 of the 5 cases investigated at the 3 different bowl luminances on the Dicon AP3000 autoperimeter enhanced sensitivity was demonstrated at the lower bowl luminance (Table 5.5). These differences in sensitivity, measured between the 3 bowl luminances, were of a similar magnitude to those of section 4.7 in a series of normal subjects. In the fifth patient the results were inconsistent, whereby the changes in sensitivity with different bowl luminances varied with location.

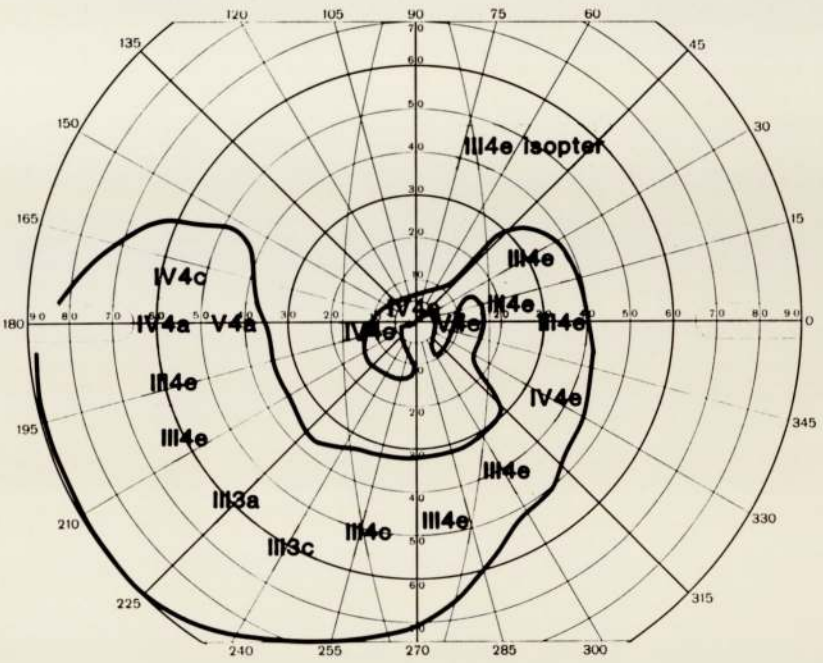
The sensitivity data, derived with Octopus Program 21 for stimulus sizes III and V, was analysed as for the first sample using the formula proposed by Gougnard (1961), to calculate the coefficient of spatial summation. Table 5.6 gives the proportion of the total stimulus locations examined, where the coefficient of spatial summation was greater than 1.

Overleaf...

Plate 5.2 A case of S.K.D. in the left eye of a 41 year old male with R.P. Top left: Octopus stimulus size III plot. Top right: Octopus stimulus size V plot. Bottom: Goldmann III_{4e} isopter and accompanying static thresholds.

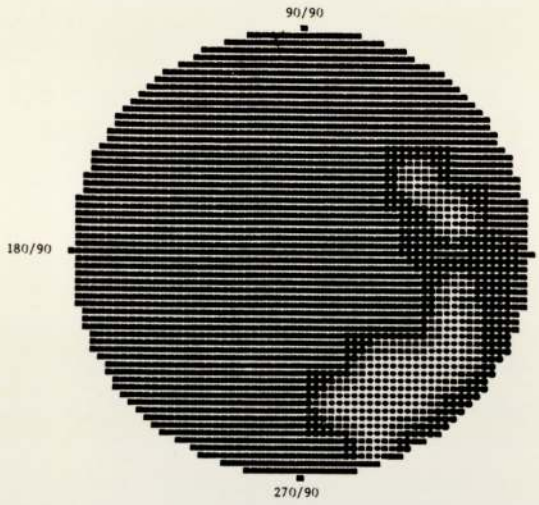
FLUCTUATIONS (R.M.S.): 4.3 DB LUM. INTERVAL: 4

FLUCTUATIONS (R.M.S.): 2.2 DB LUM. INTERVAL: 4

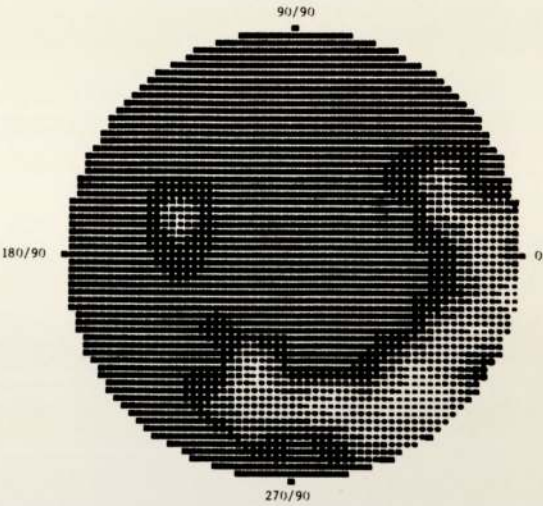


Overleaf...

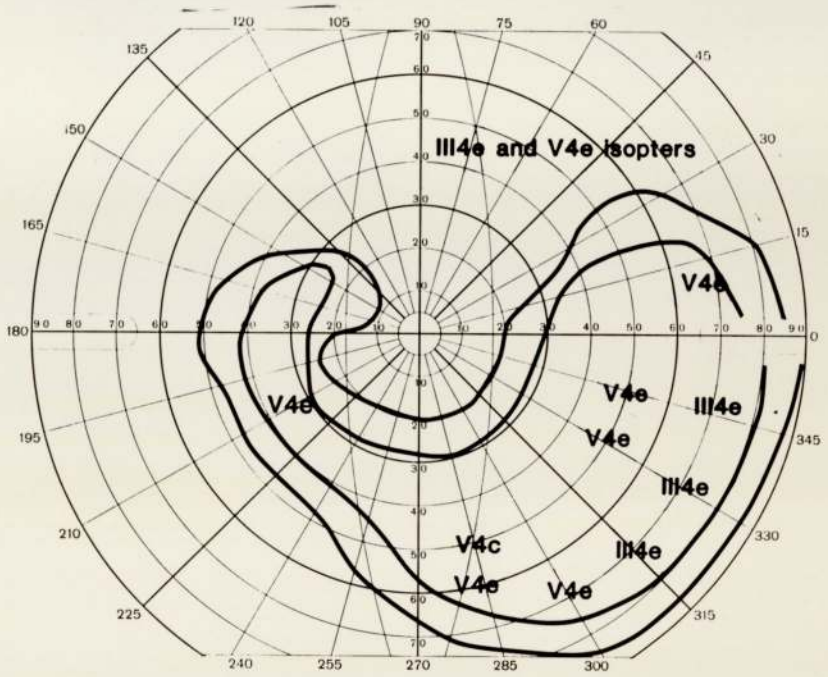
Plate 5.3 S.K.D. in the right eye of a 47 year old male with R.P. Top left: Octopus stimulus size III plot. Top right: Octopus stimulus size V plot. Bottom: Goldmann III_{4e} and V_{4e} isopters and corresponding static thresholds.



FLUCTUATIONS (R.M.S.): 0.9 DB LUM. INTERVAL: 4

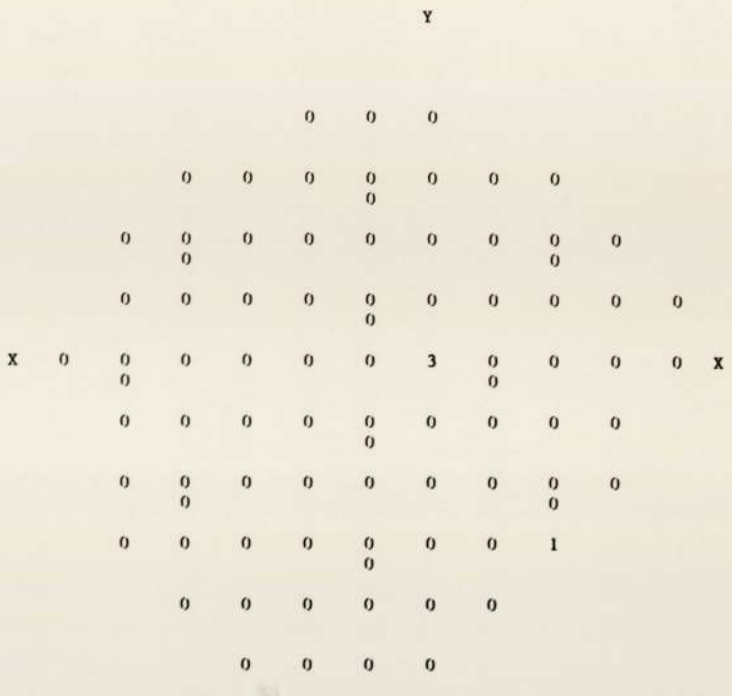


FLUCTUATIONS (R.M.S.): 2.5 DB LUM. INTERVAL: 4

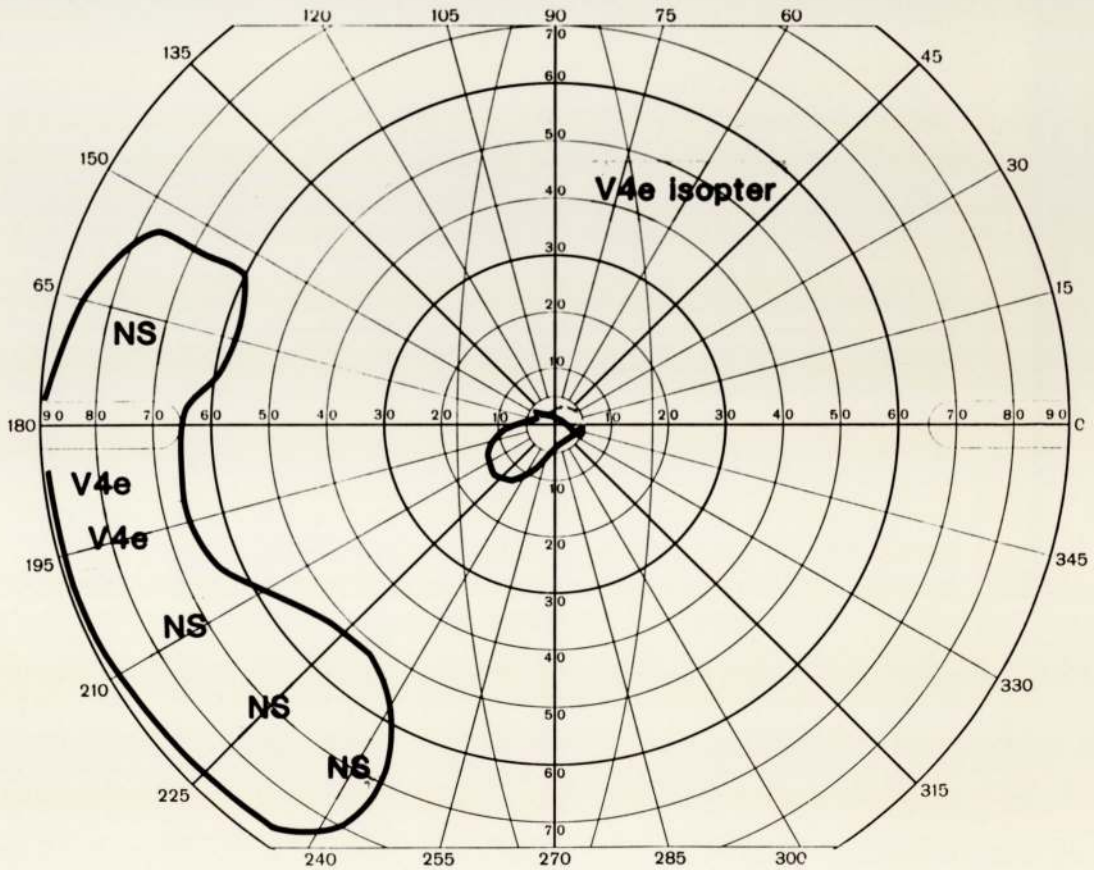


Overleaf...

Plate 5.4 S.K.D. in the left eye of a 52 year old female with R.P. Top: Octopus numeric printout of sensitivity to stimulus size V. Bottom: Goldmann V_{4e} isopter and corresponding static threshold (N.S. indicates static stimulus not seen). In this patient, Octopus stimulus size III was not visible at any eccentricity examined with Program 21.



FLUCTUATIONS (R.M.S.): 0.0 DB LUM. INTERVAL: 4



5.8.3 Discussion

The finding that R.P. patients exhibit S.K.D. has not been reported previously in the literature; the presence of S.K.D. has been demonstrated, however, in occipital lesions (Riddoch 1917), optic tract lesions (Zappia et al 1971), lesions of the optic radiations (Barbur 1979) and tumours of the anterior optic pathways (Safran and Glaser 1980). Interestingly, a minor S.K.D. has also reported in some normal subjects (McColgin 1960; Safran and Glaser 1980) where static thresholds were slightly higher than kinetic thresholds peripherally, but lower centrally (Fankhauser and Schmidt 1960). Greve (1973) attributed this physiological S.K.D. to the phenomenon of successive lateral spatial summation and demonstrated that it accounted for a difference of 0.2 log units for the Goldmann size I at a speed of $1° s^{-1}$. The differences reported here are greater than those of Greve (1973) although the stimulus sizes used are larger. In this context, the findings described in Table 5.2 for the first sample, namely the apparent discrepancy between the sensitivity recorded with stimuli of 100 ms and of 500 ms duration are in accord with the findings of S.K.D., whereby a stationary stimulus (infinitely long presentation time) yields less sensitivity than a moving one (infinitely short presentation time. The two sets of findings suggest that the kinetic nature of the stimulus is more effective in detecting small degrees of residual field in R.P. than changes in either stimulus intensity or bowl luminance.

It is possible that the S.K.D. may be related to the existence of separate channels for sustained and transient responses. These channels have been suggested on the basis both of electrophysiological studies (Enroth - Cugell and Robson 1966) and psychophysical studies (Kulikowski and Tolhurst 1973). The pattern channels are most sensitive to high spatial frequencies and are analogous to X cells, whilst the movement channels are very sensitive to low spatial frequencies and are analogous to Y cells (Tolhurst 1973; Kulikowski and Tolhurst 1973). The receptive fields of the X cells have small centres and sharp sensitivity gradients; anatomically their correlate cells have medium somas and narrow dendritic fields. Conversely, transient Y cells have large centres, sloping sensitivity gradients and their anatomical correlate cells have large somas and wide dendritic fields (Ikeda and Wright 1972; Cleland and Levick 1974). It can be speculated that in the late stages, the disease

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Octopus III)				
	I+ More	I Similar	I- Less	II Different field loss	III Normal
OCTOPUS V	_	1	6	_	_
GOLDMANN III_{4e}	_	4	3	_	_
GOLDMANN V_{4e}	_	_	7	_	_

Table 5.4a The degree of compatibility between the reference field of the Octopus stimulus size III and the comparison field of the Octopus stimulus size V and the Goldmann stimulus sizes III_{4e} and V_{4e}.

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Octopus V)				
	I+ More	I Similar	I- Less	II Different field loss	III Normal
OCTOPUS III	6	1	_	_	_
GOLDMANN III_{4e}	3	3	1	_	_
GOLDMANN V_{4e}	1	1	5	_	_

Table 5.4b The degree of compatibility between the reference field of the Octopus stimulus size V and the comparison field of the Octopus stimulus size III and the Goldmann stimulus sizes III_{4e} and V_{4e}.

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Goldmann III_{4e})				
	I+ More	I Similar	I- Less	II Different field loss	III Normal
OCTOPUS III	3	4	–	–	–
OCTOPUS V	1	3	3	–	–
GOLDMANN V_{4e}	–	–	7	–	–

Table 5.4c The degree of compatibility between the reference field of the Goldmann stimulus size III_{4e} and the comparison fields of the Octopus stimulus sizes III and V the Goldmann stimulus size V_{4e}.

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Goldmann V_{4e})				
	I+ More	I Similar	I- Less	II Different field loss	III Normal
OCTOPUS III	7	–	–	–	–
OCTOPUS V	5	1	1	–	–
GOLDMANN III_{4e}	7	–	–	–	–

Table 5.4d The degree of compatibility between the reference field of the Goldmann stimulus size V_{4e} and the comparison fields of the Octopus stimulus sizes III and V the Goldmann stimulus size III_{4e}.

	Mean perimetric sensitivity (dB)		
	10 asb	31.5 asb	45 asb
Subjects			
D.W.	6.63	4.07	3.4
C.H.	8.42	10.14	7.57
G.J.	5.32	4.21	4.89
M.P.	9.04	5.54	3.86
A.W.	6.76	4.23	3.23

Table 5.5 Mean perimetric sensitivity for 5 R.P. patients over their islands of vision at 3 adaptation levels measured with the Dicon AP3000 autoperimeter.

Subjects	Number of stimulus locations having a value of k>1 as a fraction of the total number of stimulus locations where an assessment of k was possible.
M.P.	9/15
C.H.	35/76
D.B.	8/30
A.W.	15/36
D.G.	2/21
D.W.	10/27
G.J.	14/40

Table 5.6 The number of stimulus locations where the coefficient of spatial summation derived from the equation of Gougnard (1961) was recorded as a fraction of the total number of stimulus locations where an assessment of k was possible, for 7 R.P. patients recorded with the Octopus 201 automated perimeter.

process in R.P. either affects the channels subserving sustained vision (X channels) to a greater extent than the transient channels (Y channels) or alternatively that the Y ganglion cells with their wider dendritic fields may be more resistant to damage than the X ganglion cells. The distinction between X and Y cells made on the basis of sustained and transient responses is not, however, felt to be completely satisfactory (Lennie 1980), and there is overlap in the temporal characteristics between the 2 groups (de Monasterio 1978).

The finding that perimetric sensitivity is higher at the lower adaptation levels for 4 of the 5 subjects with R.P. appeared to follow the normal laws of perimetry.

The finding that a large percentage of the coefficients of spatial summation were greater than 1 in the 7 R.P. patients of the second sample is in accord with the findings for the first sample.

It is important to note in the context of this investigation that the sensitivity values displayed by the Dicon, are not calibrated in terms of ΔL but are the absolute value of the light emitting diode (LED) stimuli and thus the validity of Weber's law cannot be verified using this perimeter. Indeed, the use of LED stimuli without reflecting covers merely measures the sensitivity of the visual system to a light flash in a black hole with the background luminance acting as a secondary stimulus. A further restriction in the use of the Dicon custom programs is the lack of stimuli beyond 60° available in the majority of the standard test programs.

5.9 Conclusions

The results confirm the hypothesis of Flanagan et al (1984b) that the sensitivity gradient of patients with R.P. behaves atypically over the dynamic range. In the study it was demonstrated that in some R.P. patients, not only is perimetric sensitivity reduced, but the temporal and spatial processing of conventional perimetric spot stimuli is also abnormal. Four of 9 patients exhibited an enhanced sensitivity to short compared to long stimulus durations which is contrary to the behavior of normal subjects who exhibit enhanced sensitivity to longer stimulus durations by virtue of

temporal summation (within the critical period). Moreover, R.P. patients demonstrated enhanced spatial summation across the islands of residual field; the presence of fluctuations in the perimetric response, however, make quantitative analysis tenuous. Furthermore, all the patients specifically investigated exhibited stato - kinetic dissociation across the peripheral islands of residual vision, where sensitivity was enhanced when the stimulus was moved as opposed to being stationary. The sample of patients in the current study is too small, however, to draw any conclusions about the efficacy of visual fields, measured under different states of parametric adjustment, in differentiating between the various genetic groups.

6. THE INFLUENCE OF INTRAOCULAR LIGHT SCATTER ON THE PERIMETRIC PROFILE

6.1 Introduction

The assessment of the visual field function of patients with ocular media opacities is confounded by the problem of separating the perimetric attenuation which arises due to optical degradation from that which arises due to neural attenuation. The optical degradation may result from defocusing of the retinal image due to uncorrected ametropia or to light scatter which may occur as a result of disturbances at the cornea, aqueous humour, crystalline lens or vitreous humour.

6.2 Light scattering theories

An understanding of the basic mechanisms of light scattering and how they apply to ocular tissues is fundamental to the investigation of the influence of ocular media opacities on the perimetric sensitivity profile. The theories of light scattering have been extensively reviewed by Kerker (1969) and Miller and Benedek (1973).

The simplest quantitative description of the light scattering power of any medium can be described by the turbidity. Scattering of light from each particle within the turbid medium is produced because the electric field in the incident light beam exerts an oscillating force on both the nuclei and the electrons of the particle. Each particle subsequently radiates out electromagnetic fields (light) in synchrony with the exciting wave.

To determine the scattered light at any given location the radiating fields must be summed. Since each of the scattered wavelets will be at different points in their oscillation cycle, known as the phase of the wave, the size of the resultant electric field will depend upon whether the constituent waves interfere constructively or destructively with one another. The difference in phase between

waves depends upon the inter - particle separation relative to the wavelength of the incident light. If two scattering particles are separated by distances comparable with the wavelength of light, the two scattered waves may be 180° out of phase, and will cancel each other out resulting in the absence of light scatter. This is known as destructive interference (Figure 6.1a) Conversely, if two scattering particles are separated by distances which are small comparable with the wavelength of light, the phases of the two waves will be nearly the same and the scattered electric field will have an amplitude which is twice as large as the amplitude of each individual wave, resulting in maximum light scatter. This is known as constructive interference (Figure 6.1b). The intensity of the resultant light scatter is proportional to the square of the total electric field and is dependent upon the relative positions of the scattering particles. In addition, if it is assumed that the light scattering is elastic i.e., there is no shift in frequency between the incident and the scattered radiation, the intensity of the scattered light will also be proportional to the reciprocal of the wavelength raised to the fourth power and is termed Rayleigh scattering.

Within a medium which is said to have independent sources of scatter e.g., gases, the constituent molecules are distributed randomly. There is thus no correlation in the position of the scattering particles relative to one another, nor in the phase of the resultant waves. If the size of the particles is increased to the point where the particles are comparable to the wavelength of light then some light scattering may occur. In contrast, the atoms in a crystal are rigidly fixed in a geometric array (lattice). Since the wavelength of the incident light is much larger than the individual sources of scatter there will always be a pair of atoms (equal scattering sources) which scatter out of phase. Consequently, there is complete destructive interference of the scattered waves which results in an absence of scattered light.

Scattering from pure liquids is intermediate between crystals and gases. A pair of atoms (much smaller than the wavelength of light) would act as independent sources of scatter which are out of phase, this results in destructive interference. Since liquids are not orderly, however, the inter - particle distances within two pairs of atoms may not be the same, therefore the intensity of the scattered light from one pair of atoms may be different from another. Consequently, destructive

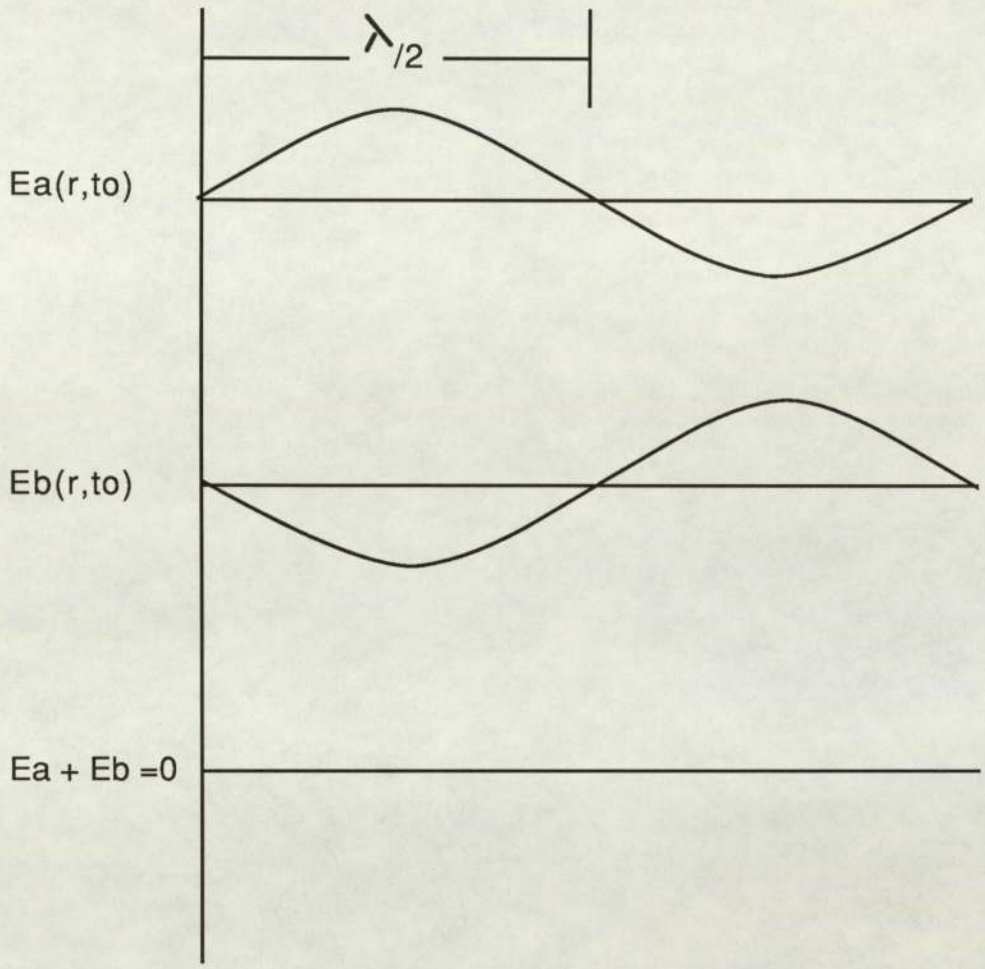


Fig. 6.1a Diagram illustrating destructive interference of two light waves (a and b), where E is the electric field, r is the radial distance and t is time. Wave a is 180° out of phase with wave b. The resultant of both waves is complete cancellation, as shown by the "flat wave" at the bottom of the diagram (after Miller and Benedek 1973).

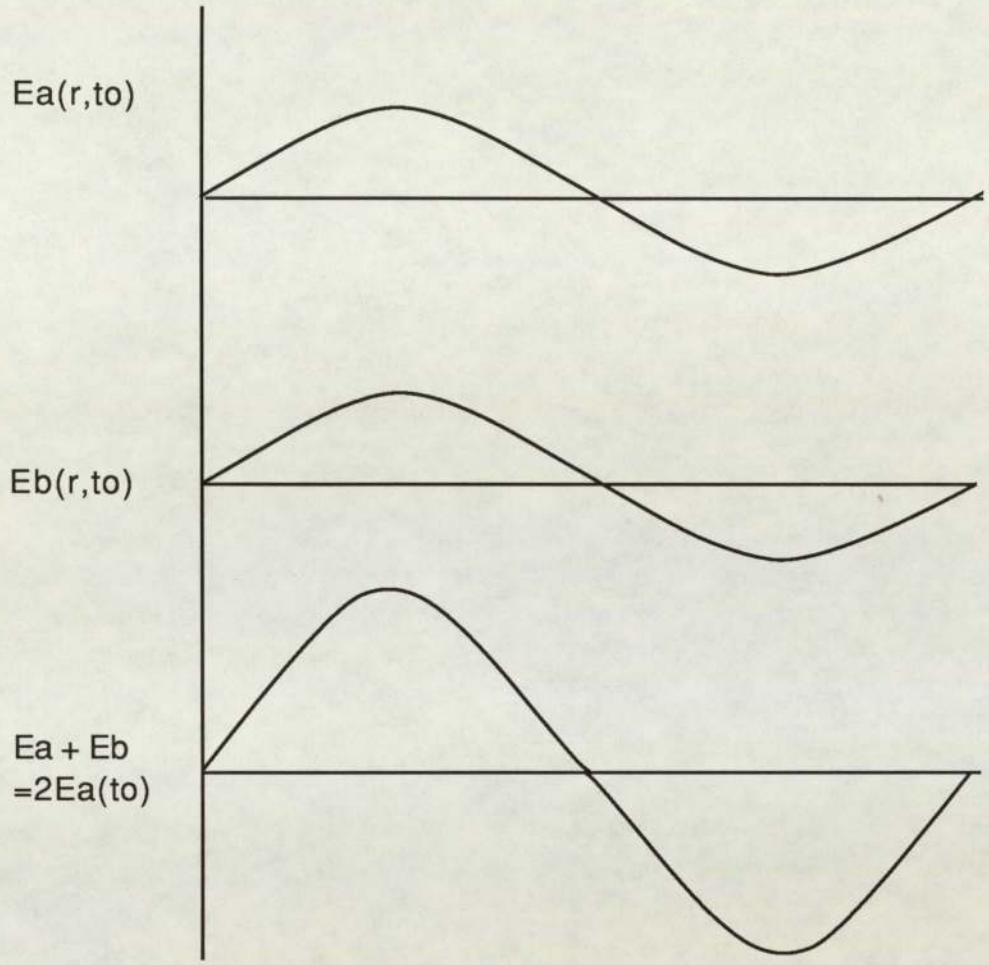


Fig. 6.1b Diagram illustrating constructive interference of two light waves (a and b), where E is the electric field, r is the radial distance and t is time. Waves a and b are in phase. The resultant wave is the summation of both waves and is twice as large in amplitude as each individually (after Miller and Benedek 1973).

interference is incomplete, and some scattering will result.

Mathematical techniques have been developed to describe particle distributions that range continuously from the perfectly random e.g., gases, to the perfectly ordered e.g., crystals. Einstein (1910) and Debye (1944) recognized that the degree of transparency or turbidity of gels or concentrated solutions depends upon fluctuations in the density of the medium. The resultant scattered light was regarded as the sum of many sinusoidal waves, each wave having a different wavelength from the other constituent waves. These theories of light scatter state that when light is scattered by a density fluctuation, only those Fourier components whose wavelengths are larger than one half of the wavelength of light contribute to scattering. Thus if a medium contains periodic fluctuations in density whose wavelength is smaller than the wavelength of light, then these will not contribute to scattering. When the size of the constituent particles becomes very large i.e., of the magnitude of the wavelength of light or greater, the scattering intensity decreases rapidly with the scattering angle and the particle - scattering becomes an oscillating function. Particles of this size in dilute solutions are treated by the Mie theory (1908).

From their treatment of the scattering of radiation by an inhomogenous material (condensed - phase models), Debye and Bueche (1949) confirmed that the intensity and angular distribution of light scattering depends upon fluctuations in refractive index (or dielectric constant) in the solid and on the sizes of the regions over which these fluctuations occur. The Debye and Bueche theory (1949) is directly applicable to gels or concentrated solutions and demonstrates that inter - particle separation as well as particle size, is important in predicting turbidity (Bettelheim and Siew 1980; 1982). An extension of the fluctuation theory is found in Stein et al (1959) for polarized light.

Transparency of the cornea is due to an imperfect lattice arrangement and is similar to that of a crystal. Indeed, perfect lattice periodicity is not required theoretically, nor is found experimentally, to maintain corneal transparency. The crystalline lens is less transparent than the cornea and has been treated as a dilute solution by Benedek (1971) in terms of light scattering properties. The scattering molecules are not in a lattice arrangement; they produce minimal scattering because there

are many particles which are smaller than the wavelength of light and there is little fluctuation in density from one region to another.

6.3 Light scattering mechanisms

6.3.1 Cornea

Light scattering theory predicts that light should traverse the cornea without appreciable scattering, by virtue of the fact that the diameter of the constituent fibrils is small compared with the wavelength of light, and their refractive index is close to that of the ground substance rendering them inefficient scatterers (Hart and Farrell 1969). The large number of fibrils compensates for their inefficiency, however, and it has been calculated that the attenuation of light by an uncorrelated distribution of the collagen fibres of the stroma would be greater than 90% (Maurice 1957). Modern theories of transparency (Maurice 1957; Hart and Farrell 1969; Feuk 1970; Cox et al 1970; Benedek 1971; Twersky 1975) have recognized that the transparency of the cornea arises from the quasi - regular, quasi - random spatial arrangement of the constituent collagen fibrils, which results in destructive interference of the light waves scattered in all directions except in the forward direction.

Feuk (1970) used the Debye - Waller theory of thermal diffuse x - ray scattering to calculate the scattering of light from an arrangement of fibres which were randomly displaced around perfect lattice positions by about one tenth of the average inter - fibre spacing. Feuk (1970) demonstrated that the theoretical magnitude of the scattering was consistent with the observed scattering from the normal stroma. This analysis does not adequately account for the effects of correlation in position of neighbouring fibres which is necessary to calculate the wavelength dependence of the scattering. Hart and Farrell (1969) alternatively computed the probability distribution for the relative positions of fibres from photographs and demonstrated that the position of collagen fibres remained correlated over two near neighbours at most. Interestingly, Twersky (1975) confirmed, by comparisons of calculated and experimentally determined values, the validity of modelling the normal cornea as a very densely packed two - dimensional gas, with the gas - particle (mechanical) radius about 60%

greater than the fibre (optical) radius.

The dependence of corneal transmission on the wavelength of the incident light was demonstrated by the short range ordering of fibrils in normal rabbit corneas and by the presence of regions void of fibrils (which were termed "lakes") in cold swollen rabbit corneas (Farrell et al 1973). These results were consistent with the electron micrograph appearance of the cornea and the theory that "lakes" are responsible for the increased light scatter in swollen corneas (Goldmann et al 1968; Benedek 1971) The results of Farrell et al (1973) were also consistent with the findings of Goldmann and Benedek (1967) who stated that light scatter theory for random arrays predicts a large degree of light scattering only if there are substantial fluctuations in the refractive index over distances of the order of the wavelength of light or greater.

McCally and Farrell (1976) demonstrated that the stromal region accounted for greater than 60% of the total light scattering over a wide range of angles (20° - 145°) and rose to greater than 75% in the backward direction. This is also in agreement with the experiments of Farrell et al (1973), although Lindstrom et al (1973) reported that the main contribution to the integrated scattered intensity from the cornea arises from regions close to the epithelium and endothelium. McCally and Farrell (1976) suggested that the differences between the two studies may, however, be accounted for by differences in experimental techniques and approximations made in the analysis.

6.3.2 Crystalline lens

It is generally accepted that increase in forward light scatter as distinct from the absorption process, produces the retinal image degradation (blur) and decreased retinal contrast (glare) of cataractous eyes (Bettelheim and Ali 1985). Indeed, Zuckerman et al (1973) demonstrated that if cataracts were merely composed of randomly distributed light absorbing, as opposed to light scattering regions, far less light would reach the retina than is the case. This view is endorsed by Philipson (1969) who reported that peaks in the visible absorption spectra of cataractous lens substances have not been found.

Increased light scattering as the physical basis for the reduction in lens transparency was first considered in detail by Trokel (1962) although the distribution and arrangement of the protein molecules within the lens cells had not been established at that time. Subsequently, Philipson (1969) demonstrated, using a quantitative microradiographic technique, that local fluctuations in the protein concentration of the lens were located at the same position as the opacities. These findings are supported by the random density and orientation theory (Stein et al 1959) which is an extension of the Debye - Bueche theory of scattering of an inhomogeneous solid (Debye and Bueche 1949). This latter theory predicts that the light scattered by the lens may be attributed to random fluctuations in the refractive index over regions which are comparable to the wavelength of the light. The validity of this theory with respect to thin sections of actual cataractous lenses has been subsequently confirmed (Bettelheim and Paunovic 1979; Siew et al 1981). Various models of light scattering in the lens were developed (Bettelheim et al 1981) from which the molecular parameters could be correlated with the measured turbidity. This facilitated the evaluation of the parameters that undergo change during cataractogenesis. Bettelheim et al (1981) predicted that three processes contribute to cataractogenesis i.e., lens turbidity: 1) a syneretic or dehydration process 2) an increase in concentration but not in size of protein aggregates 3) an association between aggregates and membrane components leading to decreased structural birefringence.

Fluctuations in refractive index or density are a consequence of a combined aggregation - syneretic process. During this process, lens protein molecules aggregate by inter - molecular cross - linking by the primary valence bonds; concurrently, the same chemical and physical forces cause intra - molecular segment - segment interactions. The net result of these interactions is a high molecular weight aggregation in a collapsed network with diminishing size (Siew et al 1981). The collapsed network and hydrated molecules exude water into the immediate environment, a process known as syneresis, which results in an increase in the refractive index difference between the aggregates and their surroundings. Indeed, the increase in scattered light from lens cytoplasm has been demonstrated to be proportional to the increase in the refractive index discrepancy (Bettelheim 1979). Furthermore, the increase in high molecular weight (H.M.W.) protein aggregates with age in bovine and human lenses is well documented (Hoenders and Van Kamp 1972; Spector and

Siegelman 1974; Jedziniak et al 1975). The insoluble protein fraction of the lens also increases with age and it is proposed that H.M.W. protein is the precursor of insoluble protein aggregates (Harding and Dilley 1976). From electron microscopy, Kramps et al (1975) demonstrated that the H.M.W. aggregates were irregular in shape and up to 500 nm in diameter. The molecular weight of H.M.W. proteins from the central lens regions, has been shown to be greater than 10^6 gm mole^{-1} up to a maximum of 3 x 10^8 gm mole^{-1} (Harding and Dilley 1976). When the size of the H.M.W. proteins within the lens becomes very large, of the order of the wavelength of light or greater, the scattering intensity increases with scattering angle and particles of this size in dilute solution may be treated by the Mie theory of scattering (Mie 1908). Indeed, quantitative mathematical analysis of lens turbidity (Miller and Benedek 1973) indicates that if protein aggregation is the correct mechanism for cataract formation, then the aggregates must have a molecular weight greater than 50 X 10^6 gm mole^{-1}, assuming that the aggregate density is approximately 20% of the lens protein mass (Benedek 1971). If these scattering centres are randomly distributed and have a different refractive index to the surrounding matrix they scatter independently of one another and severely distort incident wavelengths with the result that only low spatial frequency images are perceived.

Optical anisotropy fluctuations, in which refractive index varies with orientation, have been shown to contribute to lens turbidity (Bettelheim 1975; Bettelheim and Paunovic 1979) although they have a lesser role in light scatter production than density fluctuations alone (Siew et al 1981). Optical anisotropy arises due to the decrease in the size and therefore alignment of the optically anisotropic (birefringent) cytoskeletal bodies. The misalignment is a degradation process and decreases the intrinsic birefringence provided by the cytoskeletal bodies; optical anisotropy can be measured by birefringence (double refraction) and can be recorded by the utilization of polarization.

It was generally believed that the quantity of light scattered from the lens cytoplasm was proportional to the reciprocal of the incident wavelength raised to the fourth power, a variation of the Rayleigh scattering termed the Mie dilute solutions theory. Conversely, Hemenger (1982) using the data of previous studies (Ludvigh and McCarthy 1938; Said and Weale 1959; Zigman et al 1976) demonstrated that the light scattering in the crystalline lens was not of the Rayleigh type, but

was proportional to the reciprocal of the incident wavelength raised to the second power.

6.4 Assessment of functional integrity in the presence of media opacities

Numerous currently available techniques attempt to evaluate the functional integrity of the visual pathways in the presence of ocular media opacities.

Visual acuity assessment which measures the limit of resolution has traditionally been employed clinically, but is limited because conditions in which substantial intraocular light scattering occur cannot be modelled by defocus (Hess and Garner 1977; Hess and Woo 1978). The latter workers proposed that visual assessment of patients with cataracts should thus involve intra - resolution limit assessment by means of the contrast sensitivity function, in addition to the measurement of the limit of resolution.

Interferometric acuity assessment is a technique in which laser - generated sinusoidal gratings are projected onto the retina through a "window" in an opacity. This facilitates a direct assessment of the integrity of foveal function in the presence of media opacities since interference fringes are immune to most sources of optical blurring in the eye (Green 1970a; Green and Cohen 1971; Dressler and Rassow 1982). If the grating pattern subtends a large area and if the stimulus is very bright, visual performance in the parafoveal regions is enhanced (Enoch and Hope 1973). Consequently, relatively good readings may result even if the central fovea is non - functional. Furthermore, in cases where effective windows in the opacity do not exist, interference may be compromised to the extent where readings cannot be obtained (Williams et al 1984). It has been reported that there is a poor correlation between the visual acuity determined by interference fringes and that determined by Snellen acuity (Goldmann and Lotmar 1970) although most work conducted on cataract patients has produced good agreement between preoperatively determined laser acuity and Snellen letter acuity measured post operatively (Green 1970a; Green and Cohen 1971; Dressler and Rassow 1982).

Alternative tests of visual function which penetrate ocular opacities have similar disadvantages. Flash and flicker visual evoked potentials (V.E.P.) and electroretinogram (E.R.G.) techniques require bright stimuli in order to penetrate the opacity and to elicit a measurable response. Even a small stimulus would be scattered by the opacity and stimulate relatively large retinal areas. Under such circumstances, the peripheral retina may dominate the flicker sensitivity test and foveal function may not be discriminated from the peripheral retinal response in certain cases (Burian and Burns 1966; Fricker 1971; Spillmann and Roberge 1972).

Hyperacuity tests overcome the disadvantages of interference acuity, V.E.P. and E.R.G. and are relatively resistant to blur. An opening in the opacity is not a prerequisite for a meaningful result. Furthermore, hyperacuity falls off rapidly with retinal eccentricity, such that the fovea will produce much lower thresholds than the periphery (Westheimer 1979). An increase in intensity and contrast above a critical value therefore does not improve hyperacuity in the presence of blur.

Williams et al (1984) suggested that a vernier acuity test configuration consisting of 2 small points of light separated by a gap ranging from approximately 2' to 2° was ideal for clinical application in cases of media opacities. This test was extended to investigate regions peripheral to the foveal by the use of various fixation devices, and was termed hyperacuity perimetry (Enoch et al 1984).

6.5 Assessment of intraocular light scatter

6.5.1 Objective techniques

The degradation of the retinal image in media opacities, such as cataracts, results from an increase in forward light scattering. For the clinician using a slit - lamp alone, only the back scatter of light is available to diagnose the severity of cataract. Indeed, many investigators made the assumption that the back scatter of light by the lens provides an index of image degradation (Allen and Vos 1967; Siegelman et al 1974). It has been demonstrated, however, that there is no direct relationship between ocular scatter measured by back scatter from a slit - lamp beam (photometry) and the

deterioration in visual acuity (Allen and Vos 1967).

Slit - lamp examination by multiple adjustments of the viewing angle of the apparatus provides a three - dimensional image of the lens which is captured as a two - dimensional representation by slit - lamp photography (Brown 1969). A semi - quantitative interpretation of the turbidity in the lens is provided by scanning such photographs (Siegelman et al 1974). It is possible, however, to obtain a three - dimensional reconstruction of turbidity in the lens (with the aid of densitometry) by photography based upon the Scheimpflug principle (1906). Equipment constructed on Scheimpflug's principles has either a tilted objective, a tilted film plane, or both in combination, so that the entire plane of the slit beam and thus the optical section can be maintained in focus at the full aperture of the objective (Brown 1969; 1972). This technique has been more recently adapted to clinical requirements using the Topcon prototype of a Scheimpflug camera, fitted with a green flashing light and phototransistors to ensure reproducibility of the optical section photographs (Hockwin et al 1975; Dragomirescu et al 1978; Dragomirescu et al 1980). The technique has been shown to produce consistent results in the assessment of the cataract (Datiles et al 1987). Alternative techniques include photography in retroillumination (Hockwin et al 1975; Hendrickson et al 1977) and back - scattering testing (Ben - Sira et al 1980). The contrast (Pap/Mac) transfer ratio, which consists of the measurement of the brightness of the papilla and the macula using a photopapillometer (Hendrickson et al 1984; Robert and Hendrickson 1984) provides an evaluation of the efficiency of the ocular media. Indeed, the contrast (Pap/Mac) transfer ratio was found to be highly correlated with the visual acuity of patients with on - going cataract development (Hendrickson and Robert 1986). Recently, Weale (1986) utilized polarized light with the slit - lamp and adapted the experimental technique of Koeppe (1920) to evaluate the "real light scatter" of the human lens, and proposed that the scattering arose from specular reflections.

6.5.2 Subjective techniques

It is also recognized that patients with media disturbances, such as cataracts, suffer a greater depression of visual performance in the presence of glare light.

Since the level of disability glare is closely related to the degree of media disturbance, several workers have suggested that a glare test should be included in the preoperative evaluation of the cataract patient (Junker 1976; Cinotti 1979). The principle of this technique is the measurement of the contrast threshold, in the presence and in the absence of glare light. Miller et al (1972) introduced an instrument, known as the Miller - Nadler glare tester, in which a circular bright glare source surrounded a series of randomly orientated, constant sized, black Landolt rings. The contrast threshold was determined by varying the background luminance surrounding the Landolt ring. A simpler and less expensive device was subsequently developed by LeClaire et al (1982) which consisted of an audioviewer table - top projector with a series of slides, each of which consisted of a constant glare source and a variable - contrast central target. This method is currently utilized as a criterion for post operative success in cataracts, and has been validated in further studies (Hirsch et al 1984). Criticisms of this method include difficulty in controlling the density of the slides and the requirement for accurate positioning of the patient with respect to the screen, since misalignment of the patient's position 10 cm from the visual axis results in a 50% drop in the glare intensity (Van der Heijde et al 1985).

The assessment of Snellen visual acuity in the presence of a glare source has been advocated as a measure of light scatter by Van der Heijde et al (1985), in which the glare source consisted of a ring of 24 light emitting diodes (LEDs). Interestingly, these workers found a linear relationship between glare luminance of the target and visual acuity.

Paulsson and Sjostrand (1980) developed a system in which a quantitative measurement of the glare effect of light scattered in the ocular media was determined. These workers recognized that contrast sensitivity was a more representative description of visual ability than visual acuity measures and developed a system in which the depression in contrast sensitivity in response to the introduction of a bright light source into the field of vision was measured. A direct measure of intraocular light scattering, the light scattering factor (LSF), was calculated from these results:

$$LSF = {}^{L}/_{E}(M_2/M_1 - 1)$$

where L is the luminance of the contrast sensitivity monitor, E is the direct illumination onto the eye from the glare light source, and M_2 and M_1 are the detection contrast thresholds with and without the glare light respectively.

Subsequent studies, utilizing similar principles, employed ring glare sources and measured the LSF in a series of subjects with corneal and lenticular changes (Griffiths et al 1984; Griffiths et al 1986) with radial keratotomy (Atkin et al 1986) and with lenticular changes alone (Abrahamsson and Sjostrand 1986; Ginsburg et al 1987). Griffiths et al (1984) reported that wide angle glare sources were more appropriate for evaluating lenticular light scatter than narrow angle glare sources, since corneal epithelial haloes are not produced by the wide angle glare source. Abrahamsson and Sjostrand (1986) demonstrated that an increasing glare score is related with an increase in turbidity of the ocular media, while visual acuity had a weak correlation to the glare score. Similarly, Atkin et al (1986) noted that the glare scores obtained with their technique were not significantly correlated with a questionaire index of glare complaints or with the score obtained with the Miller - Nadler Glare Tester.

An alternative variation of these techniques was developed by Van den Berg and Speckreijse (1987) in which the glare annulus flickered instead of being constant. The flicker was compensated by adjusting a central light which flickered in counterphase with the stray light source. The luminance for minimal flicker of the central light is equal to the equivalent luminance of the scattered light, which can thus be calculated as a function of the visual angle. Van den Berg and Speckreijse (1987) validated this method on a series of patients with varying degrees and types of media disturbances.

6.6 Simulated media opacities

In any psychophysical investigations of visual processing in eyes with advanced media disturbances, the integrity of the visual system behind the opacity cannot be determined with certainty. As a consequence, a variety of media opacity simulations have been developed.

6.6.1 Corneal opacity simulation

Hess and Garner (1977) simulated corneal oedema by means of diffusing lenses (positioned close to the cornea) containing spherical particles of 19 μm diameter with an average interparticle separation distance of 30μm; this particle size was selected as it mimics the diffraction effects from an oedematous cornea (Finkelstein 1952). As a result of their investigations, which involved the measurement of visual acuity and contrast sensitivity, Hess and Garner (1977) suggested that large degrees of corneal oedema could be simulated with the diffusing lenses, however, for smaller degrees of corneal oedema, equivalent defocus was more appropriate.

6.6.2 Lenticular opacity simulation

Based upon the assumption that a cataract is an optical element containing a random distribution of scattering centres, in whom the refractive index differs from that of the surrounding matrix, Zuckerman et al (1973) simulated cataracts using a glass lens with petroleum jelly spots pressed randomly on the surface. The study evaluated the transfer function of the simulated cataract as a function of the percentage of cataract (determined by the surface area of the glass lens which was covered with petroleum jelly spots).

An alternative approach has been the utilization of diffusing lenses to simulate cataracts. Hess and Woo (1978) compared the imaging of a complex visual scene, which had been optically filtered by a diffuser (comprising 5 μm diameter spherical particles suspended in liquid media), to that of a defocus lens. The diffuser, unlike the defocusing lens, produced low frequency as well as high frequency degradation, similar to that exhibited by the cataract patients examined. Similarly, Williams et al (1984) in their work with hyperacuity tests, demonstrated that a diffusing lens more nearly simulated the optical degradation which occurred in cataract subjects than a defocus lens. Interestingly, LeClaire et al (1982) utilized varying concentrations of 10 μm diameter latex spheres in distilled water, suspended in 12 mm thick bottles, in order to simulate light scatter for the purpose of calibrating a glare tester for use on cataractous and aphakic patients. More recently, a

series of diffusing lenses, defined by their log relative transmittance, were utilized to determine the influence of opacities on the visual fields assessed with the Humphrey Field Analyser and the Octopus automated perimeters (Heuer et al In press).

Niesel et al (1978) and Niesel and Wiher (1982) suggested that both selective occluders and diascleral illumination produce stray light comparable to that resulting from lens opacities and used these techniques to model cataracts in their visual field studies. Alternative media opacity simulations have been advocated which include orthoptic occluders (Urner - Bloch In press) and neutral density filters (Klewin and Radius 1986; Eichenberger et al In press; Heuer et al In press)

6.7 Influence of media opacities on perimetric thresholds

Numerous studies have qualitatively evaluated the effect of media opacities, in particular cataract, on the visual field profile for manual perimetry. Utilizing kinetic techniques, it was demonstrated that cataract produces a general depression of the visual field and exaggerates existing scotomas (Drance 1975; Kolker and Hetherington 1976; Niesel et al 1976; Greve 1979; Harrington 1981) and produces a depression of the superior visual field (Gayer Morgan 1958). Interestingly, Lyne and Philips (1969) found that opacities situated in the cornea result in asymmetrical visual field defects which lie on the same side as the opacity, whereas the reverse is true for opacities in the posterior lens. It was suggested that visual field defects in eyes with axial lens opacities and with a miotic pupil may occur as a result of the ensuing decrease in retinal illumination (Forbes 1966; Harrington 1981). These findings were subsequently confirmed in a series of patients whose apparent glaucomatous visual field defects disappeared following cataract extraction (Bigger and Becker 1971); although the possibility that a reduction in intraocular pressure following the extraction may have resulted in a reversal of the glaucomatous defects could not be discounted.

Radius (1978) correlated the depression of kinetic threshold sensitivity arising from cataracts with the level of Snellen visual acuity in order to quantify the extent of isopter depression for the six Goldmann stimuli. Sensitivity measured with the smallest stimuli (I_{2e}) was depressed to a greater

extent than with the other stimulus sizes, which is in agreement with that of Kolker and Hetherington (1976). Problems incurred in making a quantitative analysis of the data of Radius (1978) are the use of visual acuity, which is a poor correlate of visual function in cataracts (Miller et al 1972) and the inaccuracies and inconsistencies inherent in kinetic perimetry (Berry et al 1966; Ross et al 1984).

In static manual perimetry, cataract has been shown to produce a general reduction in sensitivity, with the central field being affected more than the periphery. This results in an effective flattening of the sensitivity profile (Greve 1973; Niesel et al 1976; Greve 1979). Large stimuli have been advocated if the cataract reduced the central sensitivity by more than 1.5 log units in the centre and by more than 1.0 log unit in the periphery (Greve 1979). In this way, Greve (1979) proposed that visual field examination is possible even when the optic disc can not be visualized by ophthalmoscopy. More recently, it has been demonstrated using the Goldmann perimeter that media opacities (simulated by orthoptic occluders) affect the detection of glaucomatous defects to a greater or lesser extent dependent on their location (Niesel and Wiher 1982). These workers found that pericentral relative field defects smaller than 4° - 6° in diameter were obscured by media opacities, whereas the detection of absolute pericentral scotomas remained intact until the media opacity was far advanced. In contrast, apparent peripheral field constriction was overcome for by increasing the luminance of the stimulus by approximately 3 dB (Niesel and Wiher 1982).

The effect of media opacities on the differential light sensitivity as measured by automated perimetry has been investigated in only a few studies. Guthauser et al (1986) and Guthauser and Flammer (In press) quantified cataracts by densitometry using the Scheimpflug slit - lamp measuring system and found a high correlation with the density of the cataract and the visual field changes assessed with program G1 of the Octopus. Hendrickson et al (In press) demonstrated that the visual fields assessed with program G1 of the Octopus improved following cataract surgery and subsequent intraocular lens implantation. The workers employed the (Pap/Mac) ratio (described in section 6.5.1) to determine the imaging quality of the ocular media and to discriminate between the reduction in light sensitivity caused by media opacities and that caused by disease of the retina and

the optic nerve. Interestingly, Faschinger (In press) demonstrated, in a study of six eyes, that visual fields measured with the Octopus automated perimeter were only slightly depressed in the presence of corneal dystrophies.

6.8 Aim of the investigation

The purpose of the investigation was to quantify the attenuation in perimetric sensitivity arising from media opacities. Such a system would facilitate assessment of the integrity of the receptor and post - receptor system of those patients with media opacities.

The investigation involved the development of a means whereby the degree of intraocular light scatter could be related to the level of perimetric sensitivity. Clearly, there is no definitive method of achieving this objective. One possibility is to induce intraocular light scatter in the normal eye. In this instance the integrity of the visual system is known; however, the success of this method is dependent upon the simulation accurately reflecting the scattering effects of media opacities. A second possibility is the use of patients with unilateral media opacities, in which the clearer eye is used as the control. The absence of concomitant retinal or neural disease in the eye with the opacity cannot, however, be necessarily ascertained with certainty. Furthermore, the use of the clearer eye as the control for the perimetric assessment assumes that the right and left eyes are similar. This assumption would appear to be valid, however, since it has been reported with the Humphrey Field Analyser that the visual fields of the two eyes are symmetrical (within 6 dB) at 99 % of test locations (Brenton et al 1986).

It was therefore decided to develop a model which described the influence of intraocular light scatter on the perimetric profile in the normal eye, and then to evaluate how the characteristics of this model related to the effects of light scatter in clinical material.

It was accepted that the simulation would not consider the blurring and absorption characteristics of media opacities. Furthermore, the plane of the simulation for practical reasons, had to be situated

anterior to the corneal plane, and as such affected the degree of retinal image degradation produced, since the latter depends upon the position of the opacity (Baraldi et al In press). Indeed, it was proposed that the qualitative aspects of the relationship between light scatter and perimetric attenuation established for the simulation would be valid for any given media opacity, however, the quantitative aspects of the relationship would be expected to differ.

The intraocular light scatter of the simulation and the media opacities were quantified using the experimental set - up of Griffiths et al (1984). This method was selected as it provides an assessment of the forward light scattering characteristics of the eye. The equipment was modified by inserting a 1.0 log unit neutral density filter before the wide angle glare source in order to reduce the illumination. This allowed the assessment of the light scattering factor of patients with greater degrees of intraocular light scatter than the original technique had permitted.

The effect of the simulation and of the media opacities on perimetric sensitivity was quantified using the Octopus 201 and Dicon AP3000 automated perimeters. These perimeters were selected in order to provide two different types of stimulus configuration, namely, projection and LED stimuli and to offer the facility to vary background luminance.

6.9 Experimental work

6.9.1 Simulation

In the preliminary stages of the investigation several transparent solutions containing suspensions of different sized particles were considered as sources of light scatter. Various concentrations of methyl cellulose were employed, in which the mycels in the solution produced the light scatter. These solutions were found to be unsuitable, however, as the viscosity of the methyl cellulose prevented smooth injection of the solution into the cells by a hypodermic syringe and resulted in the production of bubbles. In addition, the concentrations of methyl cellulose available did not produce sufficient ranges of intraocular light scatter for the purpose of the experiment. A second

solution was considered as an alternative and consisted of sephadex beads of 50μ-150 μ (normally employed for gel filtration techniques) suspended in K - Y jelly. Sedimentation of the particles after approximately four hours of preparation and the unpredictable swelling of the particles in the solution, however, prevented this being a viable and reproducible technique.

Latex beads suspended in distilled water were found to be the most appropriate means of producing intraocular light scatter. Concentrations of 0.01%, 0.02% and 0.025% were selected to provide a wide range of light scatter, with minimum image degradation, compatible with visualization of the contrast sensitivity monitor and the fixation targets of the perimeters involved. A bead diameter of 500 nm was selected since it did not sediment but remained suspended in solution, permitting standardization of the light scatter produced. Furthermore, it has been demonstrated that the diameter of the protein aggregates in human (Bettelheim and Siew 1982) and calf (Delaye et al 1982) cataractous lenses is between 300 nm and 500 nm. Different concentrations of beads were utilized since it has also been demonstrated (Bettelheim and Siew 1982) that inter - particle separation is another important parameter in intraocular light scatter.

The latex bead solutions were suspended in cells which were constructed with the front and back surfaces consisting of plano powered CR39 optical lenses in order to minimize the contribution of optical distortion to the scatter. The cells were suspended as close as possible to the subject's eye. It was thought possible that the empty CR39 cells might themselves attenuate the visual function of the observers. The contrast sensitivity of one subject without glare light, was therefore measured under the same experimental conditions as in the investigation, for three conditions: without a cell, with an empty cell and with a cell containing a solution used to produce intraocular light scatter. The results are illustrated in Figure 6.2. Contrast sensitivity peaks at a spatial frequency of 4 cycles deg^{-1} for the cell - free condition. The empty cell has little effect on the contrast sensitivity function, whereas the cell containing a scattering solution depresses the function, particularly for spatial frequencies greater than 2 cycles deg^{-1}.

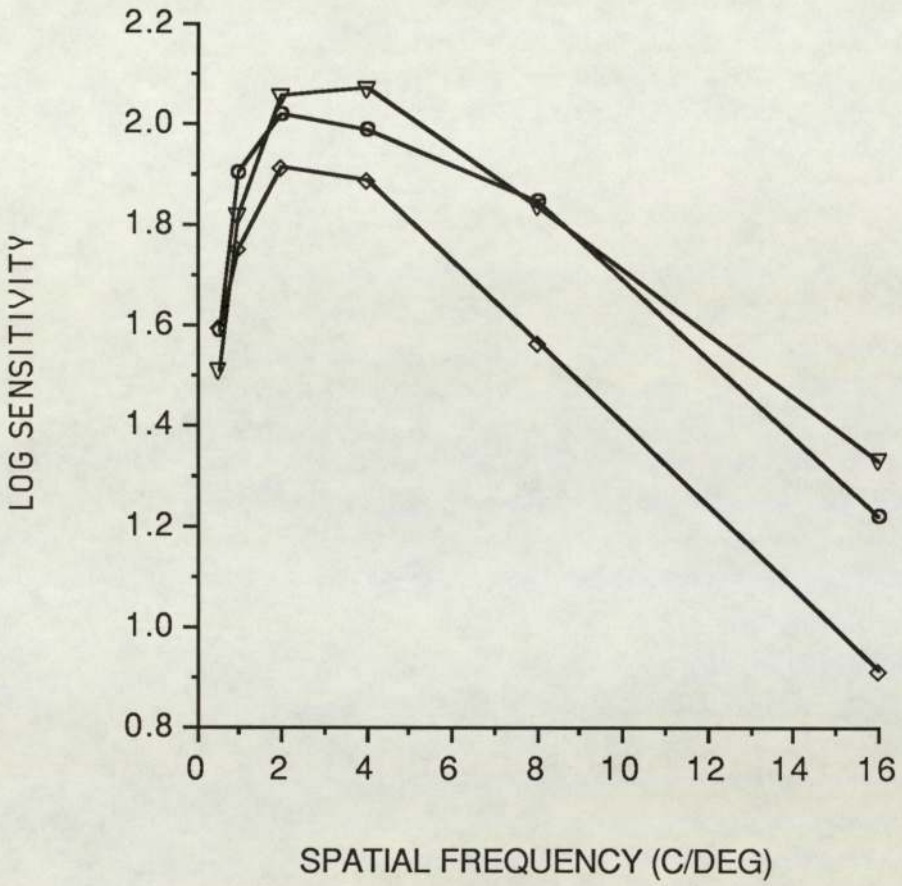


Fig. 6.2. The contrast sensitivity function of the right eye of a normal observer (open inverted triangles) compared with that of the same observer with an empty CR39 cell (open circles) and with a simulating cell (open diamonds) before the eye.

6.9.2 Materials and methods

The sample comprised 12 clinically normal age - matched subjects (mean age 24.1 years, S.D. 2.9 years; 2 females, 10 males) who were experienced observers in automated perimetry and in psychophysical techniques in general. Visual acuity was 6/5 or better in each eye. Two of the subjects were ametropes with a refractive error within 5.00 D sphere and 2.00 D cylinder. Subjects taking ocular or systemic medication were excluded from the study

Intraocular light scatter was assessed using the Nicolet CS2000, an automated contrast sensitivity apparatus. Vertical sine wave gratings were presented on a monitor 3 m from the subject. A spatial frequency of 1 cycle deg^{-1} was selected in order to avoid optical attenuation arising due to blur (Campbell and Green 1965) and the gratings were counterphased at 2 cycles deg^{-1}. The screen luminance was 94.4 cd m^{-2} and was calibrated at the beginning of each session. A circular rear illuminated diffusing screen provided a surround of the same mean luminance as the gratings.

Wide and narrow angle glare light was generated by two circular fluorescent rings concentric with, and suspended between, the screen and the subject and which subtended 30° and 3.5° at the eye respectively (Figure 6.3). The illuminance of the wide angle glare source at the eye was 4241.15 lux and that of the narrow angle glare source was 63.62 lux. Contrast sensitivity was measured, using the method of increasing contrast, in normal and under both glare conditions.

For the Octopus perimeter, a stimulus diameter of 0.431° (Goldmann size III) was presented out to an eccentricity of 30° using a square stimulus grid of 6° inter - stimulus separation (Octopus Program 31). The standard stimulus parameters, namely 4 asb bowl luminance and 100 ms stimulus duration, as described in section 3.6 were employed. For the Dicon perimeter, differential light sensitivity was measured at two bowl luminances of 10 asb and 45 asb, for eccentricities of 7.5°, 20°, 27.5° along the 85° meridian of the superior field and the 265° meridian of the inferior field using the Meridional Threshold Profile Program and for 0°, 1°, 3°, 5°, eccentricities along the vertical meridian using the Macular Threshold Program. The stimulus presentation time was the

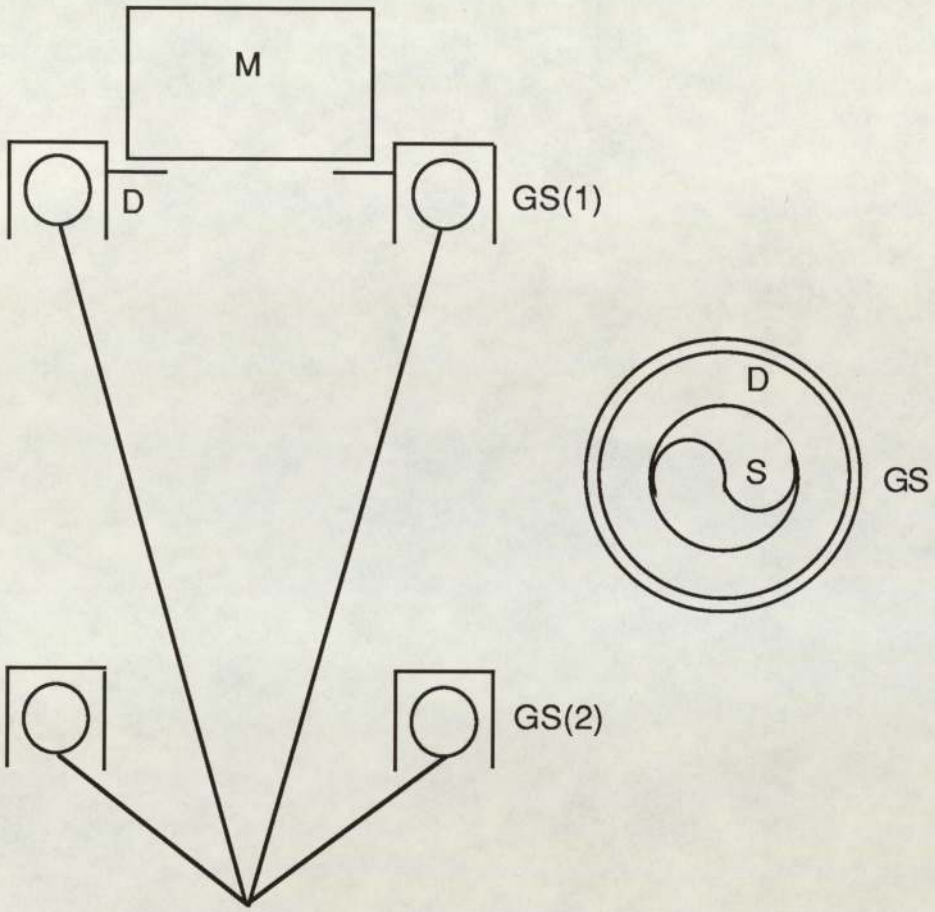


Fig. 6.3 Diagrammatic representation of the apparatus employed to derive the light scattering factor in the two experimental samples. GS(1) and GS(2) are the narrow and wide angle glare sources respectively, M is the monitor, D is the diffusing screen and S is the sine wave grating.

default value of 400 ms and the inter - stimulus duration 1 s .

Optimum distance correction was used where necessary. Natural pupils were used throughout since the procedure was intended for clinical application. Abrahamsson and Sjostrand (1986) applied a correction factor of 1.4 for a pupil variation of 3 - 4 mm during their intraocular light scatter measurements. Vos (1983), however, demonstrated that pupil size did not significantly influence his glare results. At the time of the study it was thought that pupil size had an insignificant effect on the perimetric sensitivity profile as Bedwell and Davies (1977) and Fankhauser (1979) had reported that a decrease in pupil size from 9.0 mm to 3.5 mm induced a decrease in perimetric sensitivity of the order of 0.14 - 0.20 log units. It was subsequently shown, with the Dicon, that an increase in pupil size produced a concomitant increase in perimetric sensitivity at peripheral angles greater than 10°, but that the effects (section 9.5) are unlikely to influence the results recorded here.

Using these procedures, contrast sensitivity and visual fields were measured for the right eye of the subjects both with and without the various simulating cells. The contrast sensitivity and the Dicon examinations were conducted at one session and the Octopus examination on a subsequent occasion. The order of the examinations in the first session and between the two sessions were randomized.

The intraocular light scatter factor, with and without the various simulating cells, was calculated for each subject for both wide and narrow angle glare light using the equation of Paulsson and Sjostrand (1980). The difference between the scattering factor in the presence and absence of a given simulating cell was plotted for each subject against the corresponding difference in perimetric sensitivity at a given eccentricity. In the case of the Octopus, the difference in perimetric sensitivity was expressed as a mean of the results from the 4 stimulus locations at a given eccentricity along the 4 principal meridians; for the Dicon the difference was expressed as the mean of the 2 stimulus locations at a given eccentricity along the superior and inferior meridians.

6.9.3 Results

The attenuation of perimetric sensitivity for the projected stimuli of the Octopus with variation in intraocular light scatter at fixation and at 30° eccentricity is shown in Figure 6.4 for narrow and wide angle glare light. At fixation, attenuation of sensitivity increases approximately linearly with increase in both wide and narrow angle intraocular light scatter. For eccentricities greater than 0°, attenuation increases monotonically but with a decreasing gradient for both the glare sources. For clarity, the results are illustrated for fixation and for 30° eccentricity only. The intraocular light scatter arising from the wide angle glare source is less than that for narrow angle glare light. The perimetric attenuation is lower centrally and of greater magnitude at the more eccentric location.

Perimetric attenuation for the Dicon at fixation and at 27.5° eccentricity also demonstrates a good relationship with increasing narrow and increasing wide angle intraocular light scatter which was non - linear at the 10 asb (Figure 6.5) and 45 asb (Figure 6.6) background luminances. The attenuation is greatest at the lower bowl luminance, particularly at fixation, for both narrow and wide angle glare sources.

Attenuation is greater for the Dicon (10 asb bowl luminance) at fixation than for the Octopus with increase in both narrow and wide angle intraocular light scatter (Figure 6.7) whereas at more peripheral locations the Octopus produces a greater loss of sensitivity than the Dicon (Figure 6.8).

6.9.4 Discussion

Perimetric attenuation measured with the conventional projected Goldmann III stimulus (projected diameter 0.431°) and with the LED stimulus (projected diameter 0.28°) increases with increase in intraocular light scatter. This finding is in general agreement with the results of Guthauser and Flammer (In press) who reported that there is a high correlation between visual field changes and the degree of media opacity quantified using the Scheimpflug principle. The intraocular scattering factors derived in the presence of wide angle glare light are consistently smaller than those from

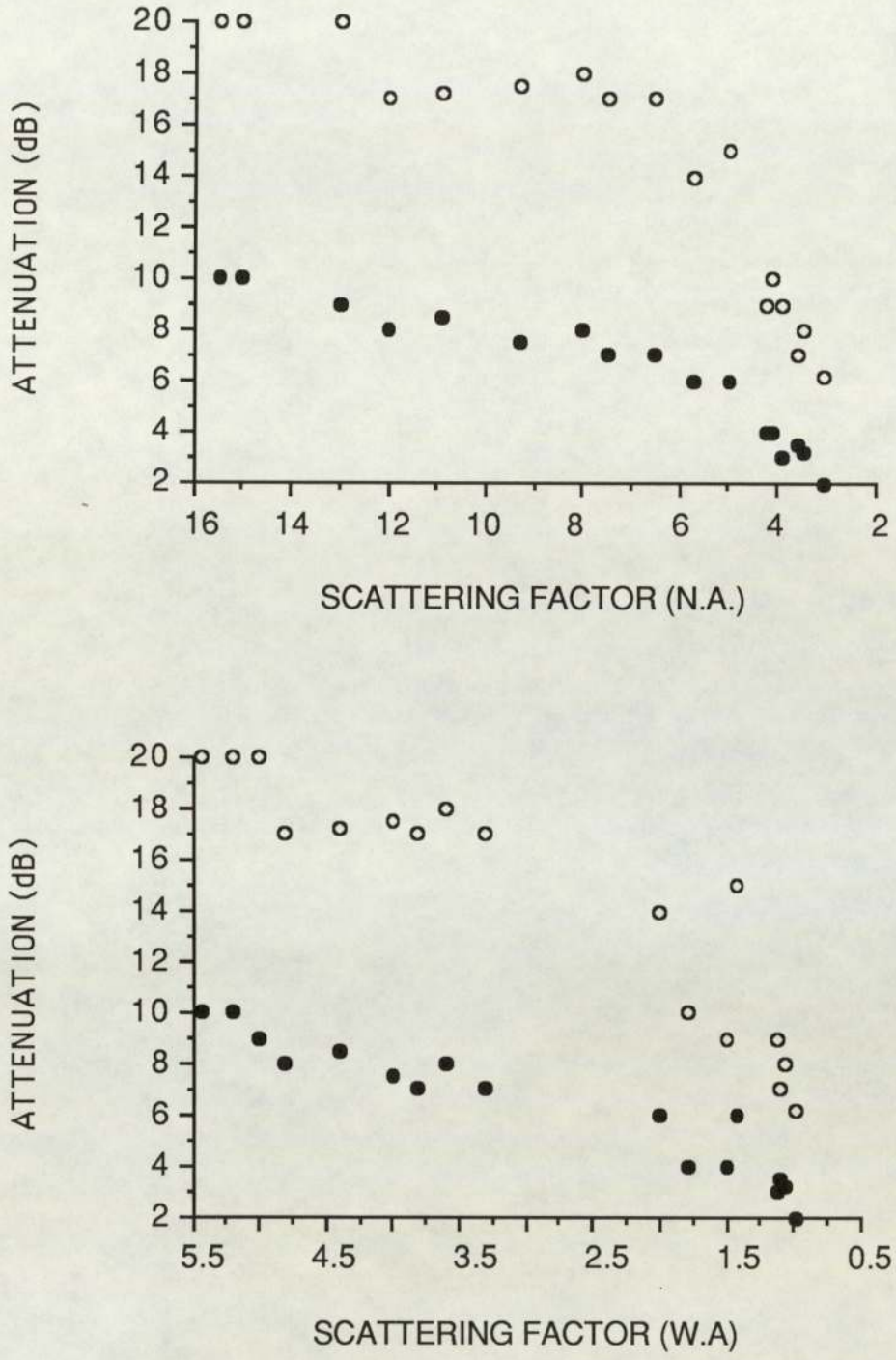


Fig. 6.4. Attenuation in perimetric sensitivity (dB) for the projected size III stimulus of the Octopus 201 automated perimeter against intraocular light scatter measured for narrow angle (top) and wide angle (bottom) glare light as a function of eccentricity (°) (closed circles 0°; open circles 30°).

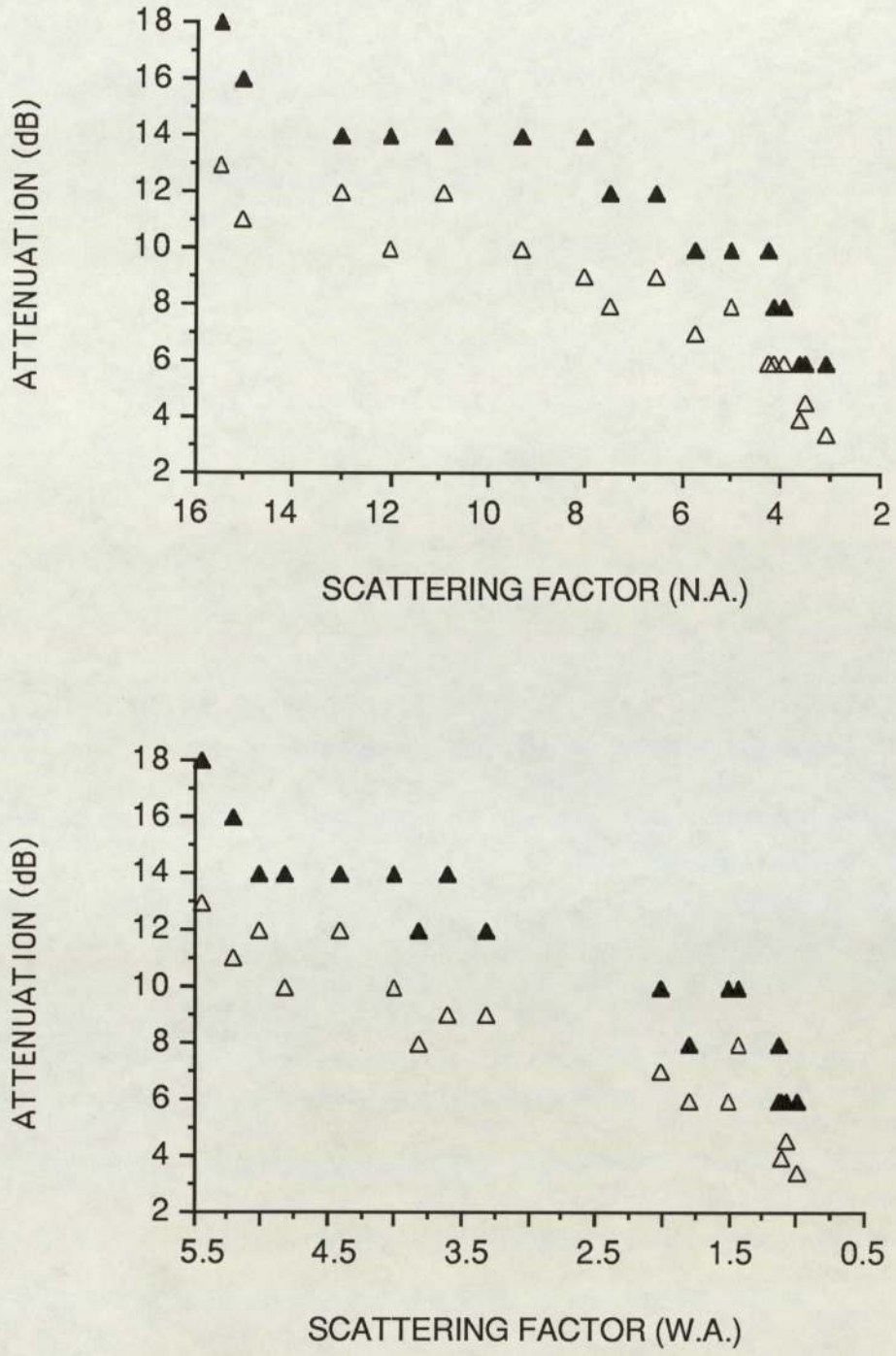
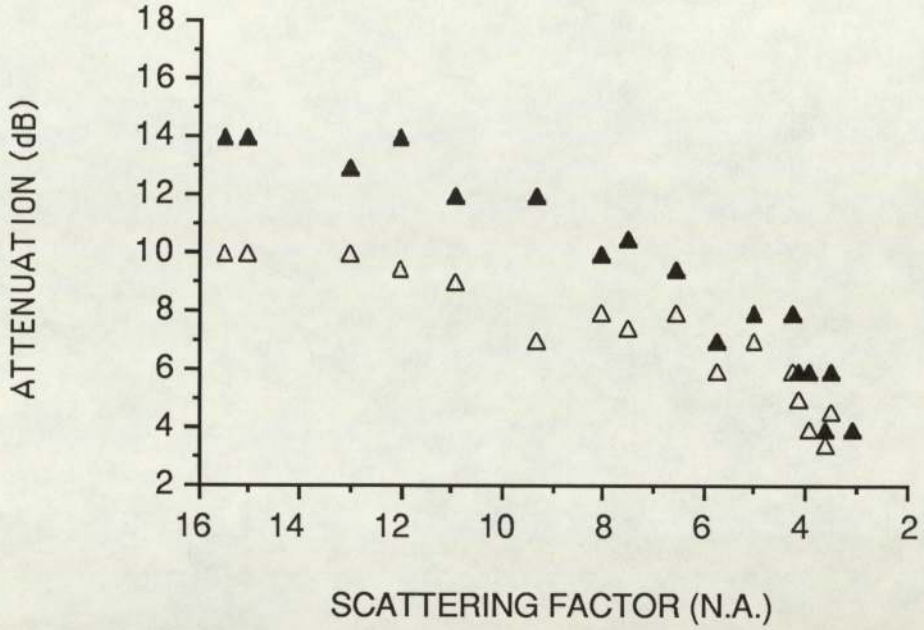


Fig. 6.5. Attenuation in perimetric sensitivity (dB) for the 1.613 mm diameter LED stimulus of the Dicon AP3000 autoperimeter against intraocular light scatter measured for narrow angle (top) and wide angle (bottom) glare light at a bowl luminance of 10 asb as a function of eccentricity (°) (closed triangles 0°; open triangles 27.5°).



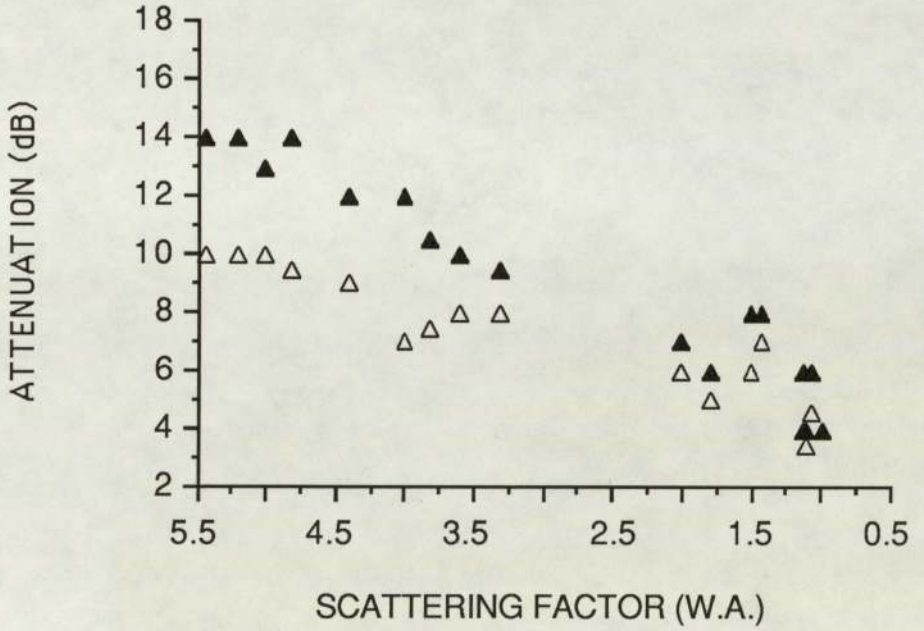


Fig. 6.6. Attenuation in perimetric sensitivity (dB) for the 1.613 mm diameter LED stimulus of the Dicon AP3000 autoperimeter against intraocular light scatter measured for narrow angle (top) and wide angle (bottom) glare light at a bowl luminance of 45 asb as a function of eccentricity (°) (closed triangles 0°; open triangles 27.5°).

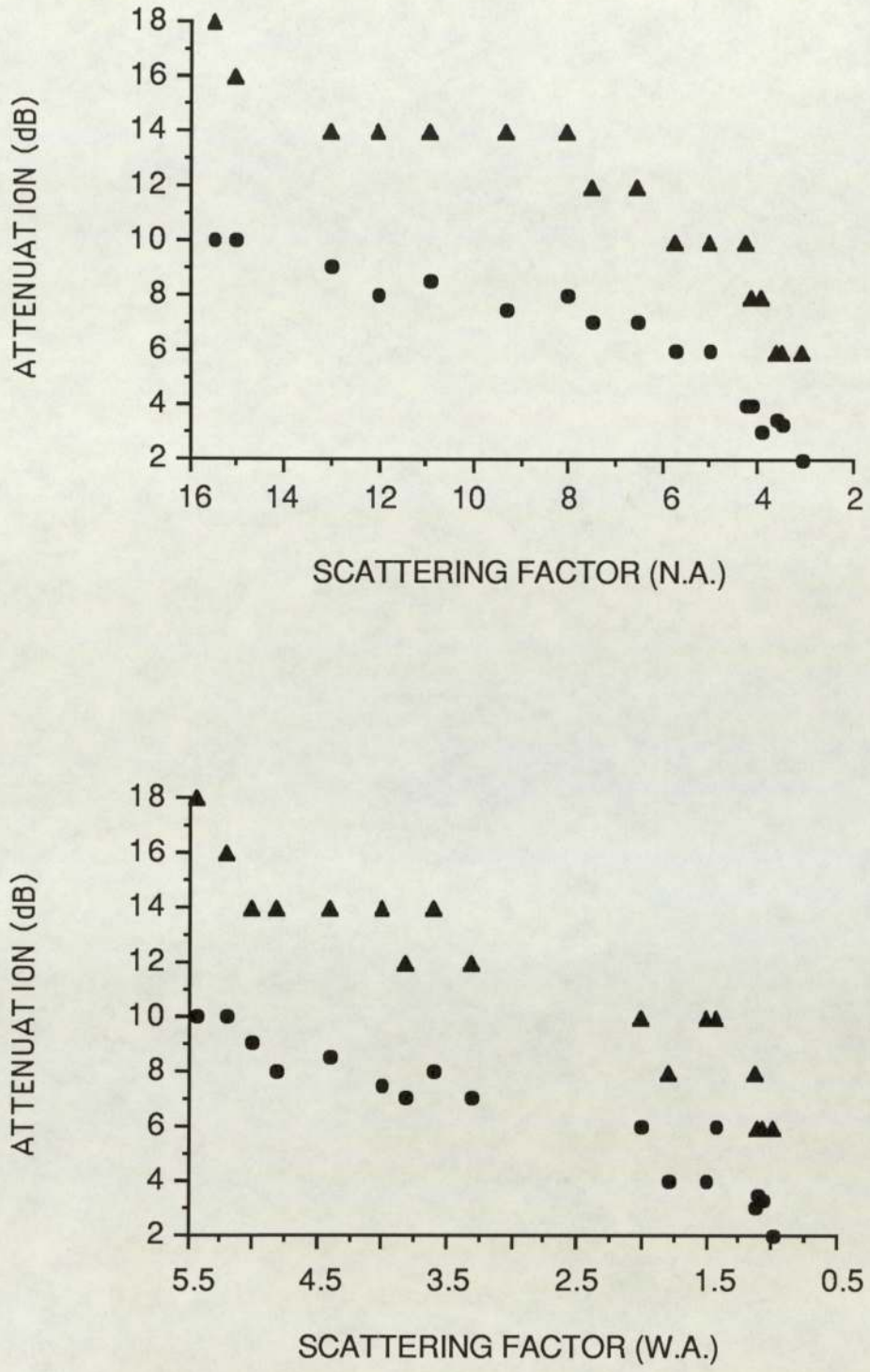


Fig. 6.7. Attenuation in perimetric sensitivity (dB) for the projected stimulus of the Octopus 201 automated perimeter (filled circles) and for the LED stimulus of the Dicon AP3000 autoperimeter (10 asb bowl luminance) (filled triangles) at fixation for narrow angle (top) and wide angle (bottom) glare light.

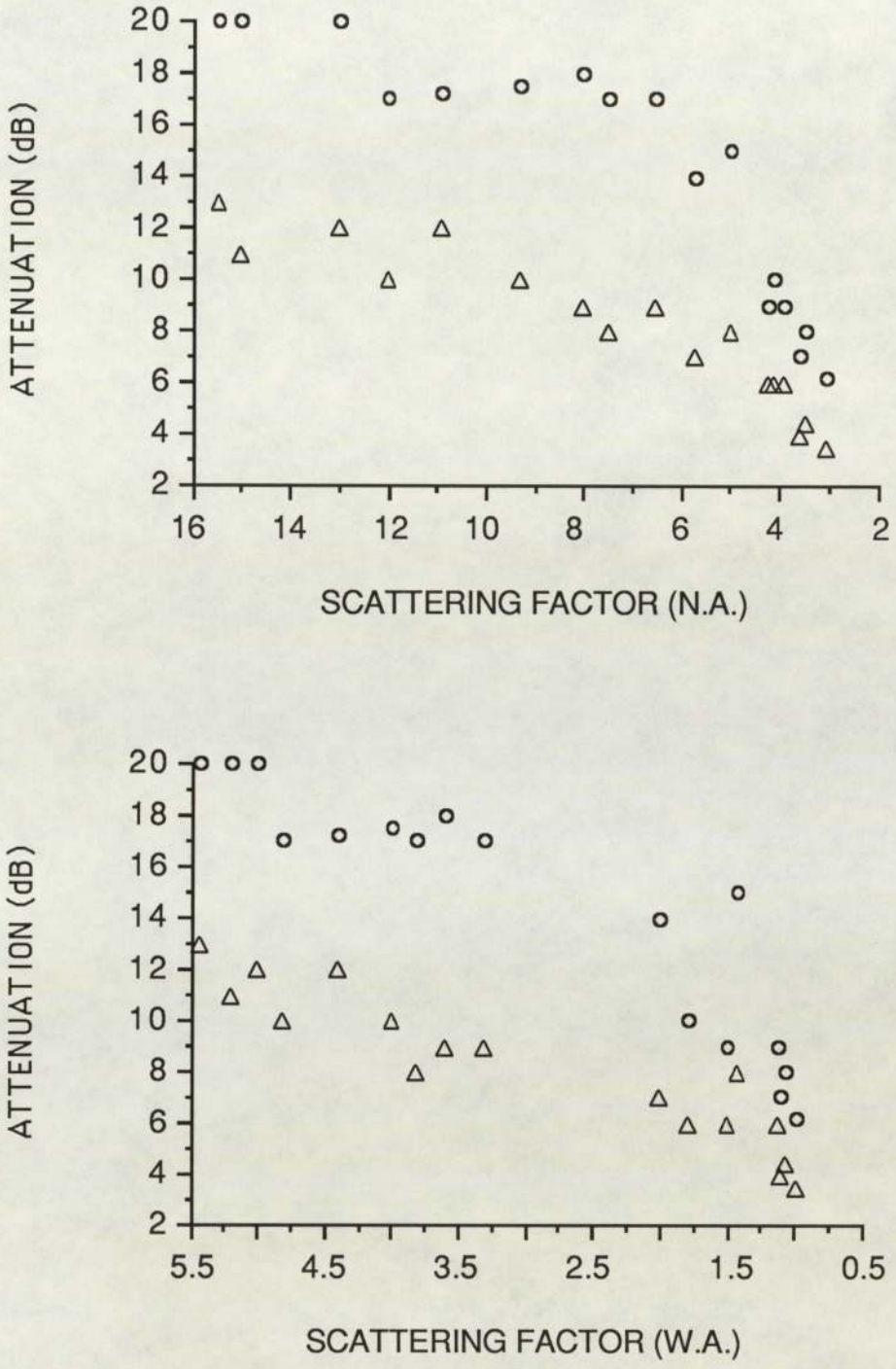


Fig. 6.8. Attenuation in perimetric sensitivity (dB) for the projected stimulus of the Octopus 201 automated perimeter (open circles) and for the LED stimulus of the Dicon AP3000 autoperimeter (10 asb bowl luminance) (open triangles) at 30° and 27.5° eccentricity respectively, for narrow angle (top) and wide angle (bottom) glare light

narrow angle glare light and arise from the form of the line spread function of the eye. The greater attenuation at the background luminance of 10 asb compared with that of 45 asb for all eccentricities is in accord with the effect on perimetric attenuation arising from neutral density filters reported in manual static perimetry (Greve 1973) and in automated static perimetry (Klewin and Radius 1986; Baldwin and Smith In press). Perimetric attenuation was of greatest magnitude at lower background luminances and was attributed to the logarithmic change in Weber's ratio at the lower photopic luminances. It should be noted, however, that pupil size was not controlled in these two studies.

The LED stimuli of the Dicon produce greater attenuation centrally than the projected stimuli of the Octopus; at peripheral locations, however, attenuation is greatest for the Octopus. The magnitude of the attenuation with increase in scattering factor, as a function of eccentricity, for each type of perimetric stimulus is illustrated by the nomograms for all eccentricities (Figures 6.9 and 6.10) constructed from second order polynomial regression equations ($r = \geq 0.96$).

The difference between the two profiles, illustrated schematically in Figure 6.11, arises in part, from the difference in size of the two types of stimuli. The combination of the larger projected stimulus and lower bowl luminance of the Octopus produces a flatter sensitivity profile in the normal eye than the Dicon. This arises because the central area is saturated in terms of incident light energy (as described in section 3.6) compared with more peripheral locations and the fovea is thus relatively insensitive to small changes in light intensity. The introduction of intraocular light scatter effectively steepens the sensitivity profile of the Octopus. This steepening has also been demonstrated with increasing age as measured with Octopus Program 32 out to an eccentricity of 30° (Jaffe et al 1986). Conversely, the sensitivity profile for the LED stimuli demonstrates the classical flattening reported in the literature for subjects with media changes (Greve 1973; 1979), namely a greater reduction in sensitivity centrally compared to the periphery. This arises because the LED stimuli of the Dicon, like the stimuli used in conventional manual perimetry are relatively small and do not saturate the central area which is therefore more responsive to reductions in the light intensity of these stimuli.

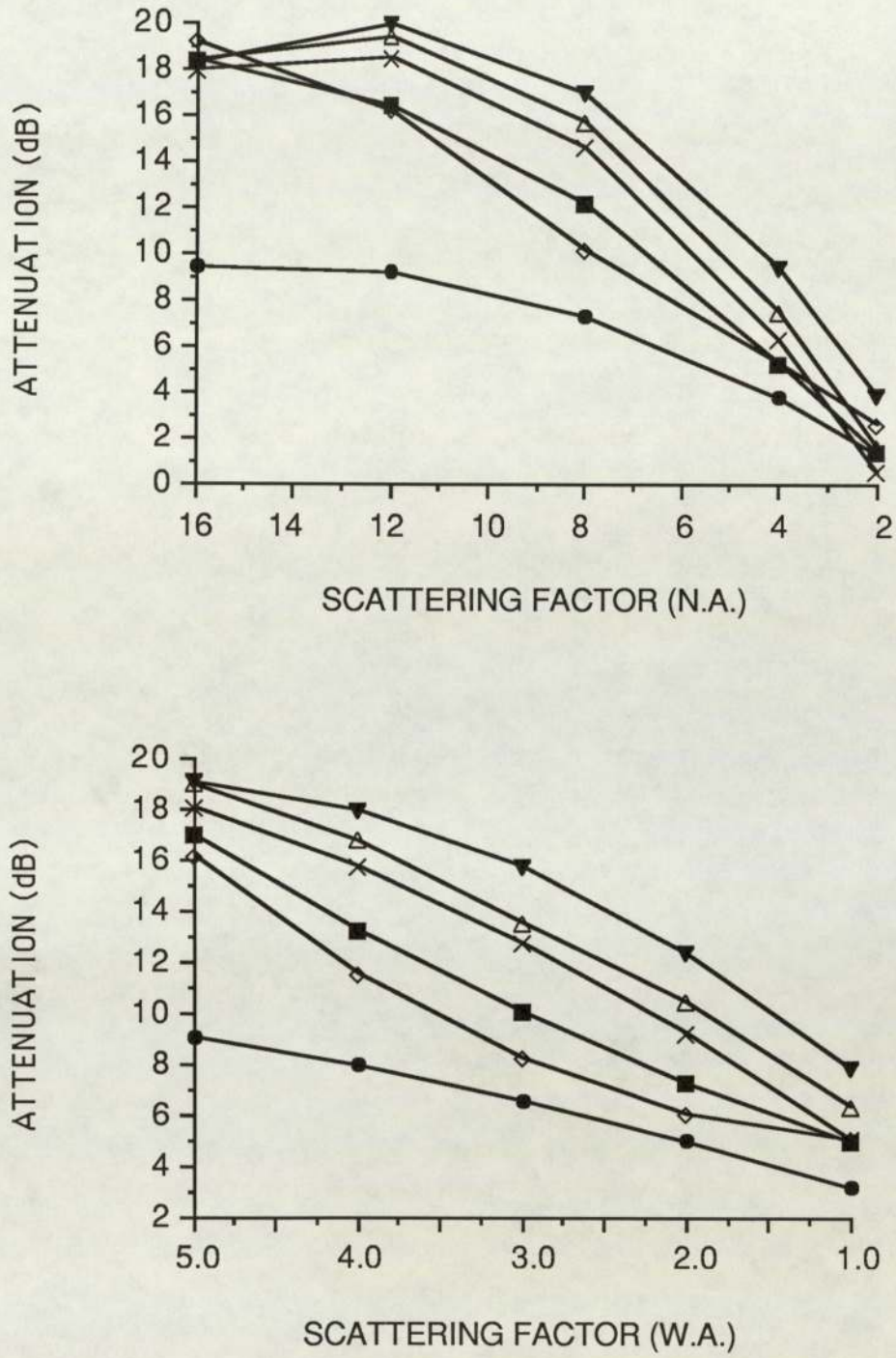


Fig. 6.9. Nomogram illustrating attenuation in perimetric sensitivity (dB) for the projected stimulus of the Octopus 201 automated perimeter for narrow angle (top) and wide angle (bottom) glare light as a function of eccentricity (°) (0° filled circles, 6° open diamonds, 12° filled squares, 18° crosses, 24° open triangles, 30° filled inverted triangles).

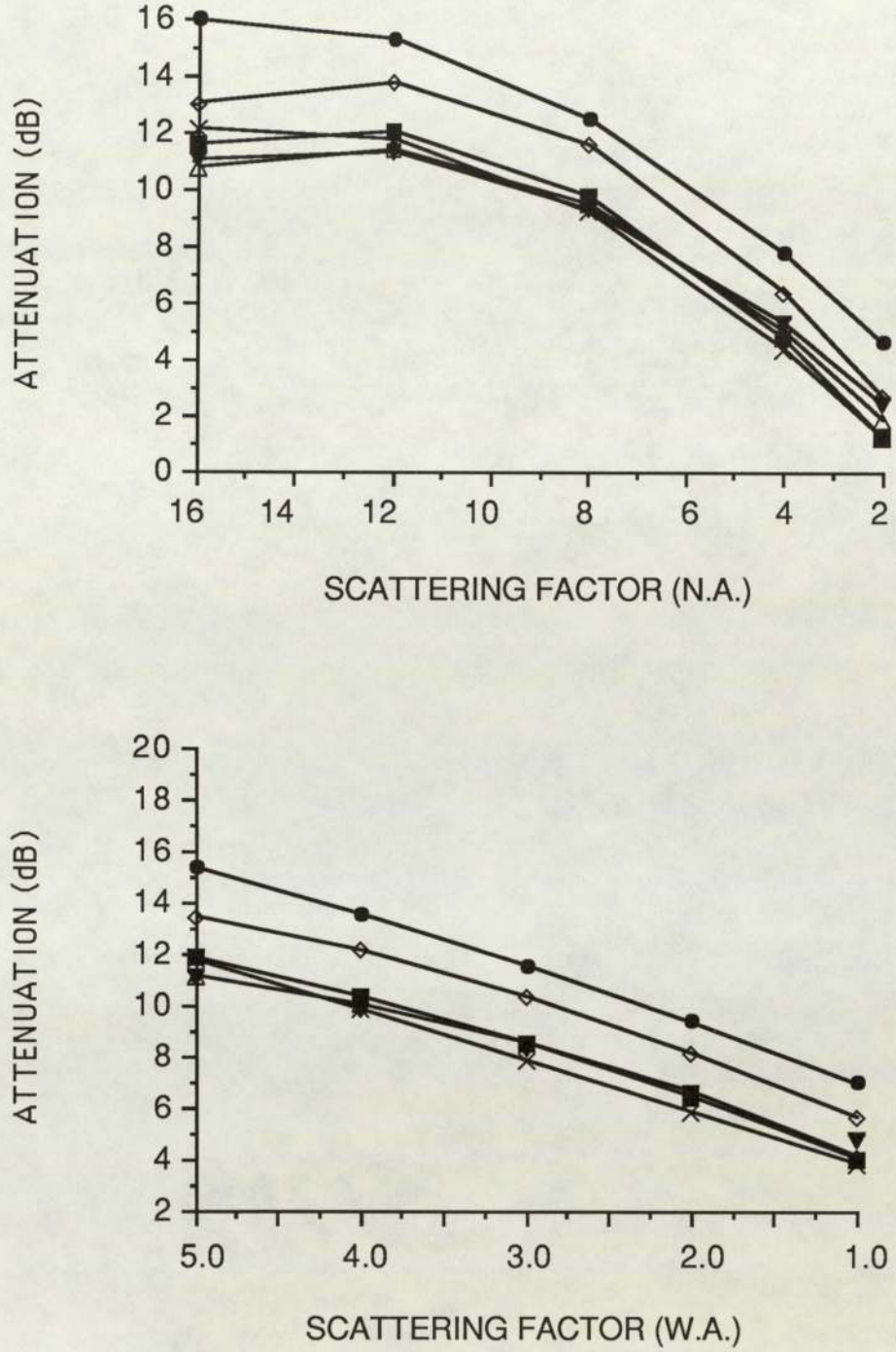


Fig. 6.10. Nomogram illustrating attenuation in perimetric sensitivity (dB) for the LED stimulus of the Dicon AP3000 autoperimeter (10 asb bowl luminance) for narrow angle (top) and wide angle (bottom) glare light as a function of eccentricity (°) (0° filled circles, 3° open diamonds, 5° filled squares, 7.5° crosses, 20° open triangles, 27.5° filled inverted triangles).

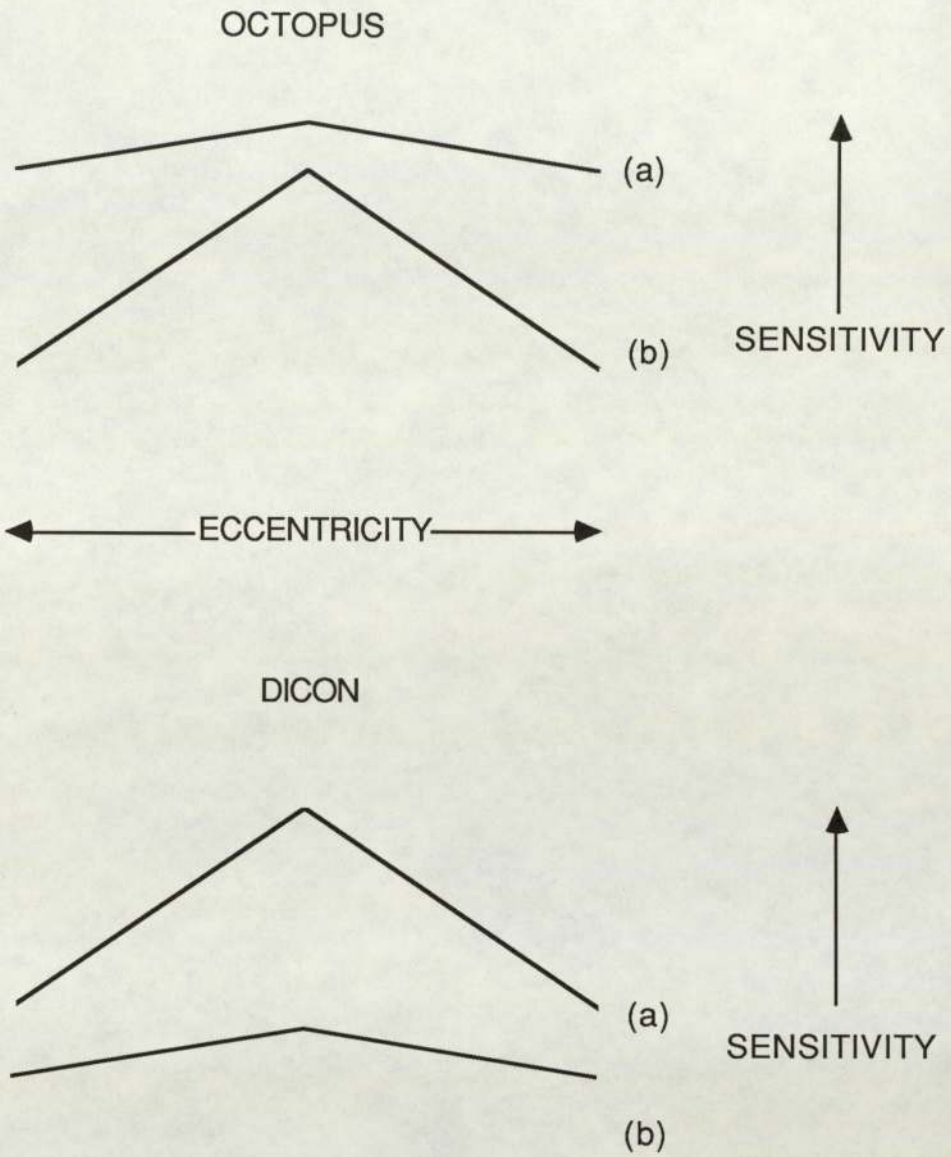


Fig. 6.11. Schematic representation of the influence of intraocular light scatter on the flat sensitivity profile of Program 31 of the Octopus 201 automated perimeter for stimulus size III (top) and on the relatively steep profile of the Dicon AP3000 autoperimeter at 10 asb bowl luminance (bottom), where a) represents the normal profile and b) the influence of intraocular light scatter on the normal profile.

If the light scattering is of the Rayleigh type, the intensity of the scattered light arising from the simulating cells should depend upon the wavelength of the incident light. In these circumstances, the Dicon LEDs with peak wavelength of 570 nm would be expected to produce less light scatter than polychromatic stimuli of the same size, since the former contain a smaller proportion of short wavelength light. Wooten and Geri (1987) stated, however, that intraocular light scatter is independent of wavelength within the range 420 nm to 650 nm.

6.9.5 Subjects with media opacities

The aim of the second investigation was to establish how the characteristics of the model (described in section 6.9.1) related to the effects of intraocular scatter resulting from disturbances of the ocular media. The experimental work was repeated with a series of patients exhibiting varying degrees of cataract. For expediency, it was decided to concentrate purely on the effect on lenticular opacities.

Prospective patients were continuously being selected from the cataract extraction waiting lists of the B.M.E.H. A total of 57 potential patients was obtained. Patients were selected in whom there were varying degrees of monocular media opacities, or in whom the degree of media opacity was markedly asymmetrical between the two eyes. It was decided that the contralateral eye should have a visual acuity of 6/12 or better to maintain a reasonable level of asymmetry between the two eyes. A signed letter was sent to each patient detailing the reasons for the study and the experimental procedures. The patients were advised that they were required to visit both the B.M.E.H. and Aston University on one occasion.

Of the thirty five positive replies, nine were rejected due to problems with travelling. Twenty six patients were therefore investigated, however, only eighteen of these proved to be suitable for the study, since the acuity of eight had deteriorated markedly since the last examination detailed in the eye hospital records; preliminary trials demonstrated that unless the vision in the poorer eye was equal to, or better than, 6/60 the contrast sensitivity monitor could not be seen with certainty.

6.9.6 Materials and methods

The sample consisted of 18 patients in whom there was no systemic disease with marked ocular complications. All patients underwent full ophthalmoscopic and slit - lamp examination prior to the investigation; the details of the patients are given in Table 6.1.

The experimental protocol was similar to that described in the previous section except that visual fields and contrast sensitivity were measured in both eyes, rather than in the right eye only. The eye with the clearest media was used as the control eye.

All the subjects underwent preliminary training in the psychophysical tasks prior to the contrast sensitivity and perimetric investigations. The distance correction was used for the contrast sensitivity measurements and the appropriate working distance corrections were employed for the two perimetric examinations. The latter were estimated from the age of the patient and from the working distance of the perimeter bowl and were verified subjectively. The scattering factor of both eyes was calculated from the results of the contrast sensitivity measurements with and without glare light; the difference between these results was plotted against the difference in perimetric sensitivity between the two eyes for both perimeters.

6.9.7 Results

The attenuation in perimetric sensitivity with the projected stimulus of the Octopus with variation in intraocular light scatter at fixation and at 30° eccentricity is illustrated in Figure 6.12 for both narrow and wide angle glare light.

The results for subjects with nuclear cataracts were then plotted separately from subjects with non - nuclear opacities, since it has been reported that the visual performance of subjects with nuclear cataracts are dissimilar from other types of cataracts in terms of the scattering factor (Abrahamsson and Sjostrand 1986) and perimetric profiles (Lyne and Phillips 1969). Indeed, subjects with nuclear

Patient	Ocular status	Visual acuity	Scattering Factor N.A.	W.A.
		R L	R L	
R.S.	R and L diffuse op.	6/9	14.0	1.37
		6/12	14.5	1.40
E.H.	R diffuse op.	6/18	1.57	0.06
		6/9	1.07	0.04
R.S.	R few lens dots	6/6-1	1.57	0.04
		6/6	1.058	0.03
R.C.	R cuneiform op.	6/18	1.2	0.16
		6/6	0.23	0.076
W.H.	L early fluid changes	6/6	1.75	0.115
		6/9	0.50	0.534
B.H.	R>L diffuse op.	6/18	2.72	0.096
		6/9	1.28	0.052
W.C.	L diffuse op.	6/9	0.728	0.036
		6/36	4.636	0.15
A.L.	R diffuse op.	6/9	1.35	0.04
		6/6	0.70	0.03
L.W.	R>L diffuse op.	6/36	6.02	0.84
		6/12	4.04	0.50
M.F.	L nuclear op.	6/6-2	0.72	0.19
		6/60		0.55
A.R.	R nuclear op.	6/60		0.284
		6/9	0.51	0.051
H.T.	R nuclear op. L IOL	6/60		0.355
		6/9	1.04	0.001
G.G.	R diffuse op. L nuclear op.	6/12	3.9	0.001
		6/36	4.58	0.034
L.B.	L>R cortical op.	6/12	3.29	0.49
		6/36	6.67	0.744
S.S.	R nuclear op. L IOL	6/60		0.466
		6/9	1.02	0.023
F.H.	R IOL L inf nuclear op.	6/6-1	0.828	0.275
		6/24-1		1.03
S.R.	R>L PSC	6/36	5.94	0.913
		6/12	2.079	0.318
P.L.	R diffuse corneal op.	6/6	0.92	0.04
		6/6	0.40	0.032

Table 6.1 Description of the visual characteristics of the cataractous sample.

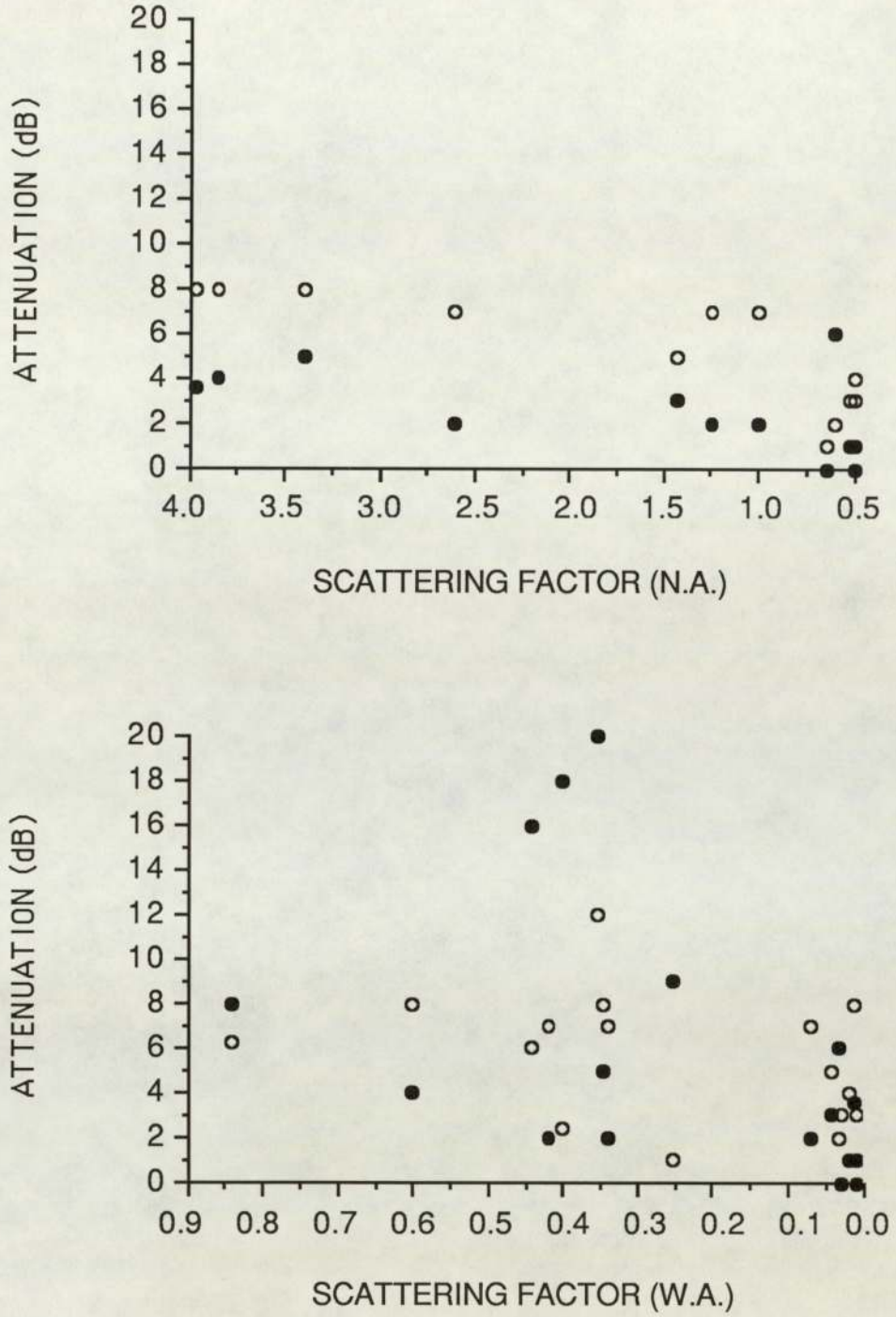


Fig. 6.12. Attenuation in perimetric sensitivity (dB) for the projected size III stimulus of the Octopus 201 automated perimeter against intraocular light scatter measured for narrow angle (top) and wide angle (bottom) glare light as a function of eccentricity (°) (closed circles 0°; open circles 30°) for all subjects with media opacities.

opacities and visual acuity better than 6/60 tended to lie at the lower limit of the contrast sensitivity scale even in the absence of glare light. The introduction of glare light in these subjects further depressed contrast sensitivity but did not produce a significant impact on the Paulsson and Sjostrand (1980) ratio.

The Octopus perimetric attenuation for subjects with non - nuclear cataracts is plotted in Figure 6.13 for both narrow and wide angle glare light and for subjects with nuclear cataracts in Figure 6.14 for wide angle glare light. These figures illustrate that the attenuation in perimetric sensitivity is greater at fixation than in the periphery for subjects with nuclear cataracts, whereas the reverse is true for all other subjects. At fixation, attenuation of sensitivity increases approximately linearly with increase in both wide and narrow angle intraocular light scatter for the non - nuclear opacities. Attenuation increases monotonically but with a decreasing gradient for both the glare sources at 30° eccentricity. The results for the subjects with nuclear cataracts are irregularly distributed.

The attenuation in perimetric sensitivity with the LED stimulus of the Dicon with both increasing narrow and increasing wide angle intraocular light scatter measured at the 10 asb and at 45 asb background luminances is shown for all subjects in Figures 6.15 and 6.16 respectively. Perimetric attenuation is greatest at fixation compared to that at 27.5° eccentricity for subjects with non - nuclear cataracts at 10 asb (Figure 6.17) and 45 asb (Figure 6.18) and for subjects with nuclear cataracts at 10 asb (Figure 6.19) and at 45 asb (Figure 6.20). The attenuation is greatest at the lower bowl luminance for both narrow and wide angle glare sources, for all subjects.

Perimetric attenuation is again greater for the Dicon (10 asb bowl luminance) at fixation than for the Octopus with increase in both narrow and wide angle intraocular light scatter (Figure 6.21) whereas at more peripheral locations the Octopus produces a greater loss of sensitivity than the Dicon (Figure 6.22) for subjects with non - nuclear cataracts.

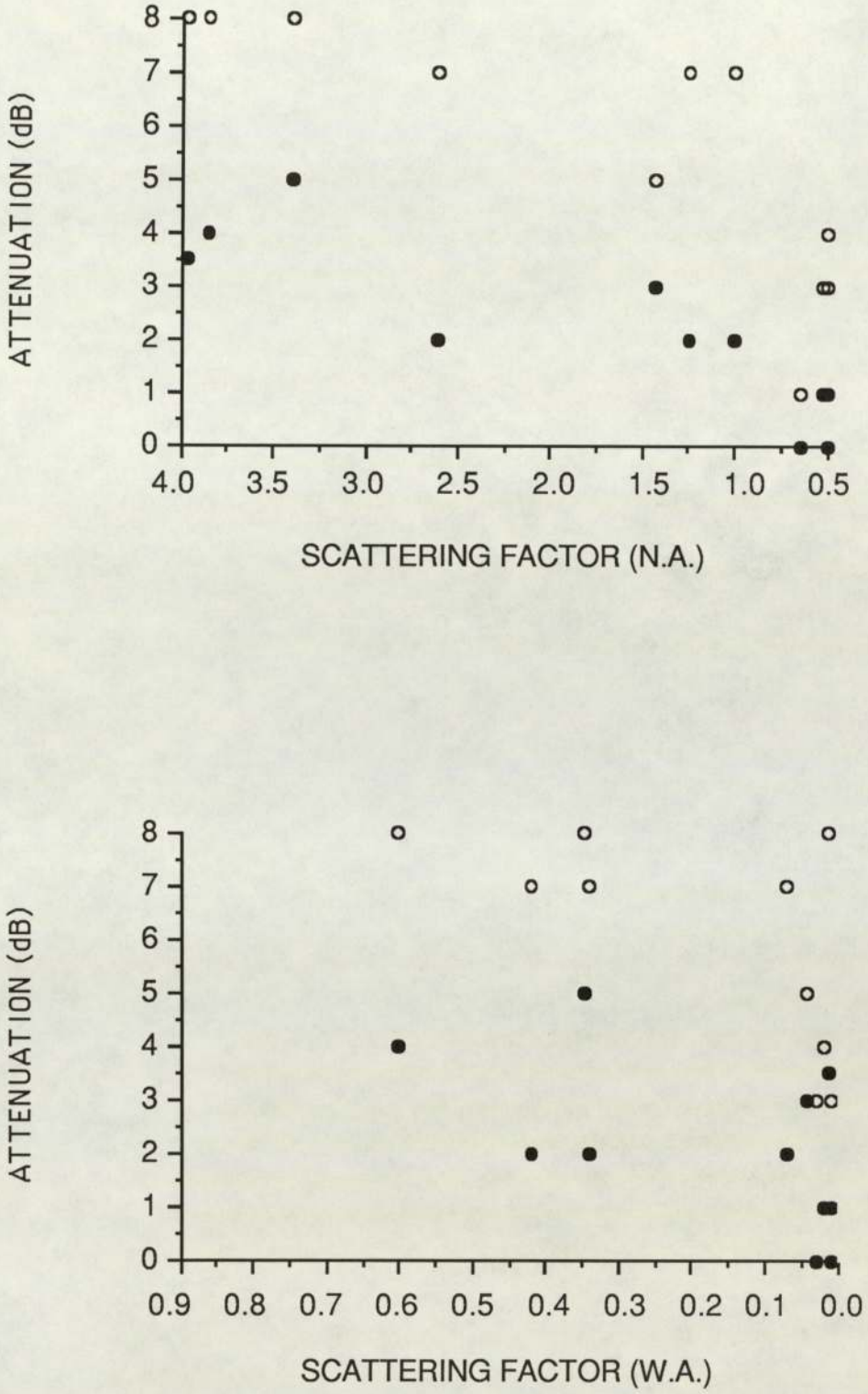


Fig. 6.13. Attenuation in perimetric sensitivity (dB) for the Octopus 201 automated perimeter stimulus size III against intraocular light scatter measured for narrow (top) and wide (bottom) angle glare light as a function of eccentricity (°) (closed circles 0°; open circles 30°) for subjects with non - nuclear opacities.

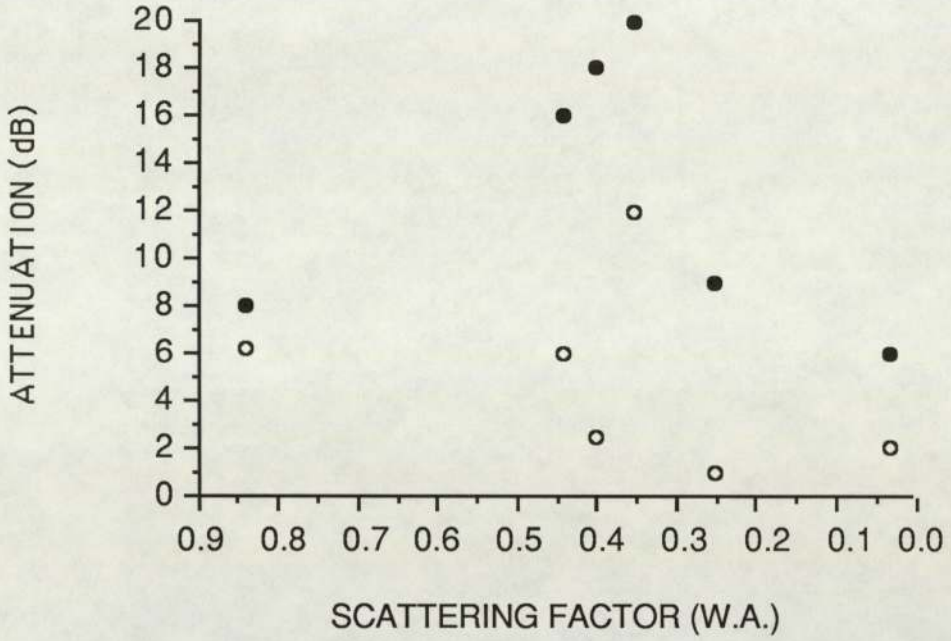


Fig. 6.14. Attenuation in perimetric sensitivity (dB) for the projected size III stimulus of the Octopus 201 automated perimeter against intraocular light scatter measured for narrow angle (top) and wide angle (bottom) glare light as a function of eccentricity (°) (closed circles 0°; open circles 30°) for subjects with nuclear opacities.

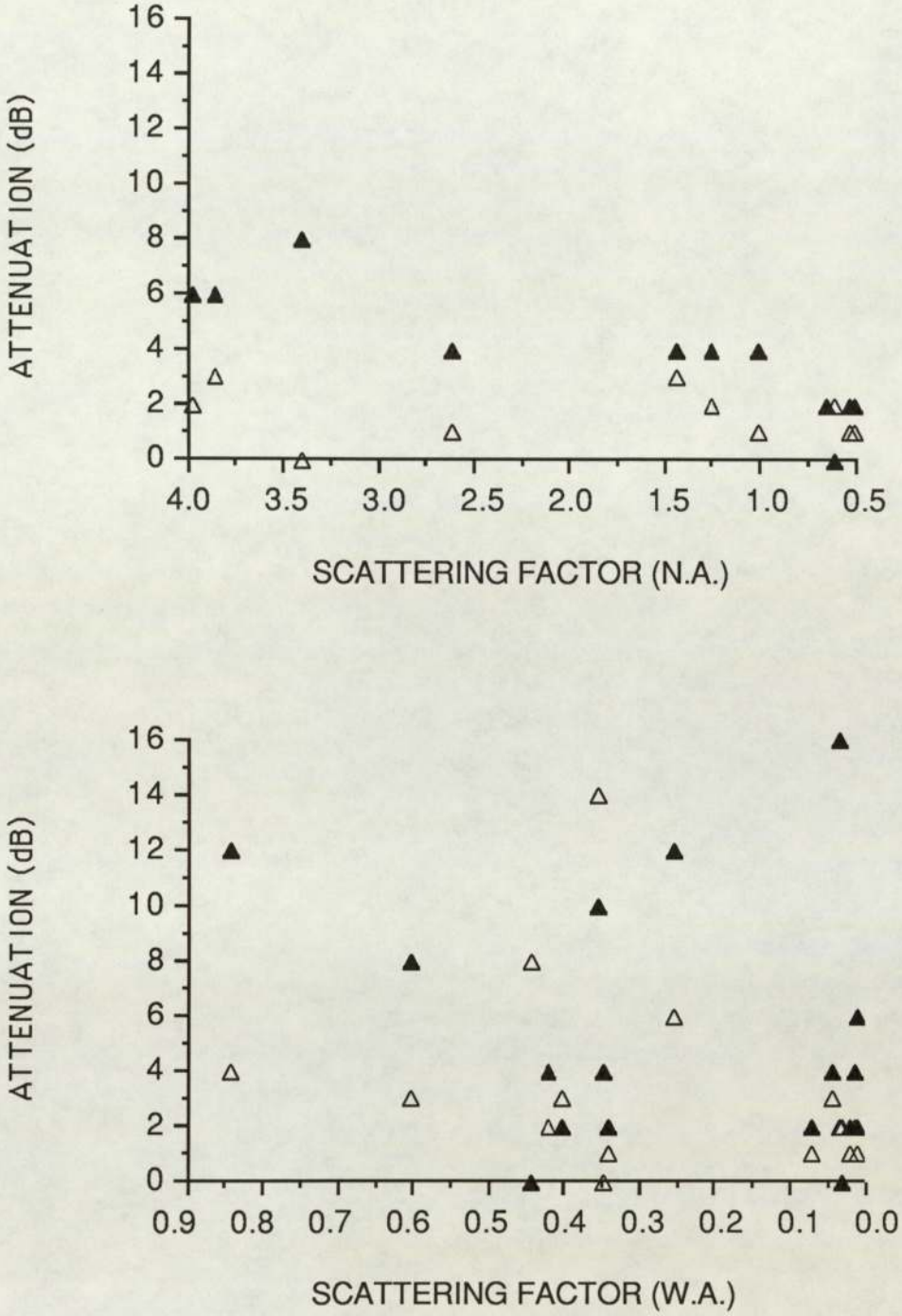


Fig. 6.15. Attenuation in perimetric sensitivity (dB) for the LED stimulus of the Dicon AP3000 autoperimeter against intraocular light scatter measured for narrow angle (top) and wide angle (bottom) glare light at a bowl luminance of 10 asb as a function of eccentricity (°) (closed triangles 0°; open triangles 27.5°) for all subjects with media opacities.

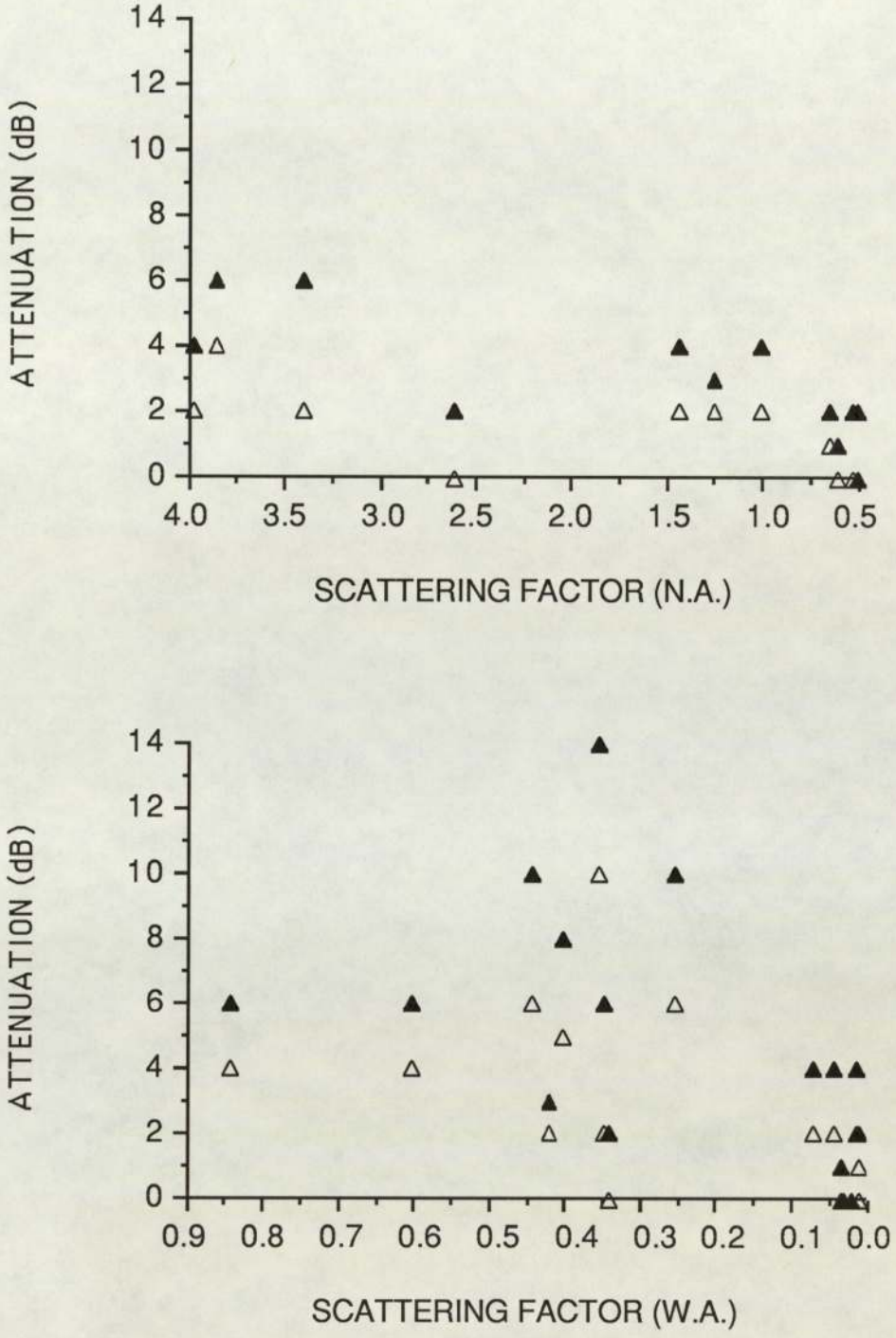


Fig. 6.16. Attenuation in perimetric sensitivity (dB) for the LED stimulus of the Dicon AP3000 autoperimeter against intraocular light scatter measured for narrow angle (top) and wide angle (bottom) glare light at a bowl luminance of 45 asb as a function of eccentricity (°) (closed triangles 0°; open triangles 27.5°) for all subjects with media opacities.

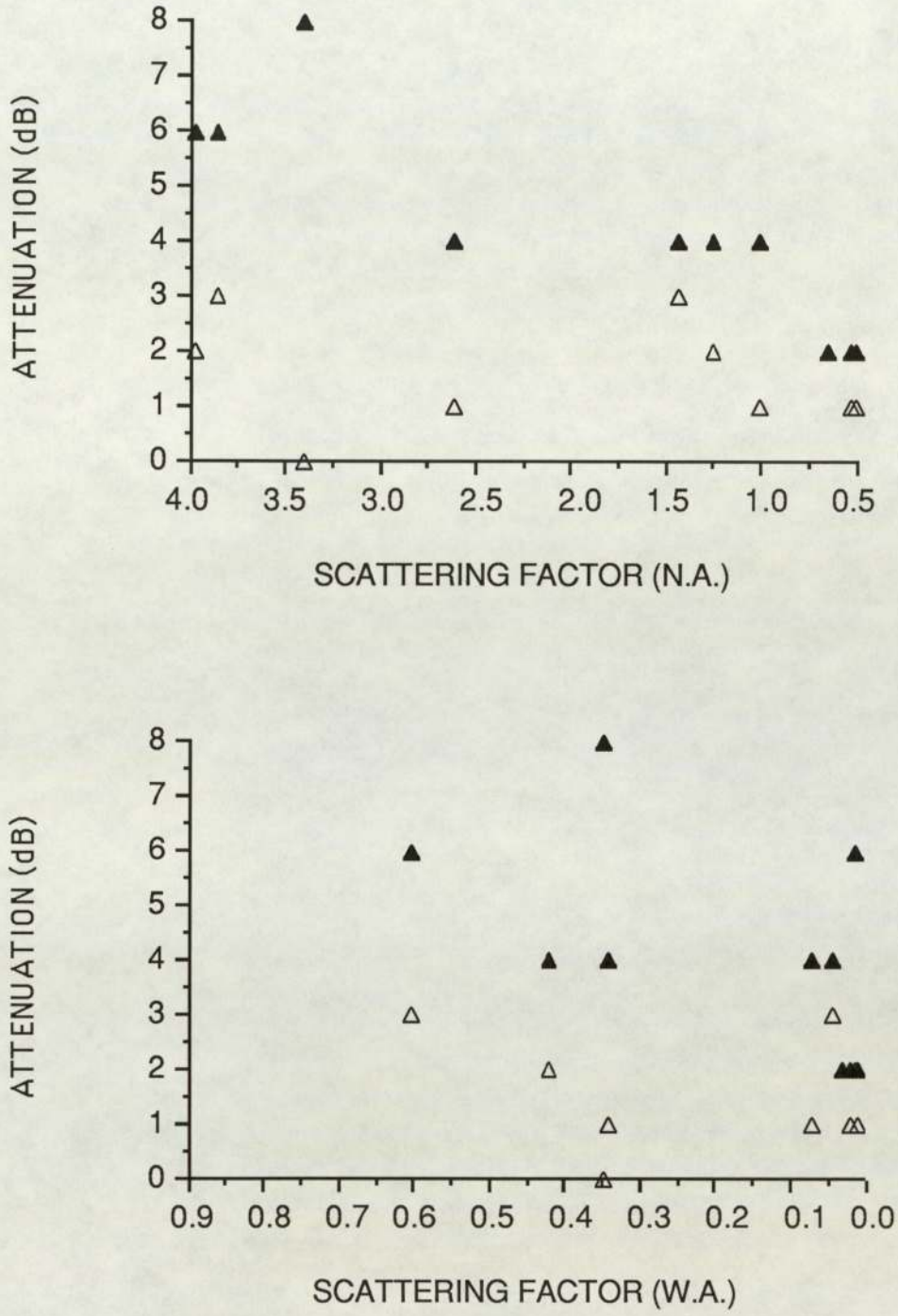


Fig. 6.17. Attenuation in perimetric sensitivity (dB) for the LED stimulus of the Dicon AP3000 autoperimeter against intraocular light scatter measured for narrow angle (top) and wide angle (bottom) glare light at a bowl luminance of 10 asb as a function of eccentricity (°) (closed triangles 0°; open triangles 27.5°) for all subjects with non - nuclear opacities.

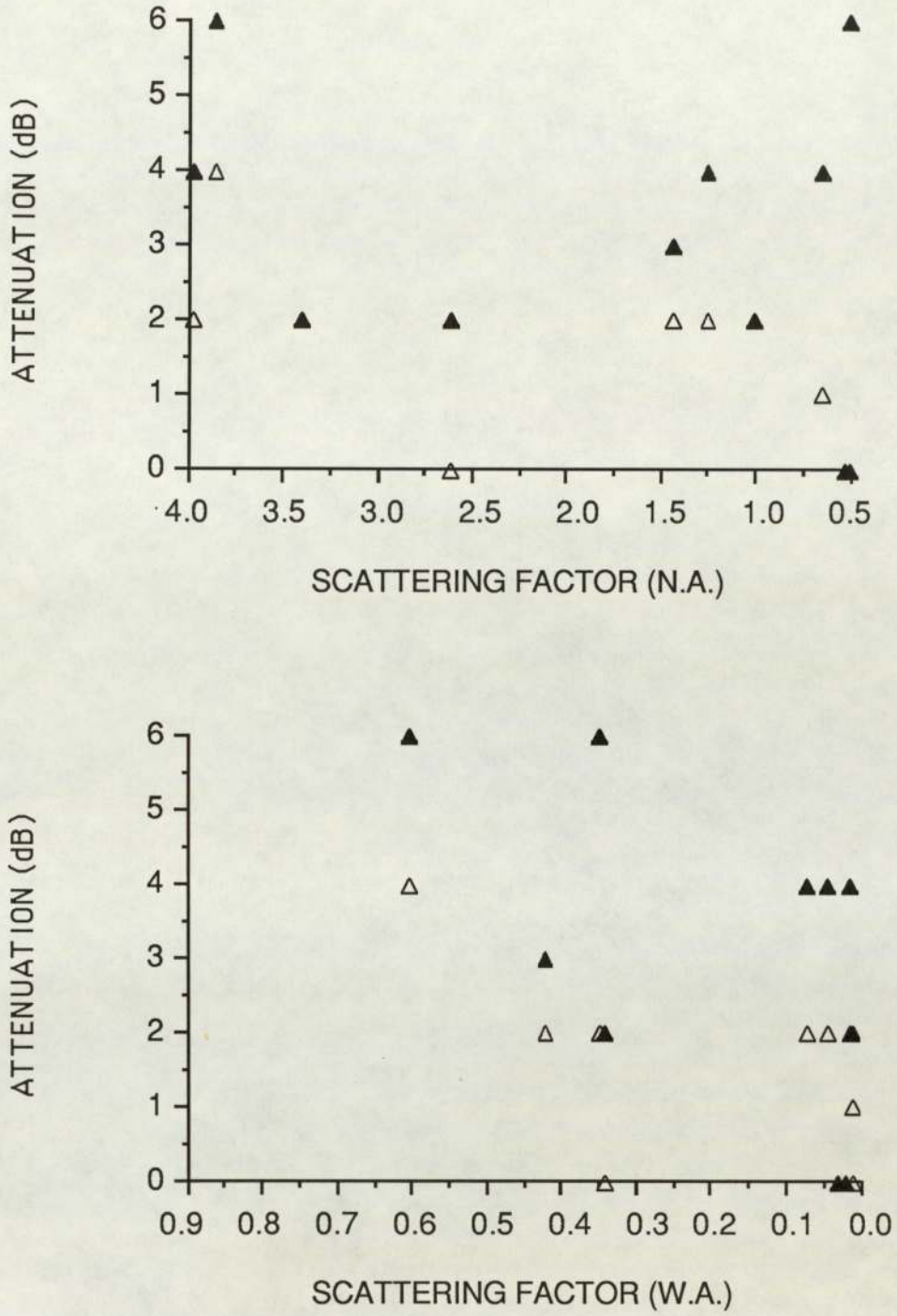


Fig. 6.18. Attenuation in perimetric sensitivity (dB) for the LED stimulus of the Dicon AP3000 autoperimeter against intraocular light scatter measured for narrow angle (top) and wide angle (bottom) glare light at a bowl luminance of 45 asb as a function of eccentricity (°) (closed triangles 0°; open triangles 27.5°) for all subjects with non - nuclear opacities.

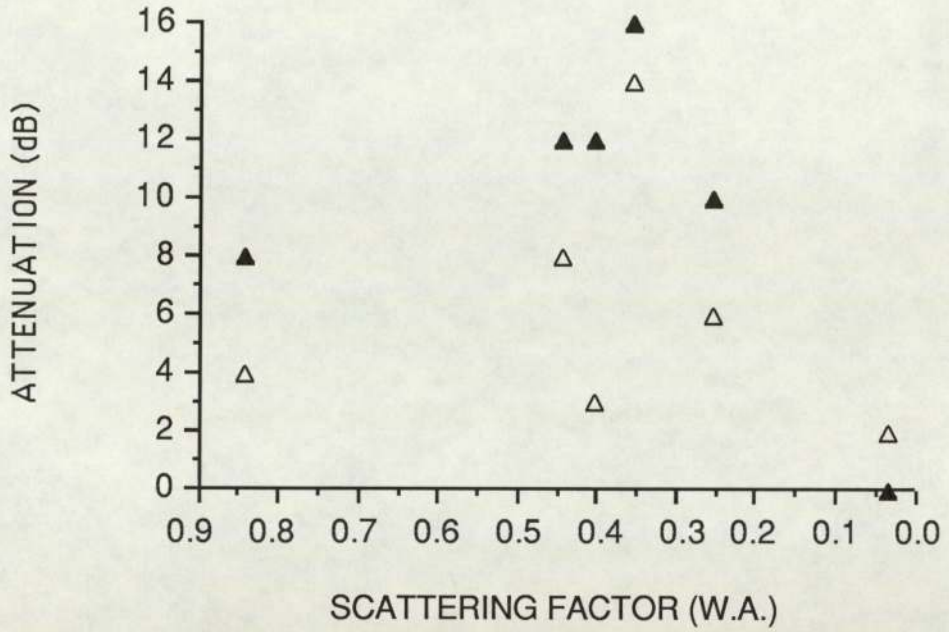


Fig. 6.19. Attenuation in sensitivity (dB) measured with the LED stimulus of the Dicon AP3000 autoperimeter against intraocular light scatter measured for wide angle glare light (bowl luminance 10 asb) as a function of eccentricity (closed triangles 0°; open triangles 27.5°) for subjects with nuclear opacities.

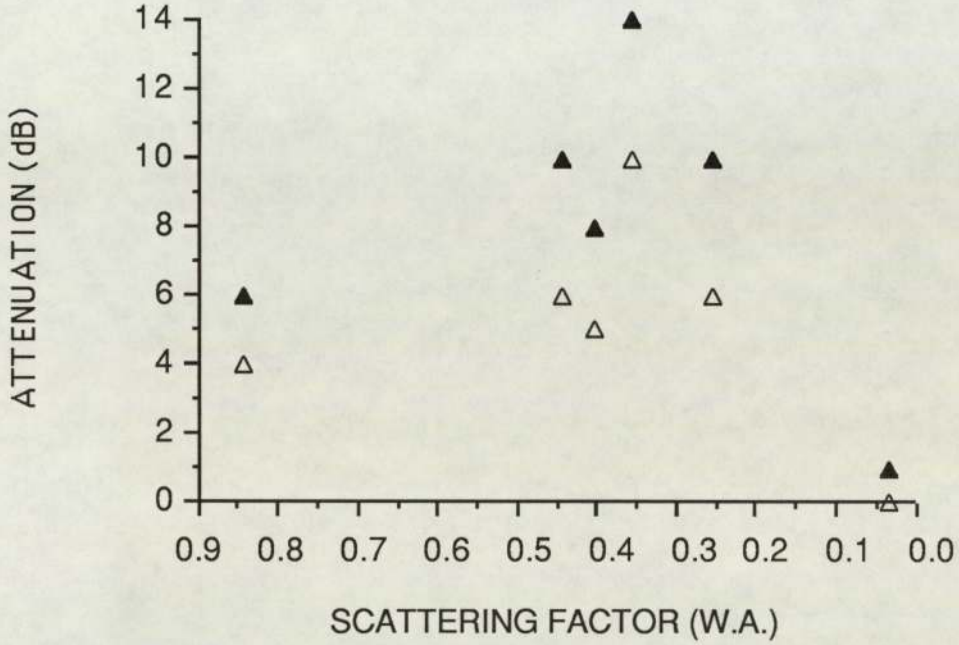


Fig. 6.20. Attenuation in sensitivity (dB) measured with the LED stimulus of the Dicon AP3000 autoperimeter against intraocular light scatter for wide angle glare light (bowl luminance 45 asb) as a function of eccentricity (°) (closed triangles 0°; open triangles 27.5°) for subjects with nuclear opacities.

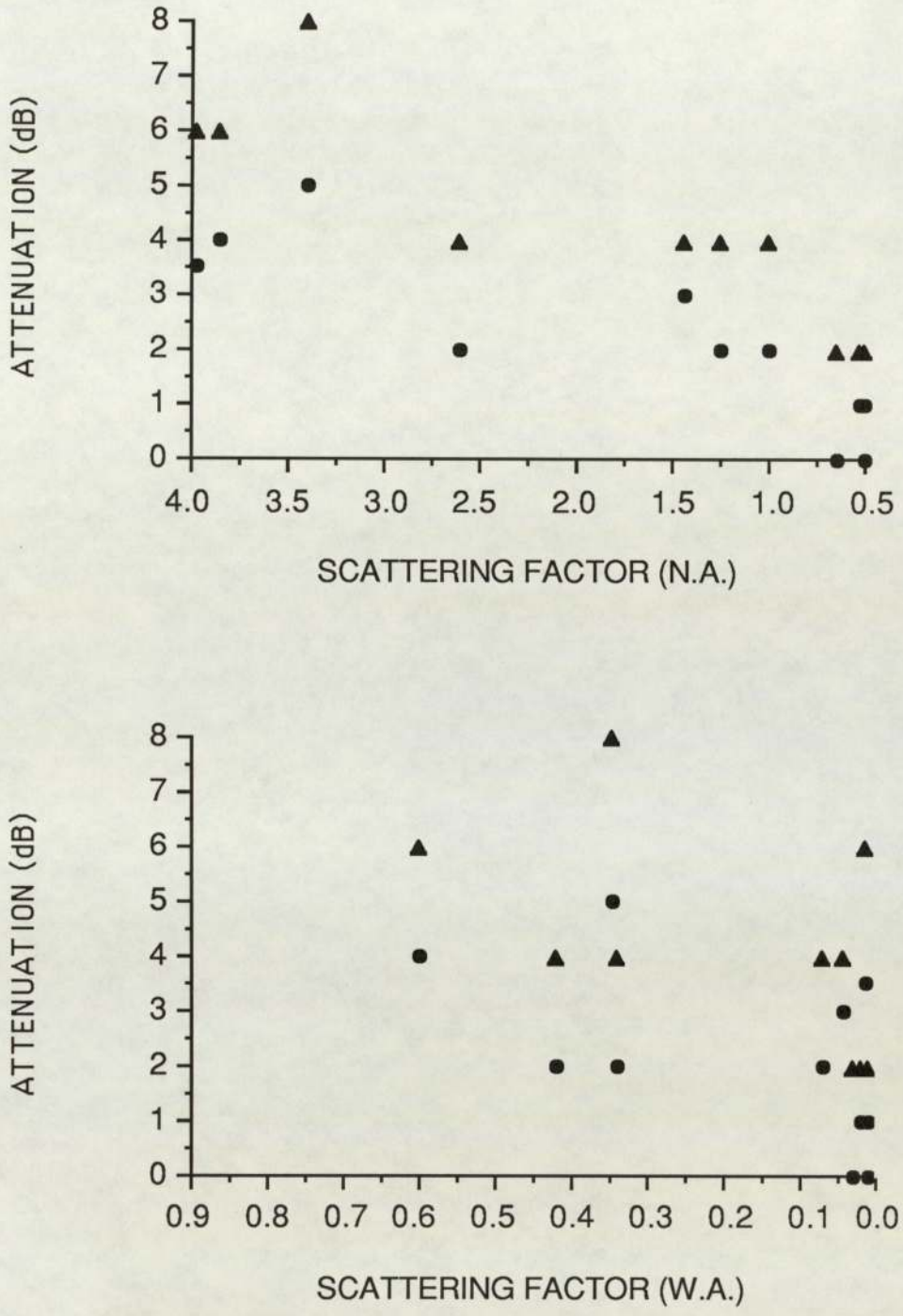


Fig. 6.21. Attenuation in perimetric sensitivity (dB) for the projected stimulus of the Octopus (filled circles) and for the LED stimulus of the Dicon AP3000 autoperimeter (10 asb bowl luminance) (filled triangles) at fixation for narrow angle (top) and wide angle (bottom) glare light for subjects with non - nuclear opacities.

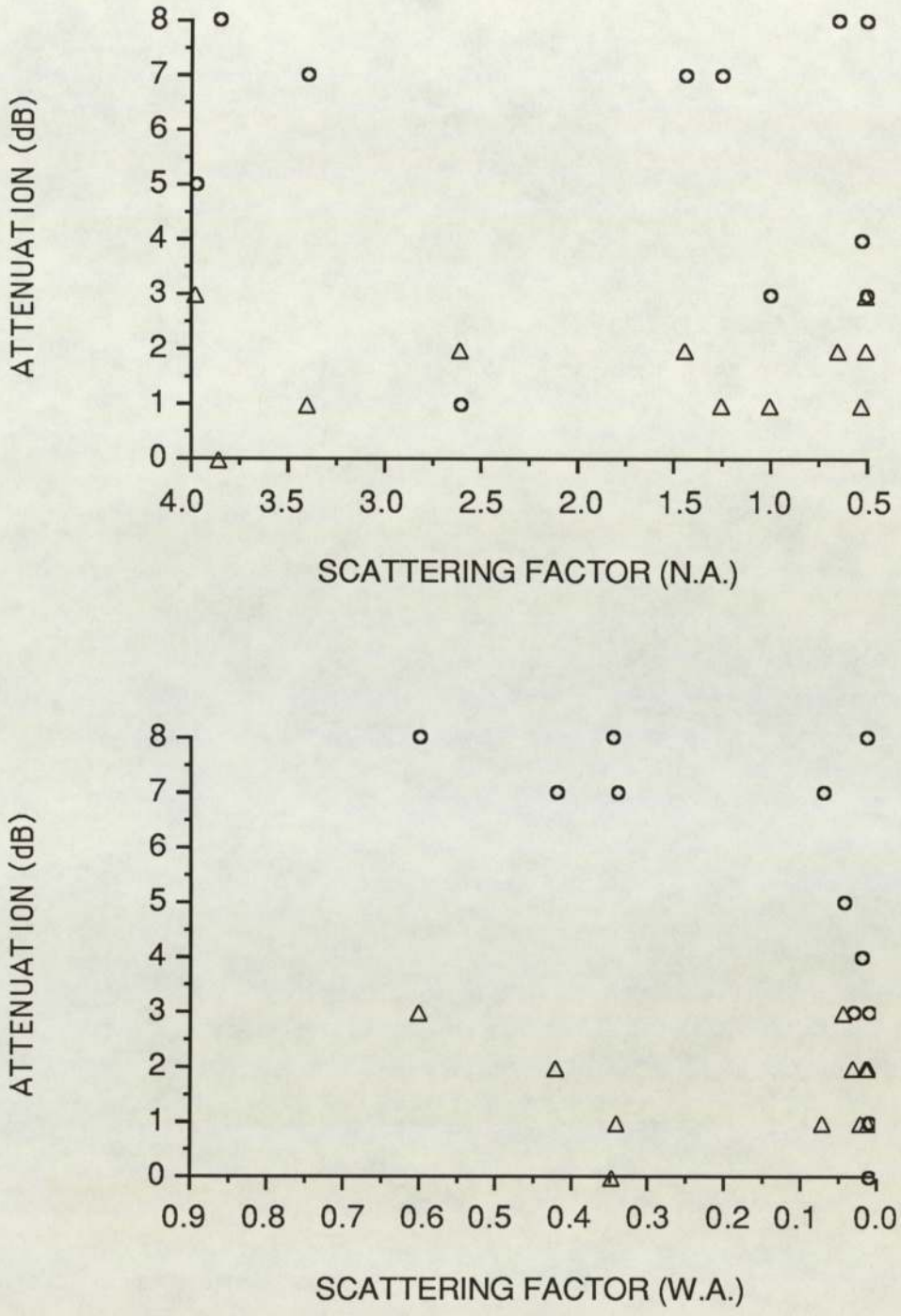


Fig. 6.22. Attenuation in perimetric sensitivity (dB) for the projected stimulus of the Octopus 201 automated perimeter (open circles) and for the LED stimulus of the Dicon AP3000 autoperimeter (10 asb bowl luminance) (open triangles) at 30° and 27.5° respectively for narrow (top) and wide (bottom) angle glare light for subjects with non - nuclear opacities.

A poor relationship exists between scattering factor and the minimum angle of resolution measured with Snellen letters for all subjects (Figure 6.23) and for those with non - nuclear opacities (Figure 6.24) for both narrow and wide angle glare light.

6.9.8 Discussion

Attenuation in perimetric sensitivity increases with increase in intraocular light scatter in all subjects with media opacities for both the projected Goldmann III stimuli of the Octopus and with the LED stimulus of the Dicon. This finding is in agreement with the model developed in section 6.9.1, however, as expected the quantitative nature of this relationship is different. The intraocular light scatter for the observers with media opacities arising from the wide angle glare source is less than that for narrow angle glare light and is in further agreement with the results for the model. Measurement of the narrow angle scattering factor was only possible for 12 of the 18 subjects, since the relatively high luminance of the narrow angle glare source prevented the gratings on the monitor being seen by those subjects in whom the level of intraocular scattering was high or in those patients with nuclear opacities.

The scattering factors of the cataractous sample for both the wide and the narrow angle glare lights were smaller than those obtained with the simulating cells, although the depression in Snellen visual acuity was consistently greater. This implies that other factors, such as absorption, are important in the visual processing of patients with cataract.

The magnitude of the perimetric attenuation with increase in scattering factor, as a function of eccentricity, for each type of perimetric stimulus is illustrated by the nomograms for all eccentricities for the patients with non - nuclear opacities (Figures 6.24 and 6.25) constructed from second order polynomial regression equations ($r = \geq 0.66$). The results for the subjects with non - nuclear opacities follow a similar pattern to that of the model, in that perimetric attenuation is greater peripherally for the Octopus and greater centrally for the Dicon. This confirms the

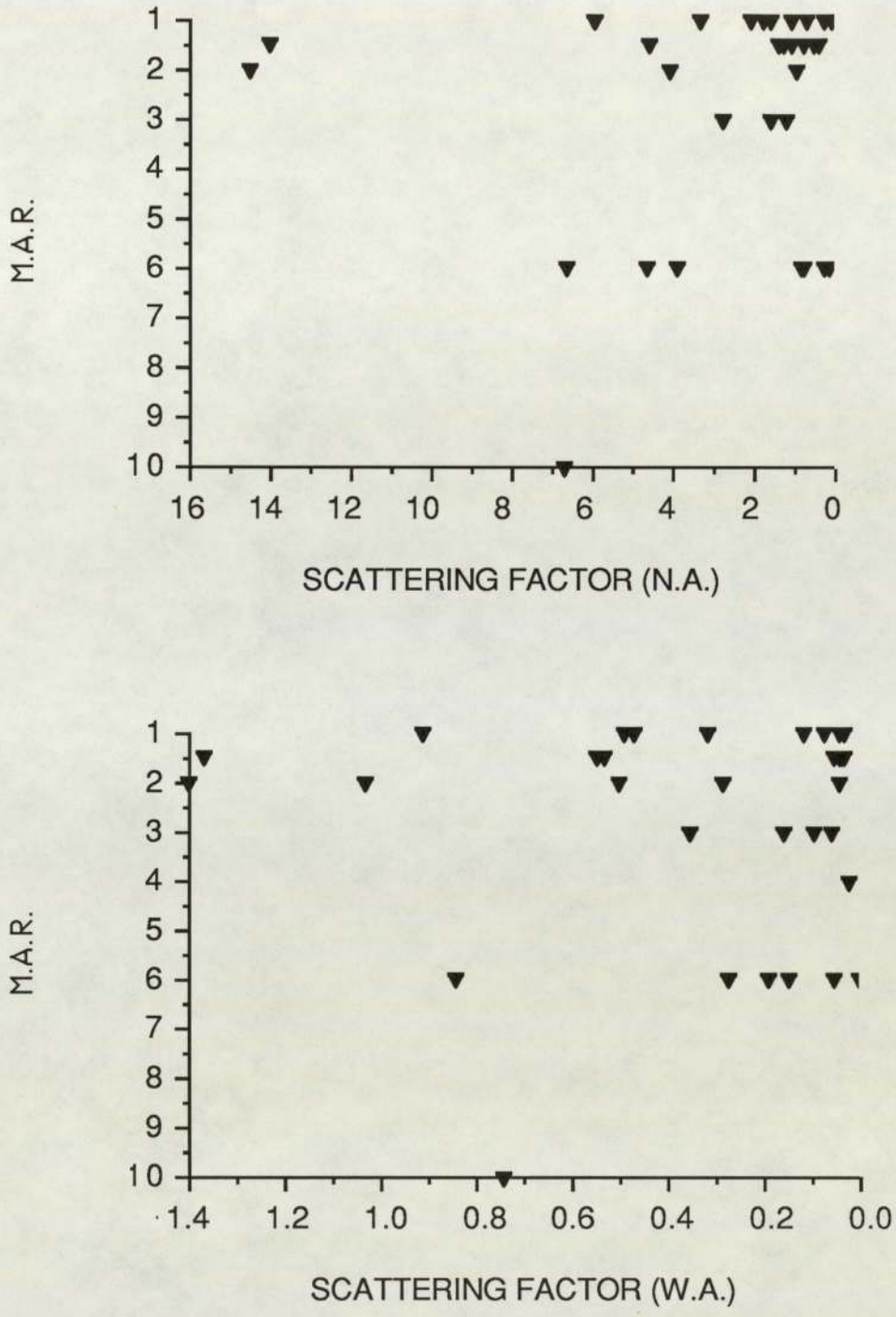


Fig. 6.23. Intraocular light scatter factor against minimum angle of resolution for all subjects with media opacities for narrow angle (top) and wide angle (bottom) glare light.

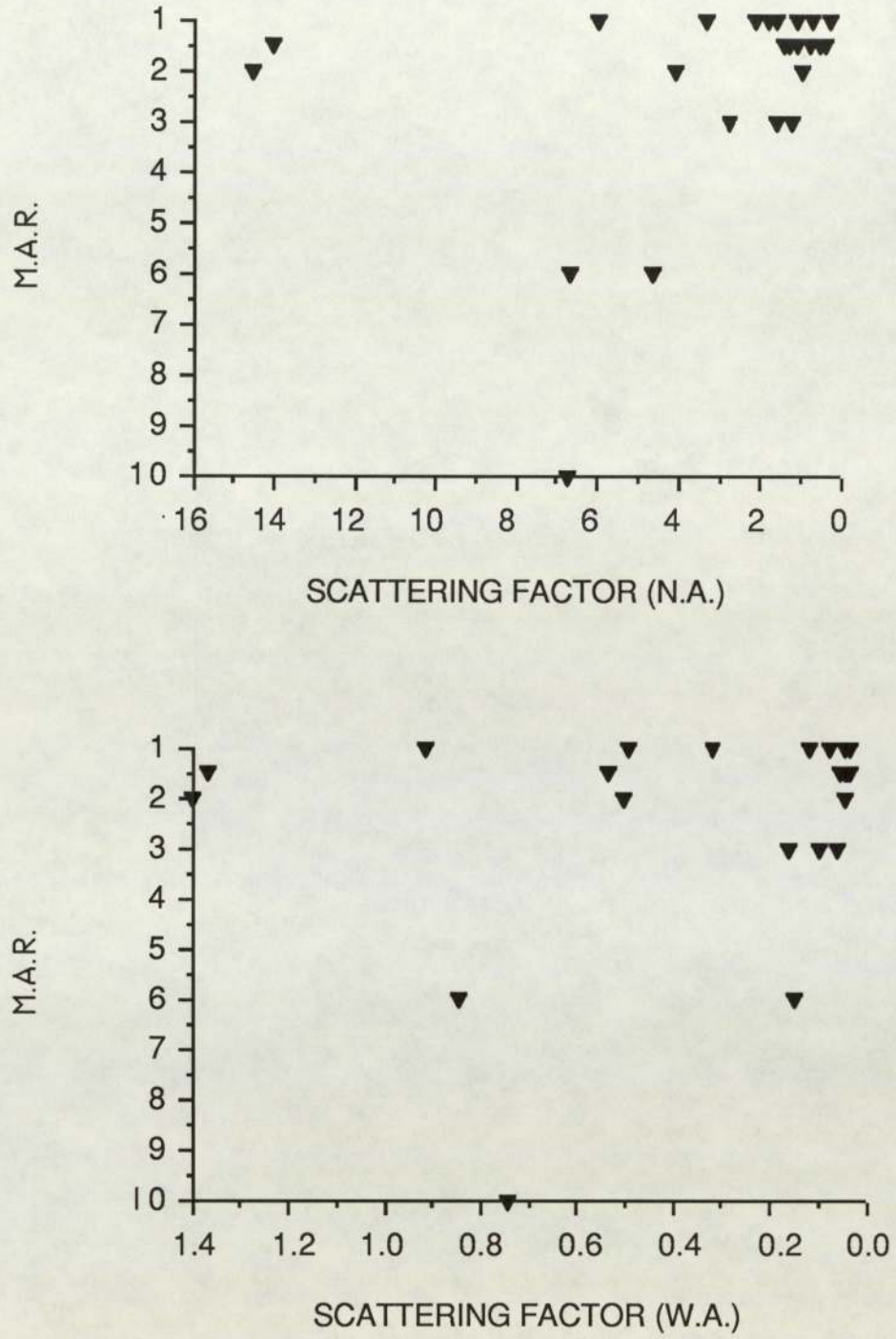


Fig. 6.24. Intraocular light scatter factor against minimum angle of resolution for subjects with non - nuclear media opacities for narrow angle (top) and wide angle (bottom) glare light.

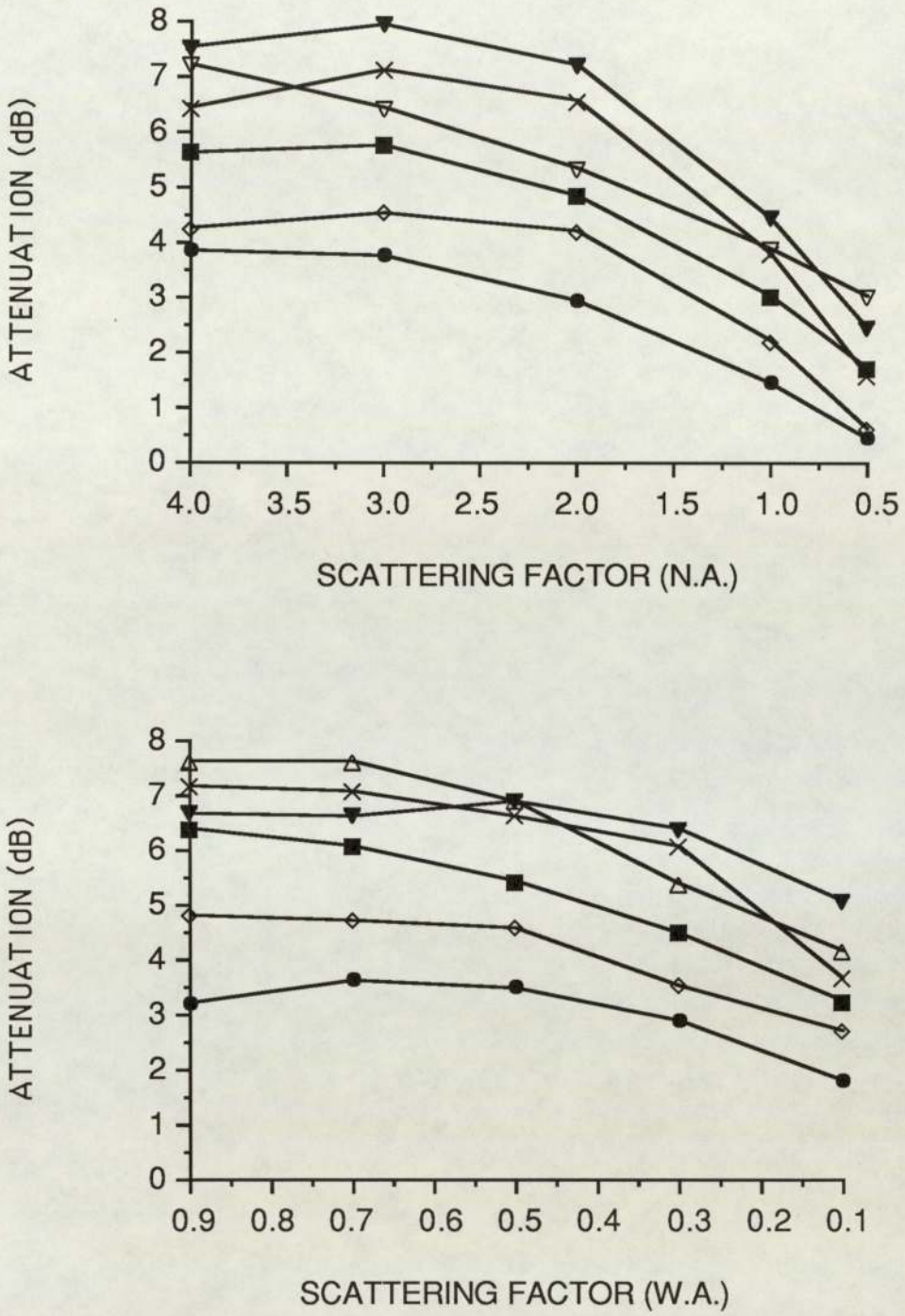


Fig. 6.25 Nomogram illustrating attenuation in perimetric sensitivity (dB) for the projected stimulus of the Octopus 201 automated perimeter against intraocular light scatter measured for narrow angle (top) and wide angle (bottom) glare light as a function of eccentricity (°) (0° filled circles, 6° open diamonds, 12° filled squares, 18° crosses, 24° open triangles, 30° filled inverted triangles) for subjects with non - nuclear opacities.

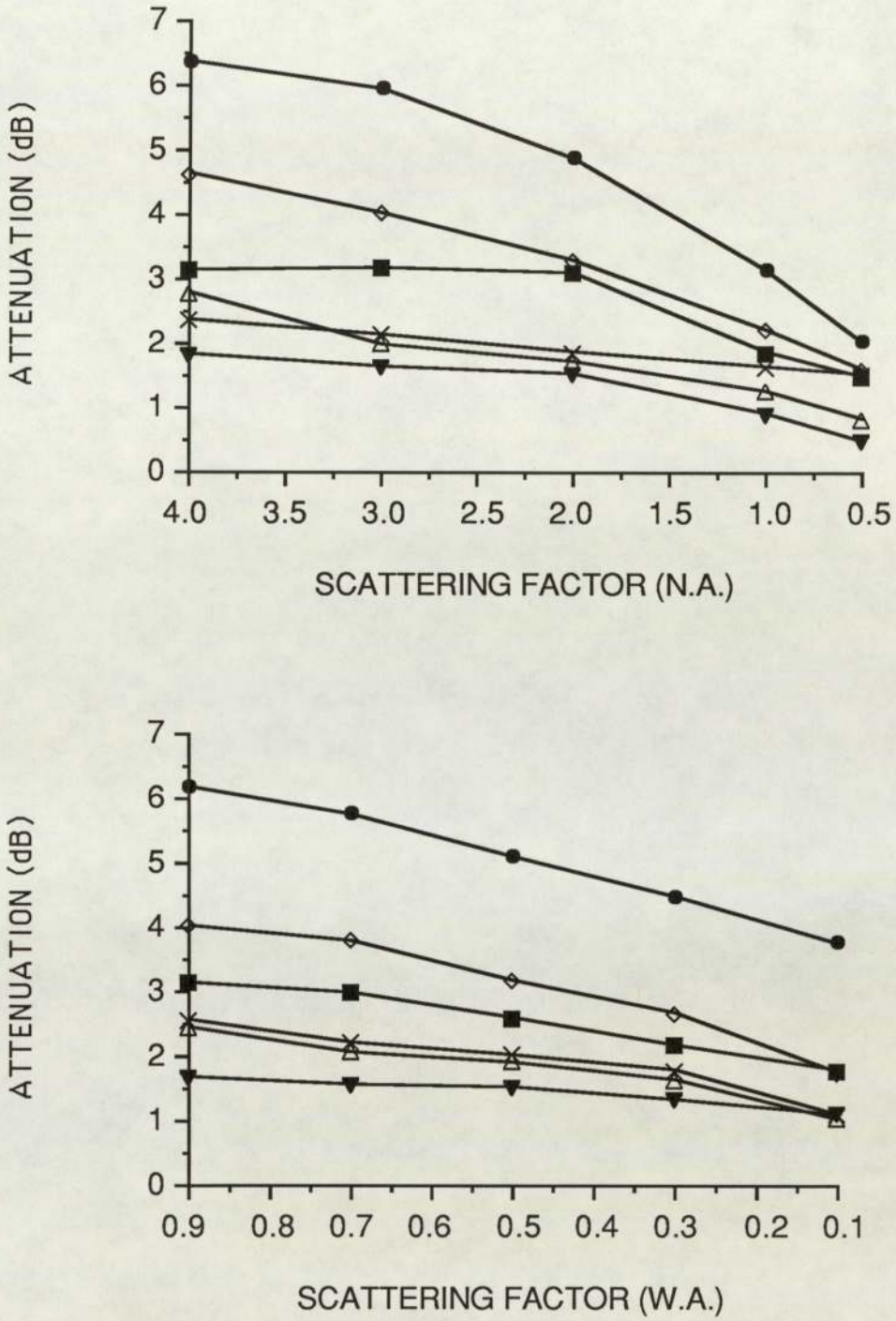


Fig. 6.26 Nomogram illustrating attenuation in perimetric sensitivity (dB) for the LED stimulus of the Dicon AP3000 autoperimeter (10 asb bowl luminance) against intraocular light scatter measured for narrow angle (top) and wide angle (bottom) glare light as a function of eccentricity (°) (0° filled circles, 6° open diamonds, 12° filled squares, 18° crosses, 24° open triangles, 30° filled inverted triangles) for subjects with non - nuclear opacities.

hypothesis, outlined in section 3.6 and further derived from the model, that relatively large projected stimuli saturate the central regions, rendering them less able to detect depressions in light sensitivity. Conversely, the results for the subjects with nuclear opacities exhibit a different relationship between perimetric attenuation and scattering factor to that of either the model or of the non - nuclear opacities. For subjects with nuclear opacities perimetric attenuation for both the Octopus and the Dicon is greater at fixation relative to more peripheral locations. Indeed, this finding is in agreement with the classic literature which states that a cataract flattens the hill of vision by depressing the central peak of sensitivity with the peripheral regions being relatively unaffected.

Interestingly, the results from one subject with a large opacity situated in the nuclear plane in the inferior half of the pupil were similar to that of a nuclear opacity in terms of perimetric attenuation, but also produced a relatively high scattering factor unlike the other patients with nuclear changes. This finding demonstrates that when position of the opacity is confined to one region rather than being diffusely distributed the position in both the horizontal and vertical planes is important.

The relationship between visual acuity and the intraocular light scattering value is poor for both narrow and wide angle glare light, and is in agreement with the results of Abrahamsson and Sjostrand (1986). This finding also endorses the opinion of several workers who have advocated that visual acuity is a poor indication of visual function of subjects with media changes (Miller et al 1972; Hess and Woo 1978). One subject with diffuse corneal opacities was investigated and produced results similar to those of the non - nuclear opacities. The data from this subject seemed to conform reasonably well with the model. Interestingly, both Faschinger (In press) and Baraldi et al (In press) suggested that the perimetric attenuation arising from corneal opacification differs from that arising from lenticular opacities. Indeed, it is envisaged that future investigations will determine the role of the plane of the opacity in perimetric attenuation.

Three of the subjects had nuclear opacities in one eye and an intraocular lens (IOL) in the contralateral eye. Although these results were included in the analysis of the nuclear opacities, it

was acknowledged that an eye with an IOL and a certain level of visual acuity is not the same as a normal eye possessing that level of visual acuity. Clearly, the relationship between the scattering factor and perimetric attenuation of different types of IOLs needs to be quantified.

6.10 Conclusions

A good relationship was found between perimetric attenuation and the intraocular light scattering function both in normal subjects with the simulated intraocular light scatter and in those patients with media opacities. The findings demonstrate that the model quantitatively represents the effect of non - nuclear media opacities on perimetric sensitivity; however, this relationship breaks down for nuclear opacities. Indeed, the type and position of the media opacity in addition to the level of intraocular light scatter determine the degree of perimetric attenuation.

It is proposed that from a measure of the light scattering function, the degree of perimetric attenuation could ultimately be predicted at any eccentricity in the central visual field. Further work must be undertaken, however, before this stage is reached. This would involve increasing the sample size, not only to overcome the inherent limitations of using non - trained perimetric observers but also to include patients with opacities at different positions within the lens, and those with media opacities at sites other than the lens, such as the cornea and the vitreous. Furthermore, modification of the light scattering apparatus to permit evaluation of patients with visual acuity < 6/60 and with high scattering factors is necessary. These proposed modifications are discussed in section 11.3.3.

7. THE INFLUENCE OF A LEARNING - EFFECT ON THE PERIMETRIC PROFILE

7.1 Introduction

The learning - effect, when applied to visual psychophysical judgements, describes the improvement in sensitivity which follows repeated trials and has been demonstrated to be perceptual rather than motor in origin (Seymour 1956). Perceptual learning refers to the increase in ability to extract information from the environment as a result of experience; there is considerable evidence that perceptual judgements can be improved (Gibson 1969). It has been suggested, however, that the learning - effect reported for the simple perceptual judgements involved in increment and absolute threshold measurements are indications of liberalized standards employed by the subject (McKee and Westheimer 1978) i.e., the observer changes his criterion for discrimination with practise, rather than manifests perceptual learning. Indeed, it has been demonstrated that thresholds remain stable if criterion - free measures are used (Green and Swets 1966).

The literature describing learning and learning theory is extensive and is beyond the scope of this study. For a comprehensive review of the theories of perceptual learning, see Gibson (1969).

7.2 Presence of a learning - effect in the measurement of visual function

7.2.1 Foveal functions

Wilcox (1936) reported that the visual resolution of a pair of parallel bars presented at different luminances improved and became more consistent with practise. He attributed this improvement in central visual acuity to a change in the subject's criterion for "doubleness". Similarly, Wittenberg et al (1969), using both the method of adjustment and the method of constant stimuli, reported a practise effect for foveal stereoacuity. In the former method, a moveable object was manipulated by

the observer to make it lie in a fronto - parallel plane containing the reference object; in the latter method, two or more objects, having a spatial displacement which was fixed for that trial, were compared and one of them was judged to be closer or farther than the other. These workers reported that the effect of practise was transferred from one method to another but did not describe the changes in threshold which occurred during the training period. More recently, foveal stereoacuity, measured by the method of constant stimuli with feedback (where the patient is informed of the accuracy of his performance), has been reported to improve with practise and to plateau after approximately 3000 - 4000 responses (Fendick and Westheimer 1983). Similarly, foveal vernier acuity, where the observer has to detect small differences in the positions of two lines, has been shown to improve with training, and to plateau after 2000 - 2500 responses (McKee and Westheimer 1978). These workers suggested that although the observer's concentration improved during training, the improvement in sensitivity represented a "fine tuning" of the neural mechanism responsible for hyperacuity. Interestingly, Kelly and Tomlinson (1987) reported that the contrast sensitivity function for vertical gratings was unaffected by training. The latter finding is consistent with that of Mayer (1983) who demonstrated that practise improved the contrast sensitivity function measured with diagonal gratings but not for gratings with cardinal (horizontal or vertical) orientations. Mayer (1983) suggested three possible theories to explain why learning - effects were apparent for diagonal gratings and not for either vertical or horizontal gratings, but advised that further work was necessary to validate these hypotheses.

7.2.2 Peripheral functions

Peripheral visual acuity has also been demonstrated to improve with practise (Low 1946; Saugstad and Lie 1964). Nevertheless, there is some discrepancy concerning the amount of practise required to produce optimal performance. According to Low (1946) the quantity of practise required, consisted of 25 sessions whilst Saugstad and Lie (1964) advocated that 15 sessions was sufficient. Indeed, Low (1946) demonstrated that trained subjects responded to peripheral visual acuity stimuli up to eleven times more efficiently than untrained subjects. The theoretical basis for the improvement in peripheral discrimination remains unclear: Low (1946) proposed that it may be due to the observers

learning to use a previously unpractised sensory area, whilst Saugstad and Lie (1964) suggested that subjects learnt to shift the maximum level of attention from central to peripheral regions of the visual field.

More recently, Fendick and Westheimer (1983) demonstrated that peripheral stereoacuity can improve with practise. The magnitude of the increase in peripheral stereoacuity reached levels of 60 - 80%; however, Fendick and Westheimer (1983) found considerable inter - subject variation in the relationship between foveal and extra - foveal practise effects. Peripheral movement thresholds have also been shown to improve with practise (Johnson and Leibowitz 1974). These workers demonstrated that the major effect of practise was realised by the 3rd session and was sustained for up to 3 months.

7.3 Learning - effect in perimetry

Aulhorn and Harms (1967) reported approximately a 1 log unit increase in sensitivity in normal subjects following 20 consecutive manual perimetric static threshold determinations within one day. The increase in sensitivity was greatest in the early trials, plateaued in subsequent sessions and was independent of eccentricity.

Several studies utilizing automated perimetry have acknowledged the presence of a learning - effect, but suggested that it was eliminated by excluding either the first (Flammer, Drance and Zulauf 1984) or the first two sessions (Wilensky and Joondeph 1984) from the analysis. Alternatively, it has been considered that any improvement in sensitivity with practise is counterbalanced by a decrease in sensitivity associated with a fatigue effect arising from the examination itself (Katz and Sommer 1986; Brenton et al 1986). Gloor et al (1981) in a retrospective study on a series of glaucomatous subjects with the Octopus, demonstrated the presence of a learning - effect of up to 2 dB magnitude out to an eccentricity of 30°. Conversely, Gramer et al (1986) with the Octopus and Kosoko et al (1986) with the Humphrey Field Analyser reported that in normals there was no effect of learning on perimetric sensitivity at these eccentricities. Interestingly, Schenkein (1987) reported

an increase across the entire visual field of patients with hemianopic visual field defects, following extensive stimulation of the defective hemi - field with bright flashing lights (400 asb luminance; 3° - 6° diameter). The visual fields were assessed with the Humphrey Field Analyser.

7.4 Aim of the investigation

Automated perimetry has minimized the influence of the perimetrist on the measurement procedure, however, the subjective components associated with the determination of any psychometric function still remain. These are manifested as the short - term and the long - term fluctuations (see section 1.5). It was hypothesized that one of the components of the long - term fluctuation might be the learning - effect which may contribute to either the homogeneous element which affects all parts of the field equally or the heterogeneous element which affects different areas of the field by differing amounts.

The purpose of the experiment was to investigate the improvement in differential light sensitivity arising from repeated examinations of the visual field by automated perimetry. In addition, the results were analysed in order to establish whether this effect was homogeneous or heterogeneous across the visual field.

7.5 Experimental work

The Octopus 201 automated perimeter was used as the instrument for the investigation (described in full in section 3.6.1). This was selected as it permits examination of the full visual field in one program.

7.5.1 Materials and methods

A homogeneous sample of young subjects was selected in order to provide the greatest potential for learning compatible with the constraints of a logistically viable experimental design. The sample

consisted of 10 clinically normal, emmetropic males (mean age 23.8 years; S.D. 2.8 years) with visual acuity of 6/5 or better in each eye. The subjects were free of ocular and systemic medication and naive to the purpose of the study, to perimetry and to other visual psychophysical techniques of measurement. Natural pupils were used throughout; the mean pupil diameter was 6.70 mm (S.D. 0.69 mm).

The full visual field of the right eye was examined with stimulus size III (projected diameter 0.431°) for a presentation time of 100 ms using Program 21. Each subject attended a total of 8 sessions comprising days 1 to 5 inclusive, and days 15, 16 and 44. Each examination was conducted at approximately the same time of day and consisted of a 10 minute adaptation period to the bowl luminance followed by the test program. The head was steadied with the head clamps and chin rest of the instrument and fixation was constantly monitored with the video camera. Subjects were encouraged to rest at intervals throughout the examination and advised if fixation was incorrect.

The results for each field plot were analysed in terms of the volume of the three - dimensional representation of sensitivity. This was determined using the Monte Carlo technique, a statistical sampling procedure based upon the binomial principle, for the evaluation of multiple integrals which are unsuited to classical mathematical methods. The application of this technique to visual field analysis has been discussed elsewhere (Wild et al In press). Volumetric analysis is an established method for analysing perimetric data (Suzumura et al 1985; Jaffe et al 1986) and was used since the derived index is dependent upon the areal dimensions of the field and can also be divided into aggregate parts.

7.5.2 Results

Figures 7.1a and 7.1b illustrate the change in volume sensitivity for each subject with consecutive examinations, where each symbol represents a single observer. Eight of the 10 subjects exhibited an increase in volume sensitivity over the 5 consecutive examinations (days 1 to 5). The sample could be divided into 3 distinct types with respect to the mode of their learning - pattern: those who

exhibited a large increase in sensitivity at the second examination (day 2) which then plateaued over the subsequent sessions (Type 1); those showing a gradual increase in sensitivity over each of the 5 sessions (Type 2); and those in whom no obvious improvement in sensitivity was demonstrated (Type 3). The increase in sensitivity persisted in the 8 subjects at the follow-up examinations on days 15, 16 and 44 and in five subjects the magnitude on each of these occasions was at a similar level to that recorded at day 5.

Figures 7.2a and 7.2b show the percentage change in volume sensitivity between examinations 1 and 5 for each subject for the superior and inferior hemi - fields and for the nasal and temporal hemi - fields excluding points lying on the vertical and horizontal mid - lines respectively. In 8 subjects, the sensitivity of the superior field increased to a greater extent than that of the inferior field.

Figures 7.3a and 7.3b illustrate the increase in perimetric sensitivity, expressed in dBs, as a function of eccentricity along the superior meridian and further confirms the trends revealed by the volumetric analyses illustrated in Figures 7.2a and 7.2b where sensitivity was shown to increase in the superior visual field with practise.

Figures 7.4a and 7.4b show the percentage change in volume sensitivity for each subject with increase in eccentricity over a series of five 15° annular zones. For 8 subjects the greatest increase in sensitivity with practise occurred beyond 30° eccentricity. At eccentricities greater than 60°, however, the magnitude of the elevation in sensitivity was reduced due to the lack of stimulus locations in this region, particularly in the superior field.

Figures 7.5a and 7.5b represent the change in sensitivity measured within the blindspot region at the 15° temporal point. Considerable inter - subject variation occurred in the depth of the blind spot. In 2 subjects the blindspot increased in depth with successive examinations over the five days; the majority of subjects, however, exhibited little change over this period. Interestingly, the 2 subjects who demonstrated no improvement in perimetric sensitivity with practise (Type 3), manifested the blindspot as 0 dBs at the first examination and at each of the subsequent examinations.

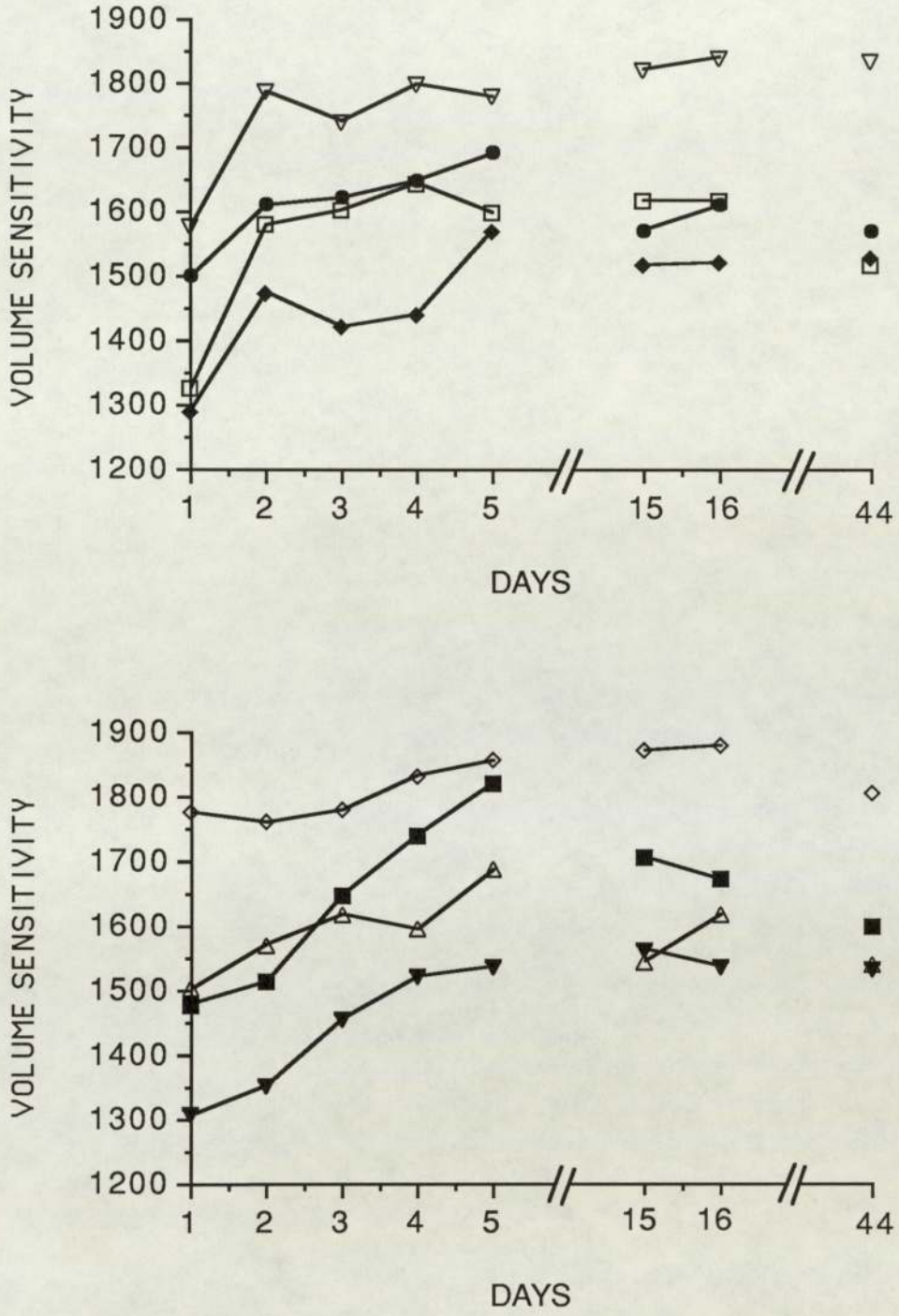


Fig. 7.1a Volume sensitivity (dB radians^2) with serial examination (days) recorded with the Octopus 201 automated perimeter. Top: 4 subjects who exhibit a large increase in sensitivity at the second examination which plateaus over the subsequent sessions (Type 1). Bottom: 4 subjects who exhibit a gradual increase in sensitivity over the five sessions (Type 2).

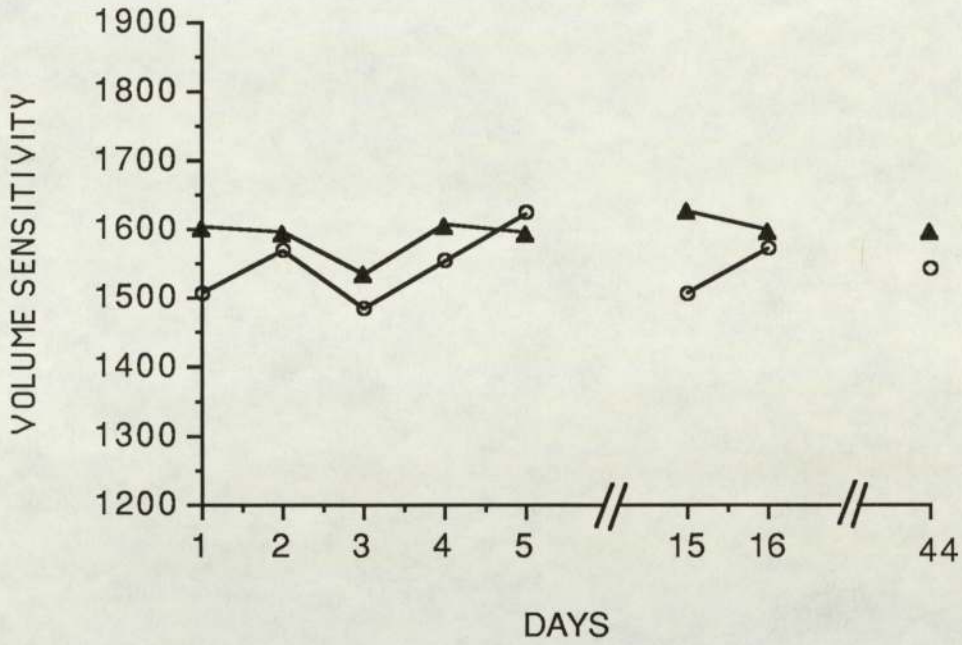


Fig. 7.1b Volume sensitivity (dB radians^2) with serial examination (days) recorded with the Octopus 201 automated perimeter for 2 subjects in whom no obvious increase in sensitivity with serial examination is demonstrated (Type 3).

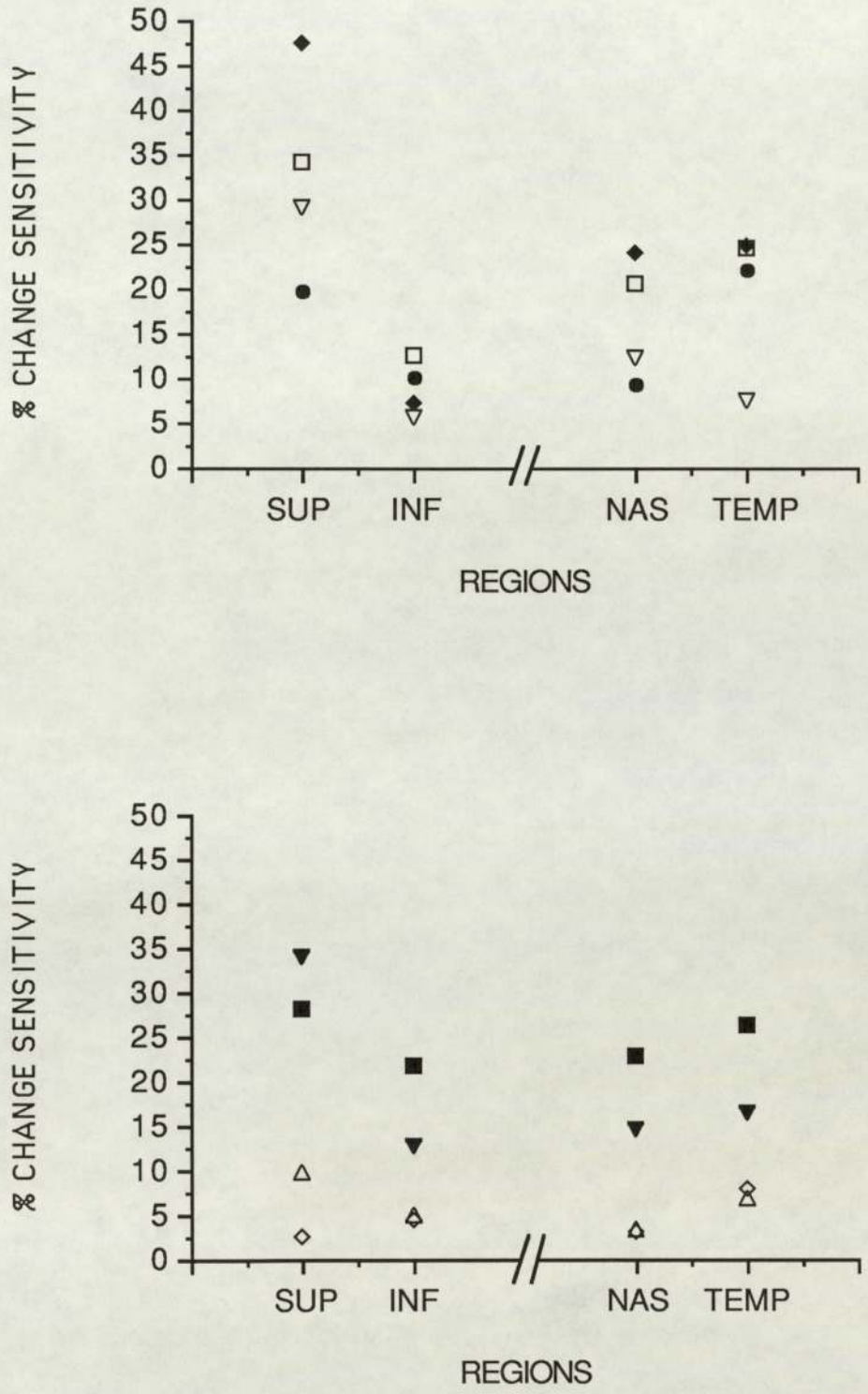


Fig. 7.2a The percentage change in volume sensitivity recorded with the Octopus 201 automated perimeter between the first and fifth examinations for the superior, inferior, nasal and temporal hemi - fields. Top: Type 1 subjects. Bottom: Type 2 subjects.

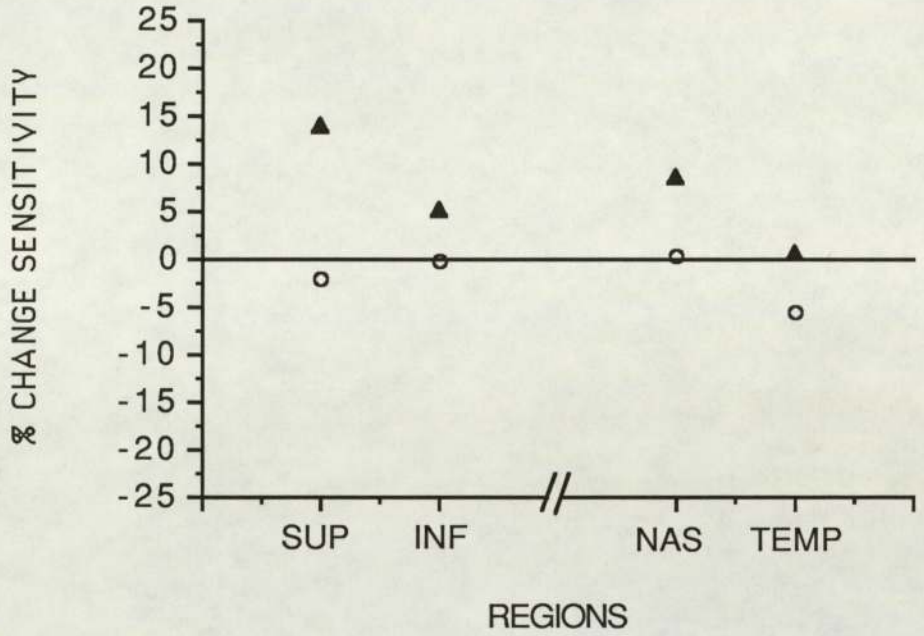


Fig. 7.2b The percentage change in volume sensitivity recorded with the Octopus 201 automated perimeter between the first and fifth examinations for the superior, inferior, nasal and temporal hemi - fields for Type 3 subjects

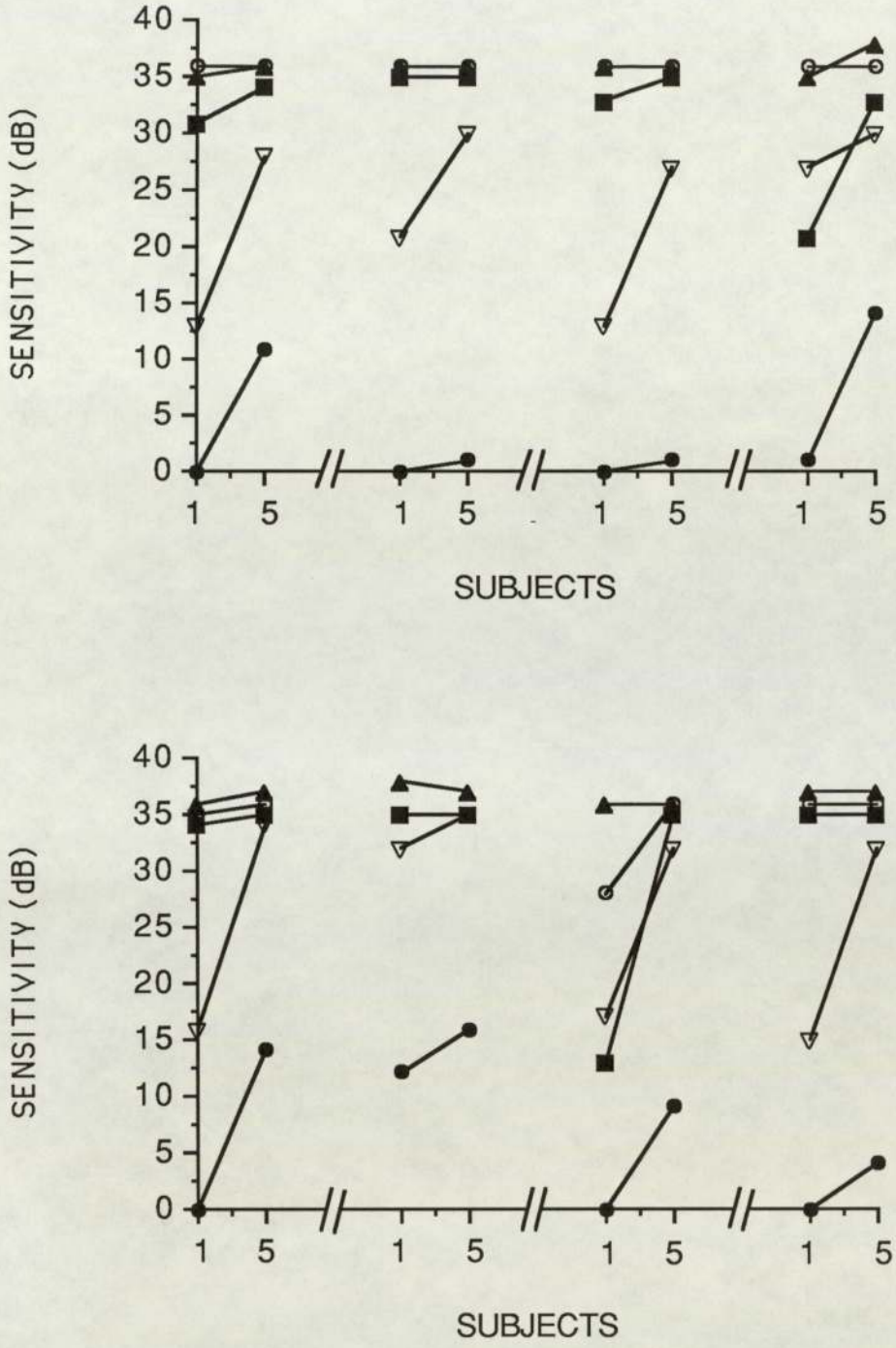


Fig 7.3a The change in sensitivity (dB) recorded with the Octopus 201 automated perimeter between the first and fifth examinations for the superior meridian as a function of eccentricity (0° filled triangles, 15° open circles, 30° filled squares, 45° open inverted triangles, 60° filled circles). Top: Type 1 subjects. Bottom: Type 2 subjects.

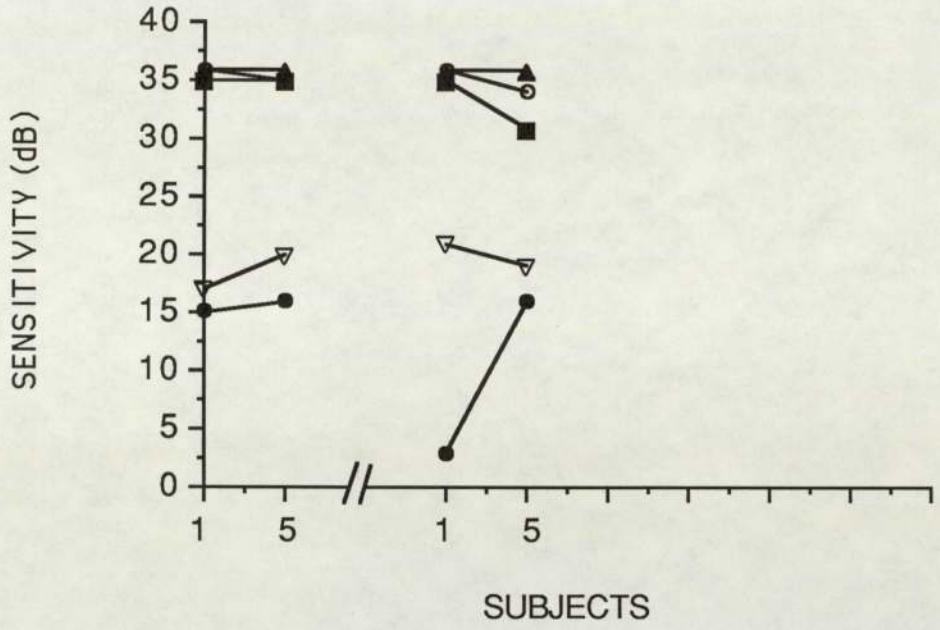


Fig 7.3b The change in sensitivity (dB) recorded with the Octopus 201 automated perimeter between the first and fifth examinations for the superior meridian as a function of eccentricity (0° filled triangles, 15° open circles, 30° filled squares, 45° open inverted triangles, 60° filled circles) for Type 3 subjects.

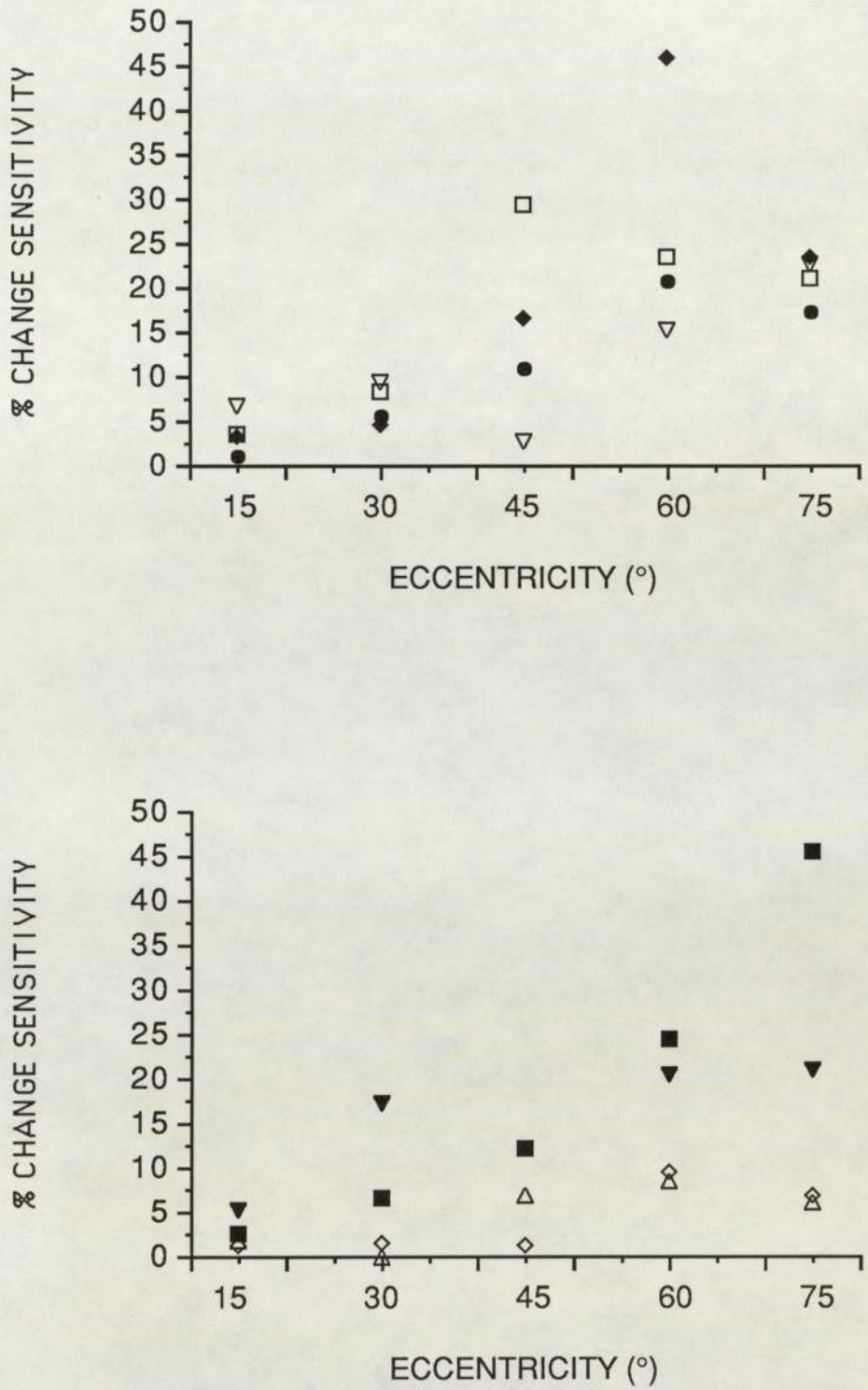


Fig. 7.4a The percentage change in volume sensitivity recorded with the Octopus 201 automated perimeter between the first and fifth examinations for the five 15° annular zones. Top: Type 1 subjects. Bottom: Type 2 subjects.

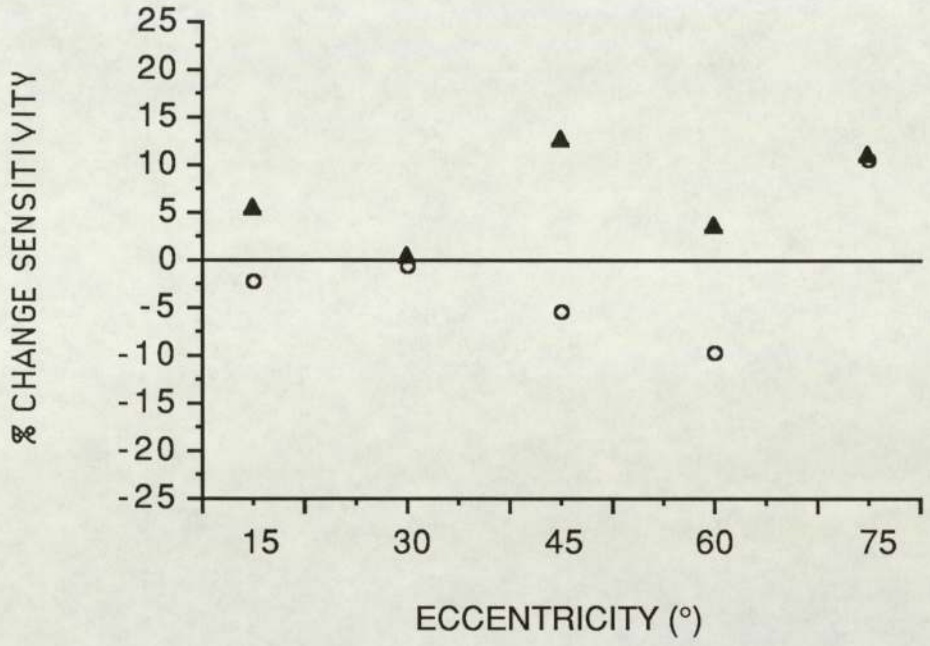


Fig. 7.4b The percentage change in volume sensitivity recorded with the Octopus 201 automated perimeter between the first and fifth examinations for the five 15° annular zones for Type 3 subjects.

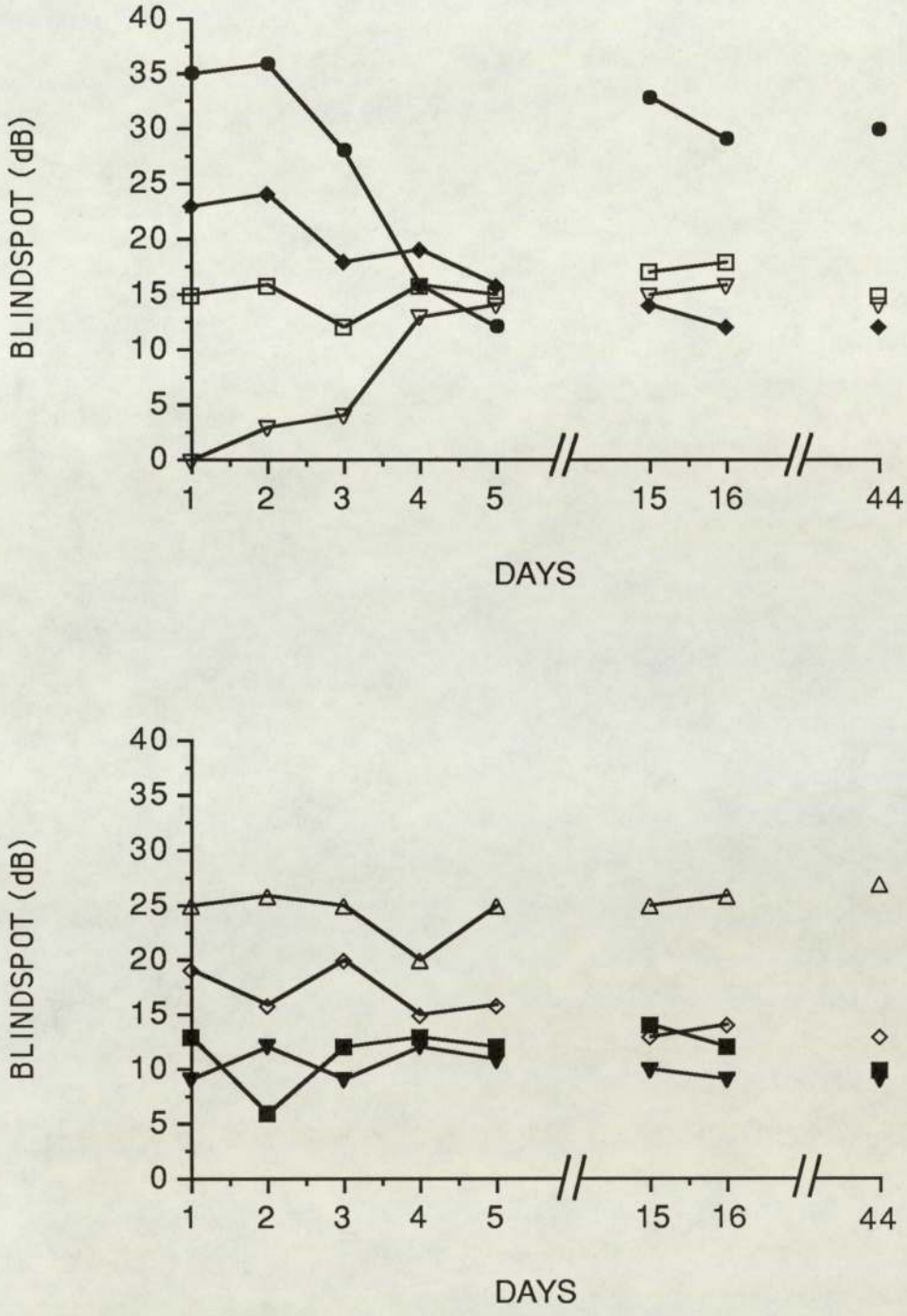


Fig 7.5a The variation in sensitivity (dB) of the blindspot at the 15° temporal stimulus location with serial examination (days). Top: Type 1 subjects. Bottom: Type 2 subjects recorded with the Octopus 201 automated perimeter.

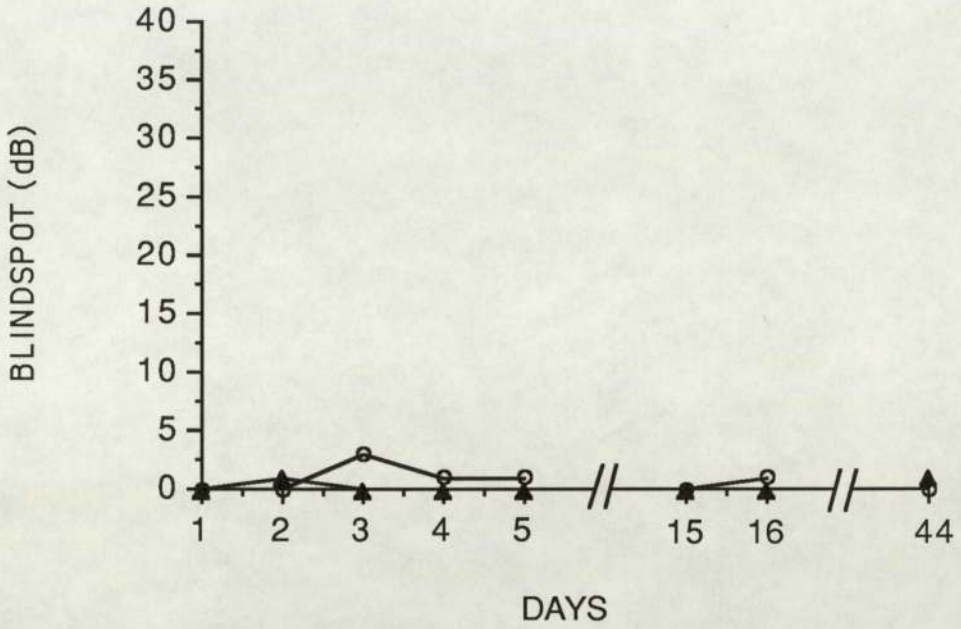


Fig 7.5b The variation in sensitivity (dB) of the blindspot at the 15° temporal stimulus location with serial examination (days) for Type 3 subjects recorded with the Octopus 201 automated perimeter.

The variability in the perimetric response during each examination, expressed as the root mean square fluctuation (R.M.S.) derived from the double threshold determination at each of 10 individual test locations, is illustrated in Figures 7.6a and 7.6b for each subject with consecutive examination. The R.M.S. value decreased in 9 subjects over days 1 to 5.

Figures 7.7a and 7.7b illustrate the variation in the mean number of false - positive responses for each subject type with serial examination. A false - positive response is recorded when a subject responds positively when no stimulus is presented.

Figures 7.8a and 7.8b illustrate this relationship for false - negative responses. A false negative - response is recorded when the subject fails to respond to a stimulus even though the stimulus luminance is well above the previously determined threshold. The variation in the mean number of false - negative and false - positive responses does not demonstrate any particular trend with serial examination.

7.5.3 Discussion

The increase in differential light sensitivity with serial examination and the retention of this effect (Figures 7.1a and 7.1b) is in agreement with the findings of Aulhorn and Harms (1967) for static manual perimetry. Considerable inter - subject variation was present in both the initial and the final sensitivity volume for the 8 subjects who exhibited a learning - effect. Interestingly, the initial and final sensitivity volumes of the Type 3 subjects were at the upper end of the range of sensitivity volumes measured for the sample as a whole. This finding suggests that Type 3 subjects performed at their optimal level at the initial session.

In 8 subjects the sensitivity of the superior field increased to a greater extent than that of the inferior field (Figures 7.2a and 7.2b). The ratio of volume sensitivity between the superior and inferior fields for these 8 subjects increased from a mean of 0.65 (S.D. 0.07) on day 1 to a mean of 0.74 (S.D. 0.03) on day 5. The low S.D.s indicate the relative constancy of this relationship between subjects in both

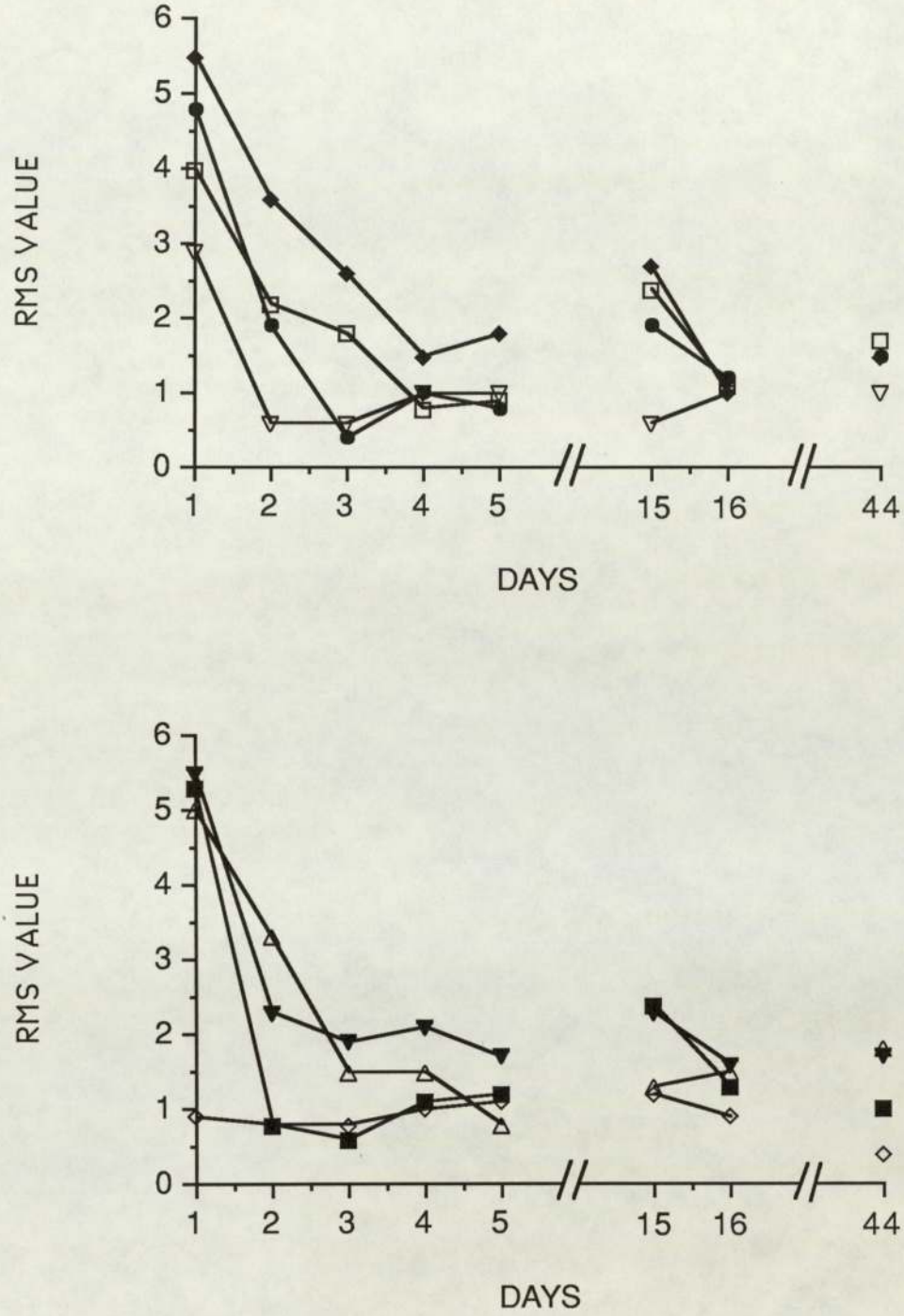


Fig 7.6a The variation in magnitude of the root mean square (R.M.S.) value with serial examination (days) recorded with the Octopus 201 automated perimeter. Top: Type 1 subjects. Bottom: Type 2 subjects.

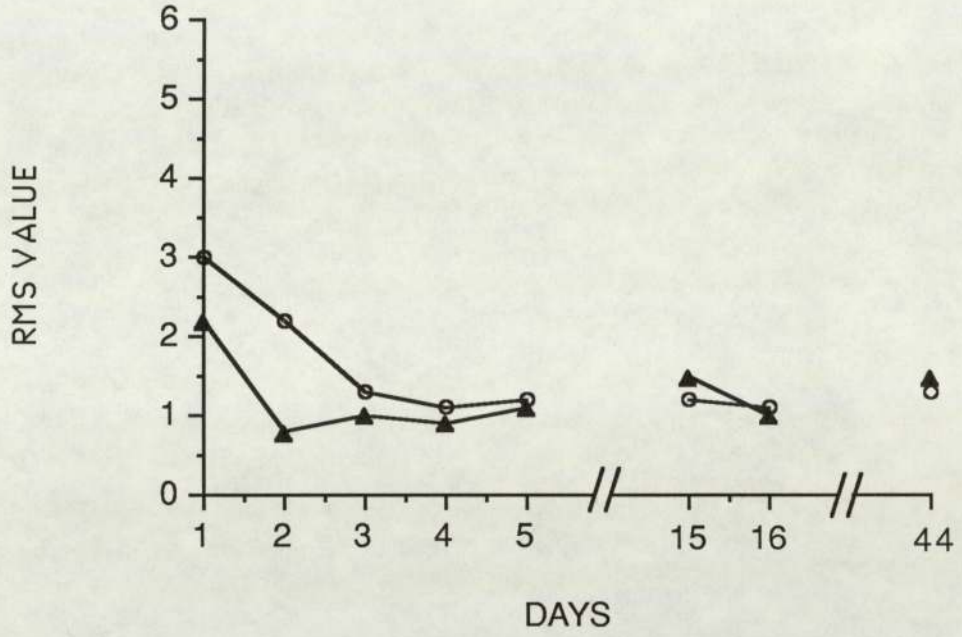


Fig 7.6b The variation in magnitude of the root mean square (R.M.S.) value with serial examination (days) recorded with the Octopus 201 automated perimeter for Type 3 subjects.

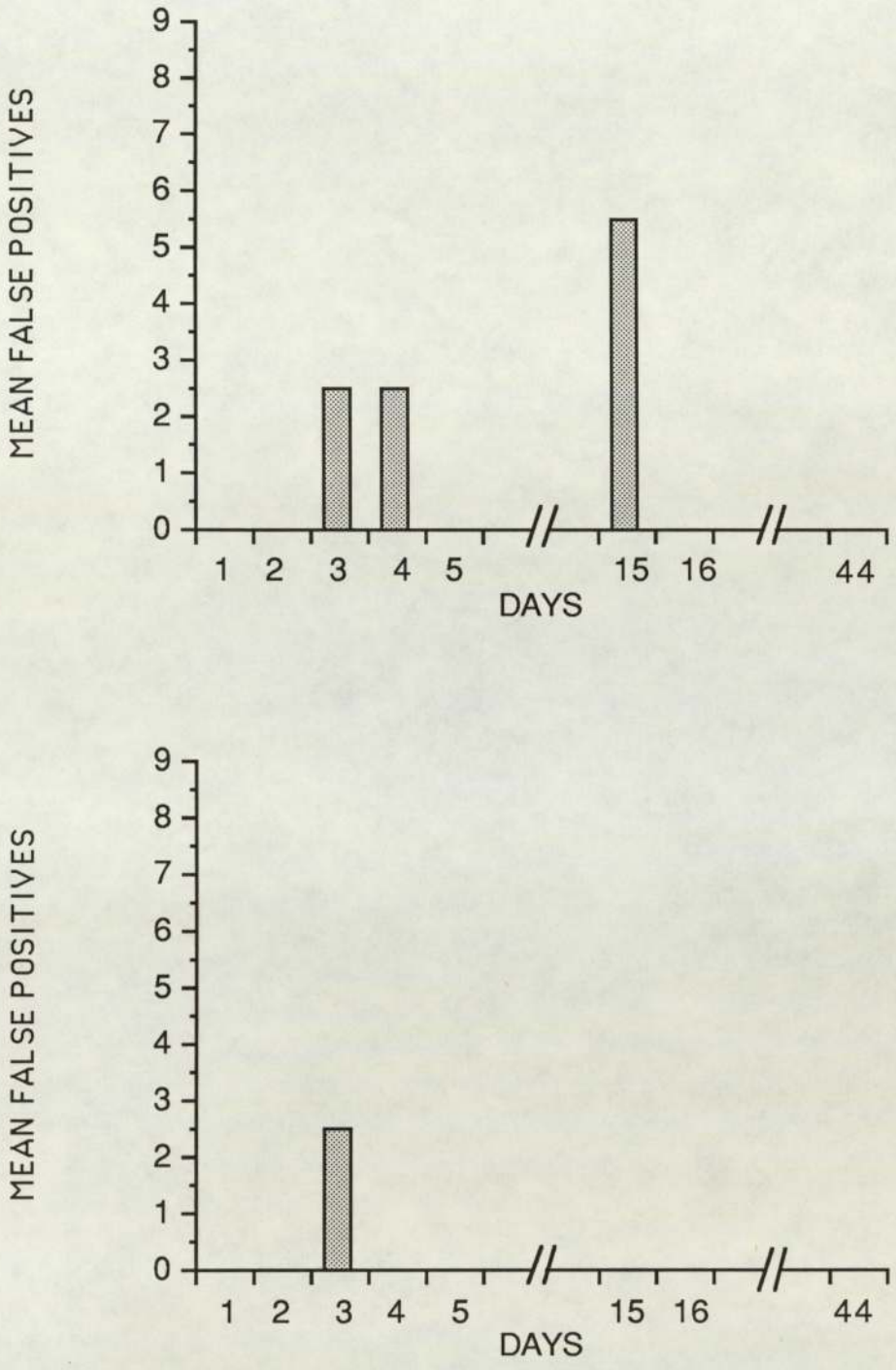


Fig. 7.7a The variation in the mean number of false - positive responses with serial examination (days) recorded with the Octopus 201 automated perimeter. Top: Type 1 subjects. Bottom: Type 2 subjects.

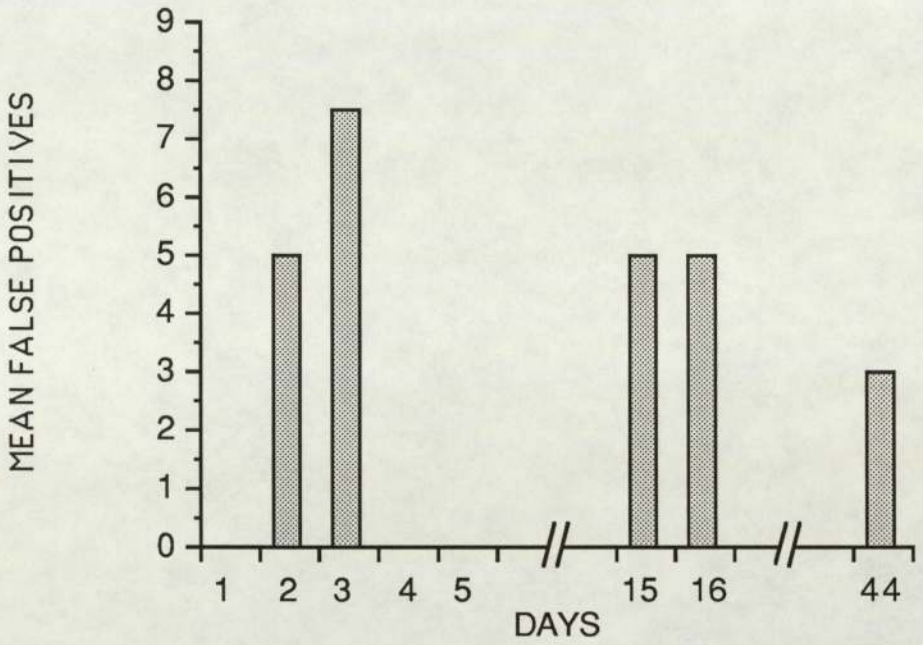


Fig. 7.7b The variation in the mean number of false - positive responses with serial examination (days) recorded with the Octopus 201 automated perimeter for Type 3 subjects.

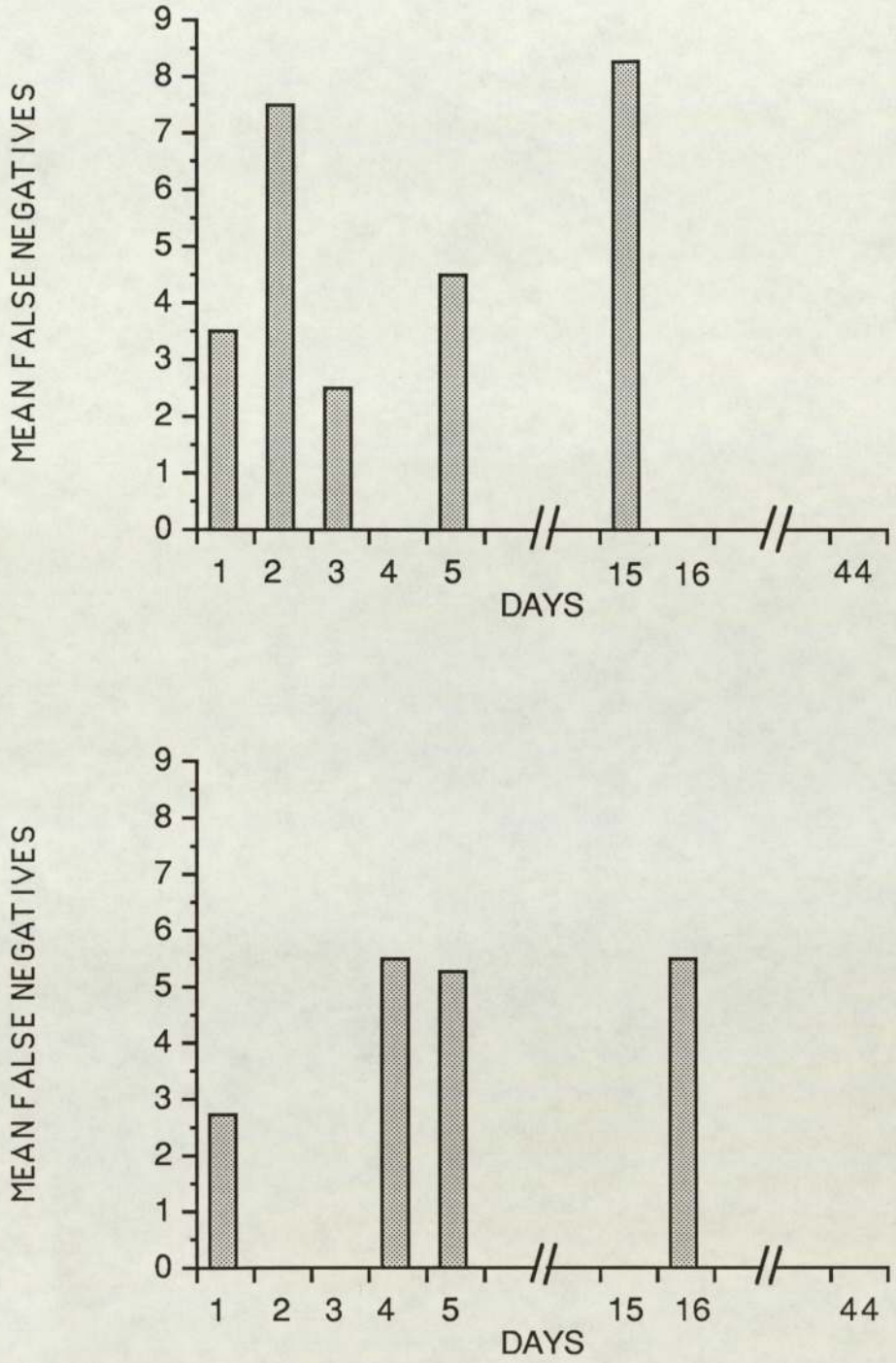


Fig. 7.8a The variation in the mean number of false - negative responses with serial examination (days) recorded with the Octopus 201 automated perimeter. Top: Type 1 subjects. Bottom: Type 2 subjects.

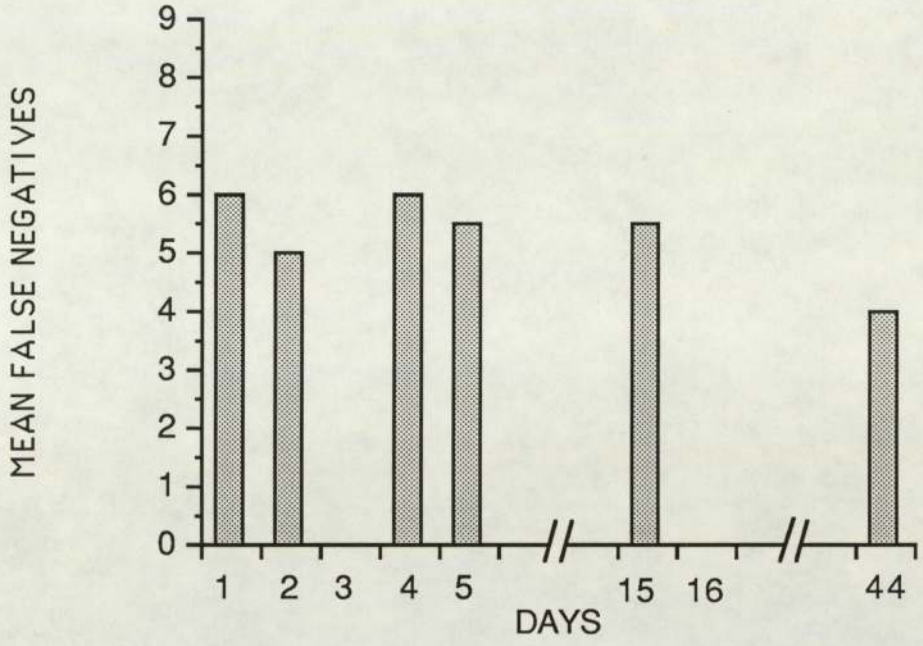


Fig. 7.8b The variation in the mean number of false - negative responses with serial examination (days) recorded with the Octopus 201 automated perimeter for Type 3 subjects.

the naive and the experienced states. The corresponding ratio for the nasal and temporal hemi - fields yielded an identical mean value of 0.45 on both day 1 and day 5 (S.D.s 0.31 and 0.28).

The greatest increase in sensitivity occurred between the 30° annulus and the 60° annulus. The interaction effect of hemi - field and annulus was not analysed owing to the limited number of common data points out to an eccentricity of 30°. The greater increase in sensitivity with increasing eccentricity is in accord with Low's (1946) concept of the periphery as an unpractised sensory area. Indeed, as previously discussed (section 7.3) a learning - effect has not been found for the central field in the retrospective study of Gramer et al (1986) with the Octopus and by Kosoko et al (1986) with the Humphrey Field Analyser, although a learning - effect was reported by Gloor et al (1981) for glaucomatous patients using the Octopus.

The decreased spread of results associated with the threshold response (Figure 7.6a and 7.6b) indicates a greater consistency in response for all subject types. This finding is in agreement with the manual perimetric results of Aulhorn and Harms (1967) and of Greve (1973) on the frequency of seeing curves of trained and untrained observers and also with the automated perimetry findings of Parrish et al (1984) Rabineau et al (1985) and Gramer et al (1986). Surprisingly, the number of false - negative and false - positive responses, which is also a measure of the subjects reliability, did not decrease with practise but varied without following any particular trend over the serial examinations for all subjects in the sample, although the Type 3 subjects made more false - negative and false - positive responses than those in the other groups. Indeed, this latter result is unexpected since the R.M.S. values of the Type 3 subjects are consistently small.

The improvement in sensitivity with practise may arise from a change in the subject's criterion as to what constitutes a "seen" response. The heterogeneous nature of the learning effect, however, tends to discount this theory. The greater increase in sensitivity of the superior field may arise from the patient learning to consciously raise the upper lid; an increase in vertical visible iris diameter was not evident, however, from observations of the video monitor during the examination. Interestingly, the superior region of the central field exhibits the highest short - term fluctuations

(Flammer, Drance, Fankhauser and Augustiny 1984; Jaffe et al 1986) and is influenced by age to a greater extent than the inferior field (Haas et al 1986; Jaffe et al 1986). The improvement in the superior field may alternatively be accentuated by the relatively small improvement in the inferior field which may be functioning at its optimum level. This latter hypothesis is consistent with the fact that in the primary position of gaze, the horizontal plane of the horopter passes through the feet.

7.6 Conclusions

The results demonstrated that sensitivity measured with the Octopus 201 automated perimeter exhibits a potential to improve heterogeneously across the visual field with serial examination. This effect is marked beyond an eccentricity of 30° particularly in the superior field. The extent of this effect can be expected to vary in the population as a function of the alteration in the general learning curve with age, but should always be considered when monitoring changes outside an eccentricity of 30°. The exclusion of the results from the first examination in serial field investigation may be acceptable in the case of those who exhibit Type 1 learning, but not for those with Type 2 learning where the potential to learn beyond an eccentricity of 30° remains until at least the fifth examination. The retention of the increased sensitivity beyond the fifth examination indicates that such an effect must also be considered in serial field analysis since the improvement was sustained over the respective follow - up examinations.

8. THE INFLUENCE OF PERIPHERAL REFRACTIVE CORRECTION ON THE PERIMETRIC PROFILE

8.1 Introduction

The peripheral dioptrics of the eye have been found to exhibit a significant error of refraction by experimental (Feree et al 1931; Rempt et al 1971; Millodot and Lamont 1974b Millodot 1981) and mathematical means (Bennett 1951; Le Grand 1967; Lotmar and Lotmar 1974; Dunne and Barnes 1987). The peripheral refractive error arises from the presence of oblique ray astigmatism, which is the difference between the tangential and saggital surface of the optical system of the eye (Sturm's interval) and increases with increasing eccentricity (Feree et al 1931; Millodot and Lamont 1974b; Millodot 1981). The refractive status of the observer, either myopic, hypermetropic or emmetropic, determines the type of peripheral oblique astigmatism manifested (either compound myopic, compound hypermetropic or mixed astigmatism) but does not influence the magnitude of the peripheral astigmatism (Millodot 1981).

The majority of the experimental determinations of peripheral astigmatism have been confined to the horizontal meridian of the eye, and have used objective retinoscopic techniques to determine refraction as a function of eccentricity. Millodot and Lamont (1974b) employed both subjective and objective methods (using an optometer and retinoscopy), and reported good qualitative agreement between the two techniques. The calculated values of oblique astigmatism have been derived from estimations based upon schematic eye models possessing spherical surfaces. Interestingly, the magnitude of oblique astigmatism derived by calculation has been reported to be higher than that determined experimentally (Bennett 1951; Le Grand 1967). Le Grand (1967) suggested that this discrepancy arose due to peripheral flattening both of the cornea and of the posterior lens surface or to the layered structure of the crystalline lens; Millodot and Lamont (1974b), however, attributed the discrepancy to variations in refractive index and curvature towards the periphery of the crystalline lens.

8.2 Influence of central refractive correction on visual function

Central visual functions are sensitive to optical defocus, however, the magnitude of this effect is dependent upon the configuration of stimuli employed.

Contrast sensitivity, measured with sinusoidal grating stimuli, is depressed by defocus of the retinal image and the tolerance to defocus is found to decrease with increasing spatial frequency (Campbell and Green 1965; Charman 1979; Kay and Morrison 1987). When the pupil size is small, however, the effects of blur became less significant at all spatial frequencies (Campbell and Green 1965; Charman 1979; Kay and Morrison 1987). Indeed, Kay and Morrison (1987) demonstrated at mesopic adaptation levels, that contrast sensitivity was reduced by half for each dioptre of defocus (up to 4 D) at all but the lowest spatial frequencies.

Visual acuity measured with high contrast Snellen letters is markedly depressed by optical defocus (Borish 1970; Westheimer 1979). The rate of degradation of hyperacuity (step displacement threshold of a line) with optical defocus is, however, significantly slower than that of both stereoacuity and Snellen visual acuity (Westheimer 1979). This finding has been interpreted as illustrating the differences in resolution (Snellen acuity) and localization (hyperacuity) mechanisms, where the former is dependent upon blur and the latter is not (Westheimer 1979). Similarly, the oscillatory movement displacement threshold, an alternative hyperacuity test, which determines the smallest amplitude of oscillation which gives rise to the perception of movement, is also insensitive to the effects of blurring and of diffusing lenses (Whitaker and Buckingham 1987).

Critical flicker frequency fusion (C.F.F.) has been reported to be independent both of variations in the steady state accommodation response (Berger and Mahneke 1953) and defocus of the retinal image (Hylkema 1944; Ong and Wong 1971). Interestingly, Jennings and Charman (1981b) demonstrated that though large (50') flickering sources were unaffected by optical defocus, small (8') sources were, such that the axial C.F.F. measured with these stimuli was halved by 2 D of blur.

The amplitude of the pattern electroretinogram (P.E.R.G.) has been reported to decrease with optical blur; the magnitude of the depression is dependent upon the spatial frequencies used for assessment (Vaegan et al 1982; Hess and Baker 1984; Persson and Wanger 1984). Similarly, the amplitude of the visually evoked potential (V.E.P.) is also decreased by optical distortion and by refractive error (Millodot and Riggs 1970).

8.3 Influence of peripheral refractive correction on visual function

The poor peripheral dioptrics of the eye represent a potential limiting factor for most visual functions which generally become relatively depressed with increasing peripheral angle from fixation. Millodot et al (1975), using Landolt rings and sinusoidal gratings, reported that there was no difference between peripheral visual acuity measured with or without correction of the peripheral refractive error. The peripheral refraction was measured with an Arnulf retinofocimeter. These findings were subsequently confirmed by Rempt et al (1976) who assessed peripheral refraction using retinoscopy. An alternative approach, consisting of the measurement of peripheral acuity by means of an interferometric technique was described by Green (1970b). In this way, interference fringes were formed directly on the retina, thus by - passing the optics of the eye. Green (1970b) demonstrated that although the optical aberrations of the eye produce a depression of visual acuity at eccentricities out to an eccentricity of 5°, they had no effect at locations more peripheral to this. Conversely, Frisen and Glansholm (1975) found that peripheral acuity measured with an interferometric technique was consistently higher than that recorded with sinusoidal gratings imaged onto the retina by the dioptrics of the eye itself. Frisen and Glansholm (1975) suggested that the discrepancies between the two studies may have arisen from technical limitations and the lack of significant oblique astigmatism in the two subjects of Green's (1970b) study.

Correction of peripheral refractive error, determined by dynamic retinoscopy, has been shown to improve peripheral motion detection thresholds and to decrease inter - individual differences (Leibowitz et al 1972; Johnson and Leibowitz 1974). Similarly, absolute sensitivity to briefly exposed stimuli is increased, and variability in response is decreased, with the correction of

peripheral astigmatism (Ronchi 1971). In addition, Ronchi (1971) reported that the correction of peripheral refraction increased both the total temporal summation time and the slope of the luminance - time relationship, he conjectured that the correction of peripheral refraction decreased the size of the minimal blur disc to below that of the retinal receptive fields. Interestingly, the peripheral refraction in Ronchi's (1971) study was determined subjectively with the aid of crossed cylinders and was thus dependent upon complete relaxation of the subjects accommodation. Conversely, Jennings and Charman (1981b) reported that the C.F.F. is insensitive to spherical and cylindrical blur at eccentricities between 10° and 40° in the nasal and temporal fields.

The finding that the correction of peripheral refractive error improves both peripheral motion detection and absolute sensitivity whilst peripheral visual acuity is unaffected poses some problems in interpretation. Johnson et al (1976) attempted to explain this discrepancy by proposing that there are two modes of processing of visual information in the visual system, namely, an identification and a localization mechanism.

8.4 Influence of central refractive correction on perimetric thresholds

The depression of perimetric thresholds by defocus within the central regions of the visual field has been reported (Harms 1950; Sloan 1961; Aulhorn and Harms 1972; Greve 1973). The effect of defocus induced by positive lenses on manual kinetic perimetric thresholds for Goldmann stimulus size II_{2e} resulted in a constriction of the isopter (Serra 1983). Similarly, the thresholds measured out to an eccentricity of 30° by static manual perimetry have been found to be markedly reduced with increasing optical blur for Goldmann stimulus size I (Fankhauser and Enoch 1962) and for Goldmann stimuli sizes I and II (Sloan 1961). The relationship between increase in optical defocus and decrease in differential light sensitivity at the fovea was reported to be a function of stimulus size by Ogle (1961), where larger stimulus sizes are relatively insensitive to defocus. Ogle (1961) stated that the findings related to the form of Ricco's law of spatial summation, whereby complete spatial summation occurs provided the blurred image of the stimulus is smaller than the critical size; the latter has, as described in section 3.6.4, been related to the size of the receptive fields

(Glezer 1965; Levi and Klein 1987). Atchison (1987) reported that for stimuli greater than or equal to Goldmann size III, that defocus had a minimal effect on manual static perimetric thresholds. Interestingly, Weinreb and Perlman (1986) reported that perimetric thresholds measured out to an eccentricity of 6° with the Octopus, were significantly depressed by defocus when measured with stimulus size III. The subjects in the latter study were, however, under cycloplegia throughout the investigation, whereas other studies relating perimetric sensitivity and defocus have utilized natural pupils. Indeed, when pupil size is increased as in cycloplegia, the ocular depth of focus is decreased since the size of the retinal blur circles increases, thus the tolerance to defocus is reduced (Campbell 1957; Ogle and Schwartz 1959; Tucker and Charman 1975; Charman and Whitefoot 1977).

Optical defocus exerts less influence on perimetric thresholds as peripheral angle increases (Sloan 1961; Fankhauser and Enoch 1962; Maguire 1971; Atchison 1987). Moreover, Benedetto and Cyrlin (1985) using automated static perimetry reported that sensitivity at fixation is depressed to a greater extent by optical defocus than at peripheral locations measured with stimulus size III. Interestingly, although the mean defect values of the G1 program of the Octopus (which measures sensitivity out to an eccentricity of 26° with stimulus size III) were found to increase with optical blur, other visual field indices such as corrected loss variance, skewness, short - term fluctuations and reliability were not significantly affected (Goldstick and Weinreb 1987). It is significant to note that none of the studies relating optical defocus and the accompanying perimetric attenuation report any depression in perimetric sensitivity with optical defocus beyond 30°. Interestingly, the tolerance to defocus has been shown to decrease with decrease in adaptation level (Johnston et al 1976).

8.5 Influence of peripheral refractive correction on perimetric thresholds

Fankhauser and Enoch (1962) demonstrated that out to an eccentricity of 30°, the retina is sensitive to blur. They found that for a given retinal location, there was an optimum lens which provided the lowest increment threshold. The study was conducted with manual static perimetry using a Goldmann perimeter for stimulus size I. Indeed, although this study is consistently cited as having assessed the effect of peripheral refraction on increment thresholds, correction of the best sphere

rather than correction of peripheral refraction was achieved, as only spherical lenses were employed. It has been suggested that asymmetry of peripheral refraction can produce refraction scotomata (Greve 1973). These have been measured with the Friedmann Visual Field Analyser (Greve and Verduin 1972) and the manual Tubinger perimeter (Aulhorn and Harms 1972) and generally take the form of bi - temporal refraction scotoma (field defects in the temporal regions of both eyes).

8.6 Aim of the investigation

The investigation was stimulated by the absence of any data relating the influence of correction of peripheral refractive error on differential light sensitivity.

8.7 Experimental work

Perimetric sensitivity was assessed using the Octopus 201 automated perimeter (described in section 3.6). This perimeter was selected since it provides the facility to vary stimulus size and, by the use of the SARGON program (described in section 1.6.3), permits repeated measurement of sensitivity at user defined stimulus locations.

The peripheral astigmatism was assessed using the commercially available Canon Autoref R - 1, an infra - red optometer which has been used in studies of accommodative function (McBrien and Millodot, 1985; Bullimore et al 1986) and is capable of producing an accurate measure of refractive status at approximately 1 s intervals. An infra - red optometer was selected in order to minimize the influence of pupil size changes on the measurements. Accurate and repeatable values of oblique astigmatism have been obtained using a modification of the standard instrument; the values of oblique astigmatism were similar to those obtained with the Hartinger coincidence optometer (Dunne personal communication 1987). The latter instrument is similar to those used in the studies of Feree et al (1931) and Millodot (1981).

8.7.1 Materials and methods

The sample consisted of 10 clinically normal, emmetropic subjects (mean age 22.4 years; S.D. 2.5 years), who were experienced observers in automated perimetry and in general psychophysical investigative procedures. Visual acuity was 6/5 or better and subjects were free of any systemic or ocular medication.

Ocular astigmatism was measured at 0°, 20° and 40° along the horizontal temporal meridian (temporal retina) of the right eye using the Canon Autoref R - 1. The Canon Autoref R - 1 has the unique feature of permitting an open binocular view of a distant target, thus eliminating instrument myopia. It is a table mounted instrument that incorporates a power range of +/-15 D sphere and +/-7 D cylinder, in steps of 0.12 D, and measures the cylindrical component in 1° increments. To reproduce the working conditions of the Octopus 201 automated perimeter, several modifications to the standard apparatus were made (Figure 8.1). The fixation targets, which consisted of a series of letters (equivalent to 6/6 Snellen acuity), were mounted upon a matt surface, semi - circular arc of radius 50 cm which was interposed between the subject and the instrument. The luminance of the arc was 1.27 cd m^{-2} (4 asb) to match the bowl luminance of the Octopus 201 automated perimeter. The illumination was regulated by a diffusing lamp and measured prior to each session using a spot photometer.

The patient was instructed to steadily fixate each target in turn, whilst 10 consecutive readings of the sphero - cylindrical power of the eye were taken. The order of eccentricities measured was randomized throughout the sample. The peripheral refraction of each subject was expressed, in sphero - cylindrical form, as the mean of the 10 measurements.

Pupil size was measured, prior to, and at intervals throughout the examination, using the monitor of the Canon Autoref R - 1. Measurement resolution was 0.10 mm, and the pupil size expressed as the mean of the readings taken throughout the assessment.

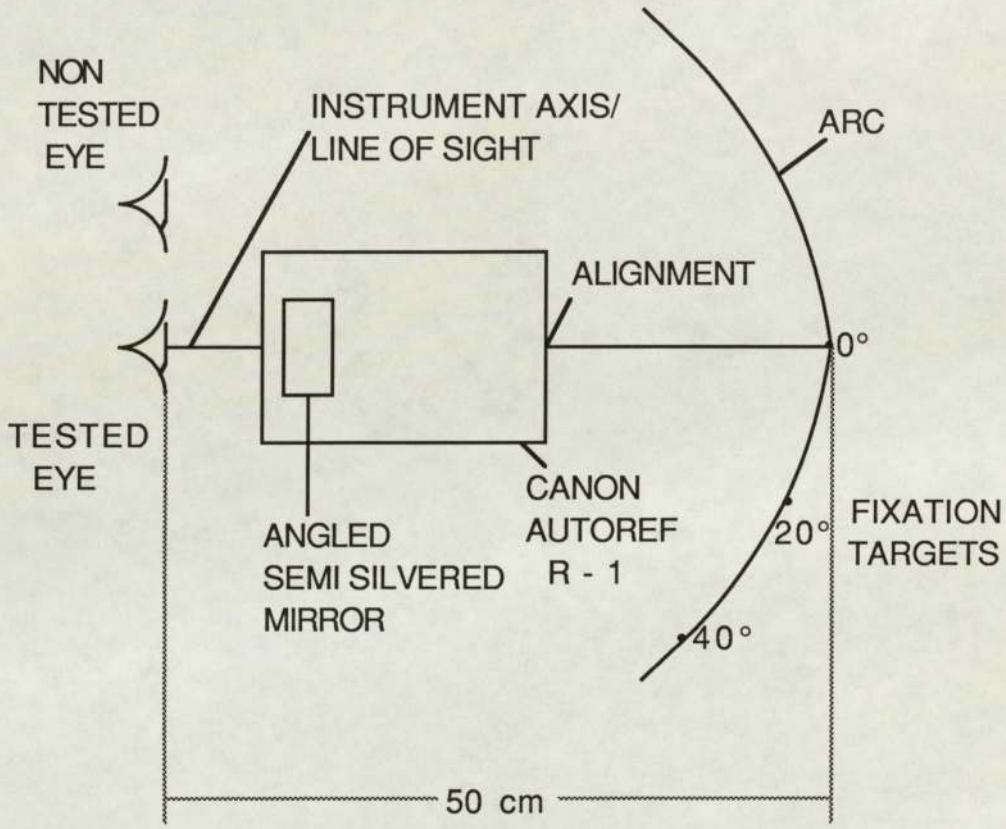


Fig. 8.1 Schematic diagram of the experimental set - up of the Canon Autoref R - 1 used to measure peripheral astigmatism at eccentricities of 0°, 20° and 40° along the horizontal meridian of the nasal field of the right eye.

Trial lenses were glazed to the mean refraction of each subject at each of the 3 eccentricities less an allowance of 2 D. It was recognized that for the dioptric distance of 2 D employed in the study, the perfect observer would accommodate by 2 D (Morgan 1944). The real observer, however, exhibits an accommodative lag, i.e. an under - accommodation of the visual system, for near targets (Morgan 1944; Nadell and Knoll 1956; Heath 1956). For the stimuli employed in the study the under - accommodation would be of order of 0.25 D (Morgan 1944); this value, however, varies in magnitude between individuals (Morgan 1944; Denieul 1982). The accommodative lag is believed to result from the antagonistic action of sympathetic and parasympathetic innervation to accommodation (Cogan 1937; Morgan 1944; Toates 1972). Furthermore, McBrien and Millodot (1985) reported that the Canon Autoref R - 1 overestimates the power of the sphere and of the cylinder by -0.25 D compared to subjective findings. McBrien and Millodot (1985) attributed the discrepancy between the spherical component measured with the Canon and that determined subjectively, to the fact that subjective techniques aim to obtain an end - point of the maximum plus lens consistent with best vision. The subjective method thus relaxes all of the subject's accommodation, whereas the Canon may not. Thus the observers underaccommodate by 0.25 D and the Canon overestimates the power of the sphere and cylinder by - 0.25 D. The central refractive findings for each subject were glazed in full aperture trial lenses. The refractive findings at 20° and 40° were glazed such that only the nasal half of the lens was employed. The negative cylinderical axis was marked with reference to the vertical edge of the lenses. One plano full aperture and one plano vertical half lens were also glazed, to assess the perimetric sensitivity without refractive correction centrally and peripherally respectively.

Perimetric sensitivity of the right eye of each subject was measured for stimulus sizes 0 and III (projected diameters of 0.054° and 0.431°). Three SARGON programs were written, in which sensitivity within each program was measured 4 times at the given selected eccentricity (0°, 20° or 40°) and twice at 15° above and 15° below this eccentricity along the horizontal nasal meridian (temporal retina) of the right eye. Sensitivity was measured at the stimulus locations above and below the horizontal meridian in order to prevent the subject anticipating where the stimulus would appear, as would have occurred had one location been repeatedly measured during a single

examination. The results from these latter locations were not included in data analysis. Each of the SARGON programs was of approximately 3 minutes duration.

Each subject attended one perimetric session which consisted of 12 presentations of the SARGON Program. Each of the 3 designated eccentricities was examined with 4 programs: once with the correcting lens before the eye and once with a plano lens before the eye for each of the two stimulus sizes. The trial lenses were suspended at a 12mm vertex distance corresponding to that of the Canon Autoref R - 1, using a modified ocular of a standard trial frame. The vertical axis of each lens was set at 90°. The ocular had been adapted and mounted in the perimeter bowl, such that it could be rotated vertically around it's axis. For the peripheral stimulus locations, the half lenses were set perpendicular to the stimulus location, with the glass region of the lens in the nasal half of the patients visual field. This permitted visualization of the peripheral stimuli through the appropriate corrective lens, whilst the central fixation target was visualized, without being blurred by the peripheral refractive correction, through the empty half of the lens.

The order of program, stimulus size and status of correction was randomized throughout the sample. The patient was allowed to rest at frequent intervals during the perimetric examination to avoid fatigue. The head was steadied with the head clamps and chin bar of the instrument and fixation was monitored throughout the examination. The duration of the perimetric examination was approximately 45 minutes in total, including rest periods.

Pupil size was measured prior to, and at intervals throughout, the perimetric examination using the video monitor of the Octopus, and was expressed as the mean of the readings taken. The measurement resolution for pupil size was 0.5 mm. It was essential to the validity of the results, that the pupil size during the perimetric examination was comparable to that during the measurement of peripheral astigmatism, since the latter varies as a function of pupil size (Van Meeteren 1974; Koojiman 1983; Dunne and Barnes 1987) whereby peripheral astigmatism increases with increase in pupil size.

8.7.2 Results

Table 8.1 illustrates the mean and standard deviation of pupil size for each subject, measured for the Canon Autoref R - 1 and for the Octopus 201. The pupil sizes for each subject are of a similar order for both examinations, as further illustrated in Figure 8.2, where the pupil sizes measured during the examination with the Canon Autoref R - 1 and with the Octopus are plotted against one another. There is a linear relationship between the 2 functions ($y=0.94x + 0.35$)

Table 8.2 illustrates the group mean values of peripheral refraction (in sphero - cylindrical form) for the 10 subjects as a function of eccentricity. Astigmatism increases with peripheral angle and reached a maximum value of 6.50 D for one subject at 40°.

Table 8.3 represents the group mean proportionate change in sensitivity with correction of the peripheral refractive error with respect to sensitivity recorded without correction, as function of eccentricity for each of the two stimulus sizes. The magnitude of the proportionate change in sensitivity is less than 1.5 dB, which is only 0.5 dB above the measurement resolution of the Octopus.

Figures 8.3 - 8.4 illustrate the relationship between differential light sensitivity measured with correction against that without correction of the refractive error as a function of eccentricity for stimulus sizes 0 and III respectively. Figure 8.5 is a combination of these two graphs, and demonstrates more clearly for both stimulus sizes a strong linear relationship between the two functions.

Table 8.4 illustrates the 4 - way ANOVA where perimetric sensitivity is the dependent variable. Eccentricity and stimulus size both significantly influence perimetric sensitivity at the $p<0.001$ level. Correction of the peripheral refraction does not, however, significantly affect perimetric sensitivity.

Pupil diameter (mm)	
Canon Autoref R - 1	Octopus 201
5.85 (0.70)	5.77 (0.68)

Table 8.1 Group mean pupil diameter measured during assessment with the Canon Autoref R - 1 and perimetric examination with the Octopus 201; one standard deviation is given in brackets.

	Eccentricity		
	0°	20°	40°
+ Sph. (D)	0.55 (0.26)	0.75 (0.26)	2.05 (0.84)
- Cyl. (D)	0.50 (0.17)	2.15 (0.61)	5.07 (0.93)
Axis (°)	71.5 (16.67)	67.25 (5.83)	80.0 (7.73)

Table 8.2 Group mean central and peripheral refraction measured with the Canon Autoref R - 1; one standard deviation, of the respective parameters, is given in brackets.

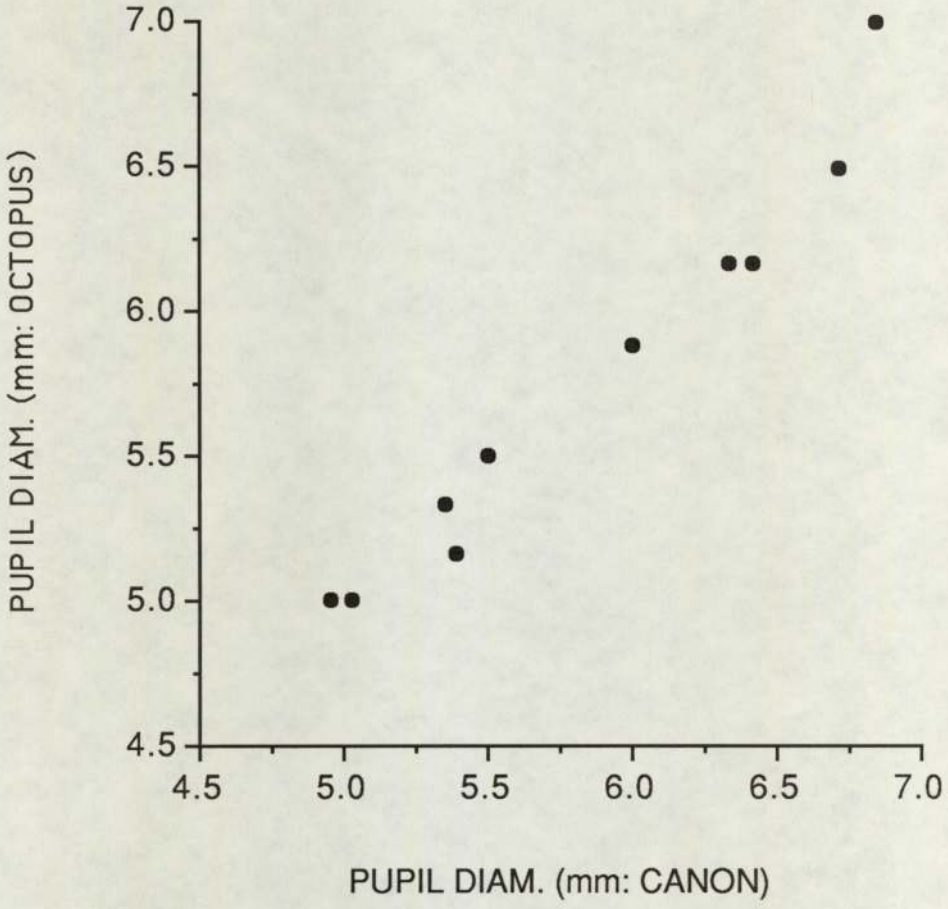


Fig. 8.2 Pupil diameter (mm) for each subject measured during examination with the Octopus 201 automated perimeter against that measured during examination with the Canon Autoref R - 1.

	Proportionate change in sensitivity (dB)		
	Eccentricity		
Stimulus size	0°	20°	40°
0	-1.48	-0.15	-0.075
III	+0.36	+0.52	+0.745

Table 8.3 Group mean proportionate change in perimetric sensitivity as a result of correction of the peripheral refractive error relative to sensitivity without correction recorded at eccentricities of 0°, 20°, 40°.

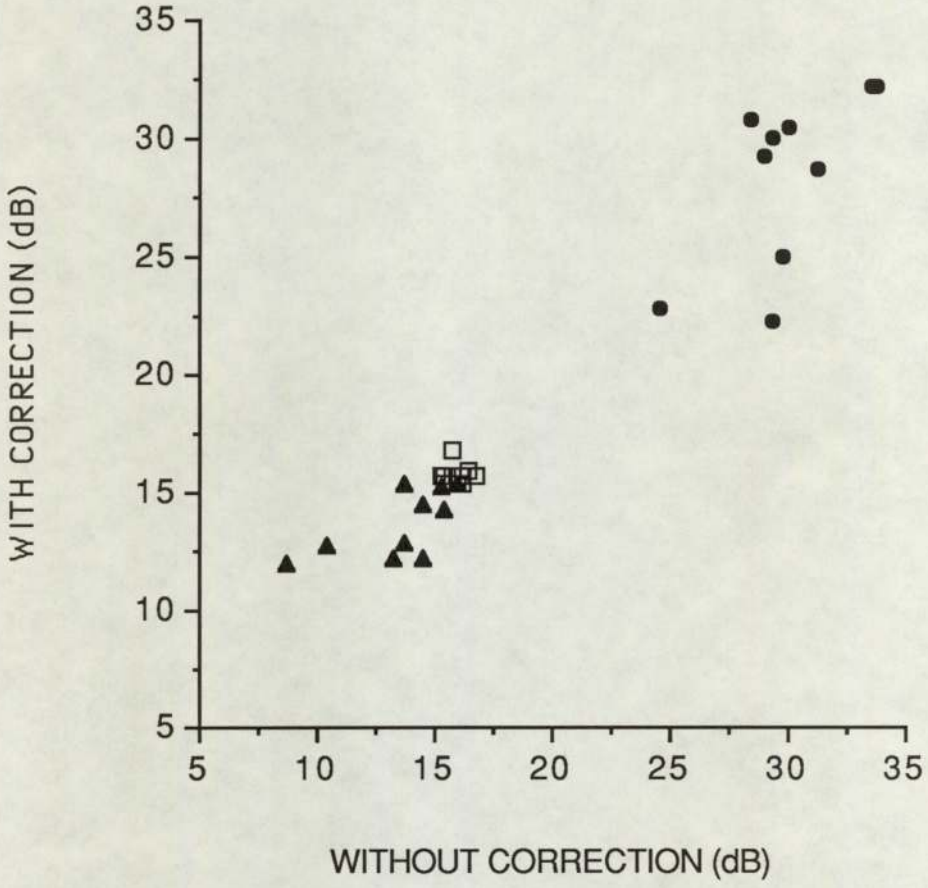


Fig 8.3 Differential light sensitivity for stimulus size 0 measured with correction of the refractive error against that without correction of the refractive error at eccentricities of 0° (filled circles), 20° (open squares) and 40° (filled triangles) along the nasal meridian recorded with the Octopus 201 automated perimeter.

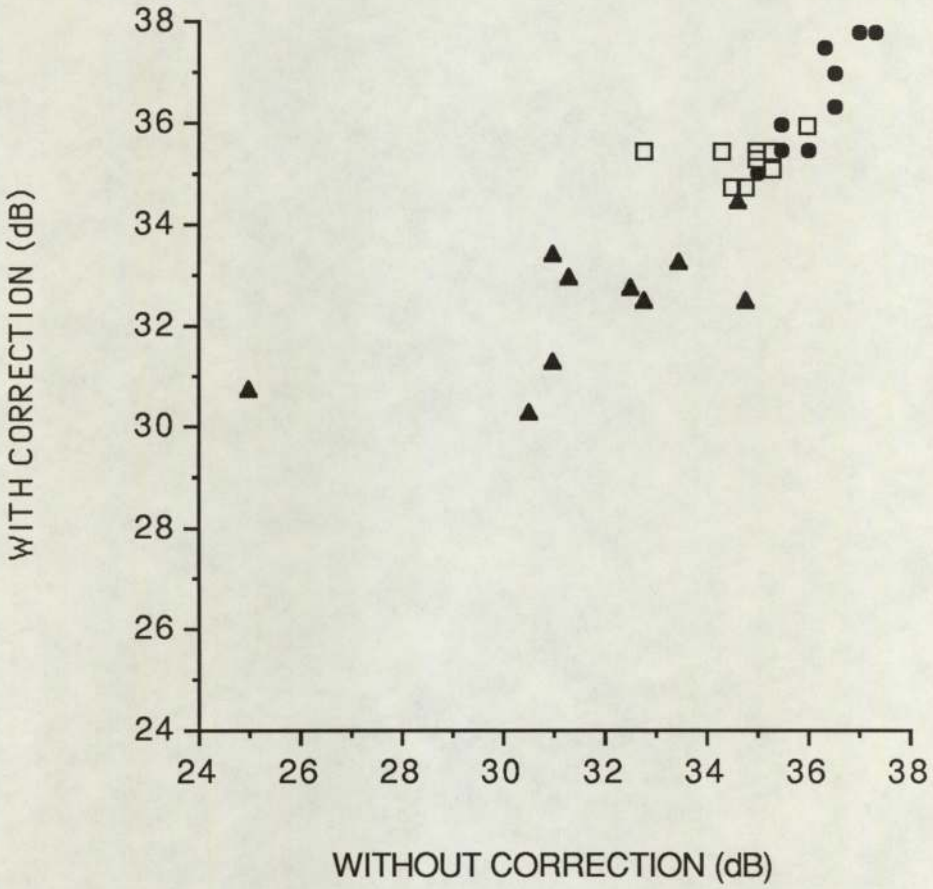


Fig 8.4 Differential light sensitivity for stimulus size III measured with correction of the refractive error against that without correction of the refractive error at eccentricities of 0° (filled circles), 20° (open squares) and 40° (filled triangles) along the nasal meridian recorded with the Octopus 201 automated perimeter.

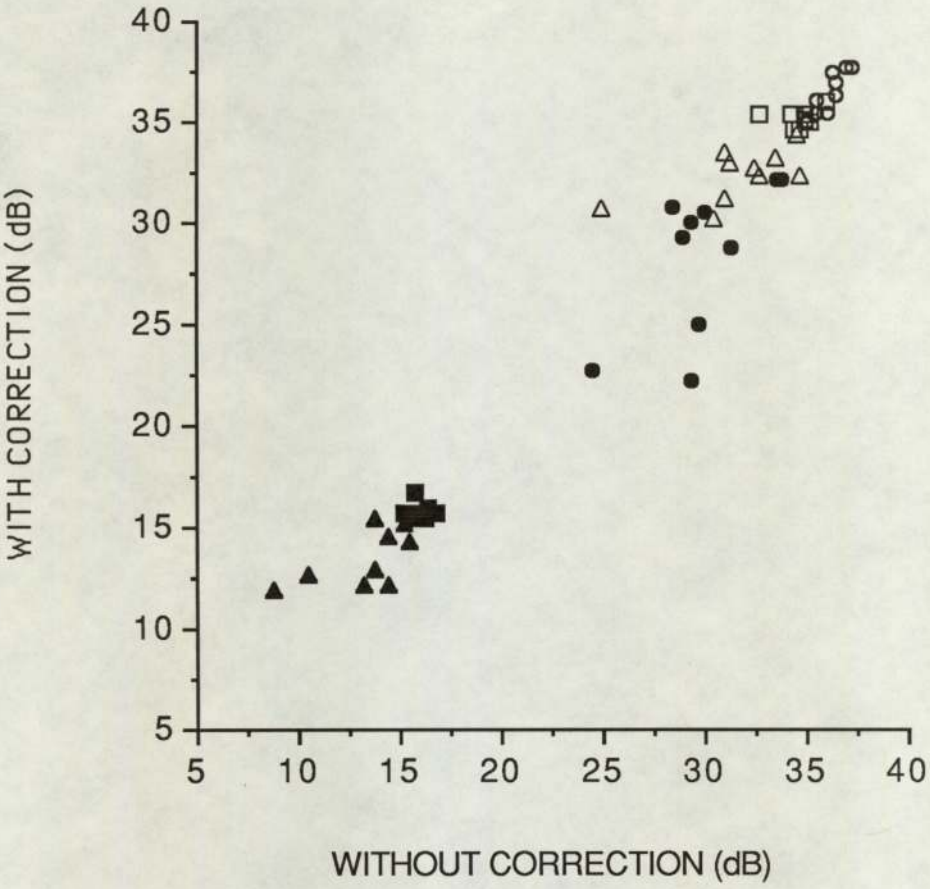


Fig 8.5 Differential light sensitivity for stimulus size 0 and III measured with correction of the refractive error against that without correction of the refractive error for stimulus size 0 at eccentricities of 0° (filled circles), 20° (filled squares) and 40° (filled triangles) and for stimulus size III at eccentricities of 0° (open circles) 20° (open squares) and 40° (open triangles 40°) along the nasal meridian recorded with the Octopus 201 automated perimeter.

Source	SS	DF	MS	F	Significance Level
Eccentricity (A)	2139.53	2	1069.77	195.204	p<0.001
AS	98.66	18	5.481		
Stimulus Size (B)	6690.13	1	6690.13	3323.083	p<0.001
BS	18.12	9	2.013		
AB	879.431	2	439.716	120.369	p<0.001
ABS	65.755	18	3.653		
Correction (C)	0.243	1	0.243	0.221	NS
CS	9.853	9	1.094		
AC	7.638	2	3.819	2.54	NS
ACS	27.034	18	1.501		
BC	7.4	1	7.4	4.561	NS
BCS	14.606	9	1.622		
ABC	2.698	2	1.349	1.015	NS
TOTAL	10090.0	119			
Subjects (S)	104.931	9	11.659	8.773	

Table 8.4 Four - way analysis of variance with perimetric sensitivity as the dependent variable.

Figures 8.6 - 8.7 illustrate the relationship between the short - term fluctuations in sensitivity (expressed as the root mean square (R.M.S.) value in dBs which is representative of the fluctuations in perimetric sensitivity during a single examination) measured with and without correction as a function of eccentricity for stimulus sizes 0 and III respectively. Figure 8.8 is a cumulative representation of the Figures 8.6 and 8.7 and demonstrates that although there is no clear pattern, short - term fluctuations show a slight tendency to increase with increase in eccentricity, with decrease in stimulus size and with correction of the central and peripheral refraction respectively. These findings are supported by the 4 - way ANOVA. illustrated in Table 8.5, where the R.M.S. value is the dependent variable. Eccentricity and stimulus size both significantly influence perimetric fluctuations at the $p<0.001$ level and $p<0.005$ levels respectively whilst the influence of correction of peripheral refraction is not statistically significant.

8.7.3 Discussion

The astigmatism of all subjects increased with eccentricity which is in agreement with previous studies (Feree et al 1931; Rempt et al 1971; Millodot and Lamont 1974b; Millodot 1981) and conforms to the Type A of Feree et al (1931) and the Type 5 of Rempt et al (1971). The peripheral astigmatism of all the subjects was mixed, as opposed to compound myopic or compound hypermetropic, which is in agreement with the findings of Millodot (1981) who found that emmetropes manifested mixed astigmatism, whilst myopes and hypermetropes manifested compound myopic and compound hypermetropic astigmatism respectively .

Correction of the central refraction depressed perimetric sensitivity in 6 observers with stimulus size 0 (Figure 8.3) and in 2 observers with stimulus size III (Figure 8.4) although the overall effect of the correction was not significant (Table 8.5). These results are in contrast to previous reports which state that the correction of refractive error within the central regions increases differential light sensitivity (Sloan 1961; Fankhauser and Enoch 1962; Ogle 1961). Indeed, since the observers were all essentially emmetropic (based upon independent retinoscopic and subjective assessments), no difference in sensitivity with or without the correction would be expected within the central

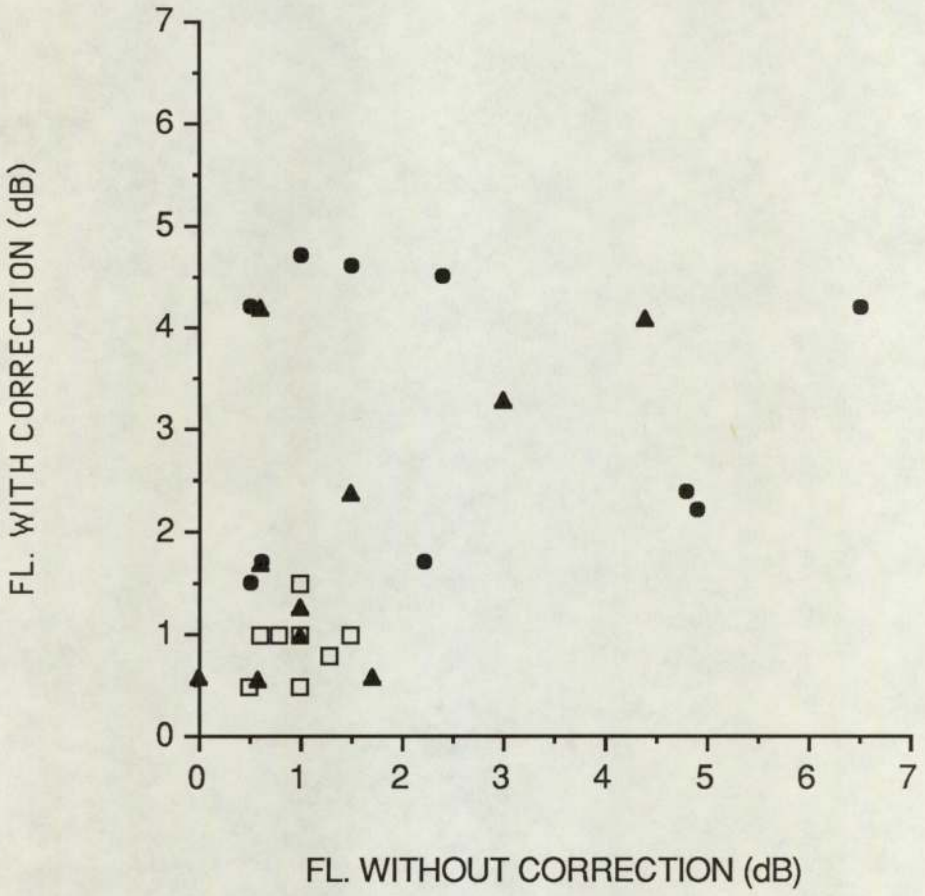


Fig 8.6 R.M.S. fluctuations in differential light sensitivity measured with correction of the refractive error against without correction of the refractive error for stimulus size 0 at eccentricities of 0° (filled circles), 20° (open squares) and 40° (filled triangles) along the nasal meridian recorded with the Octopus 201 automated perimeter.

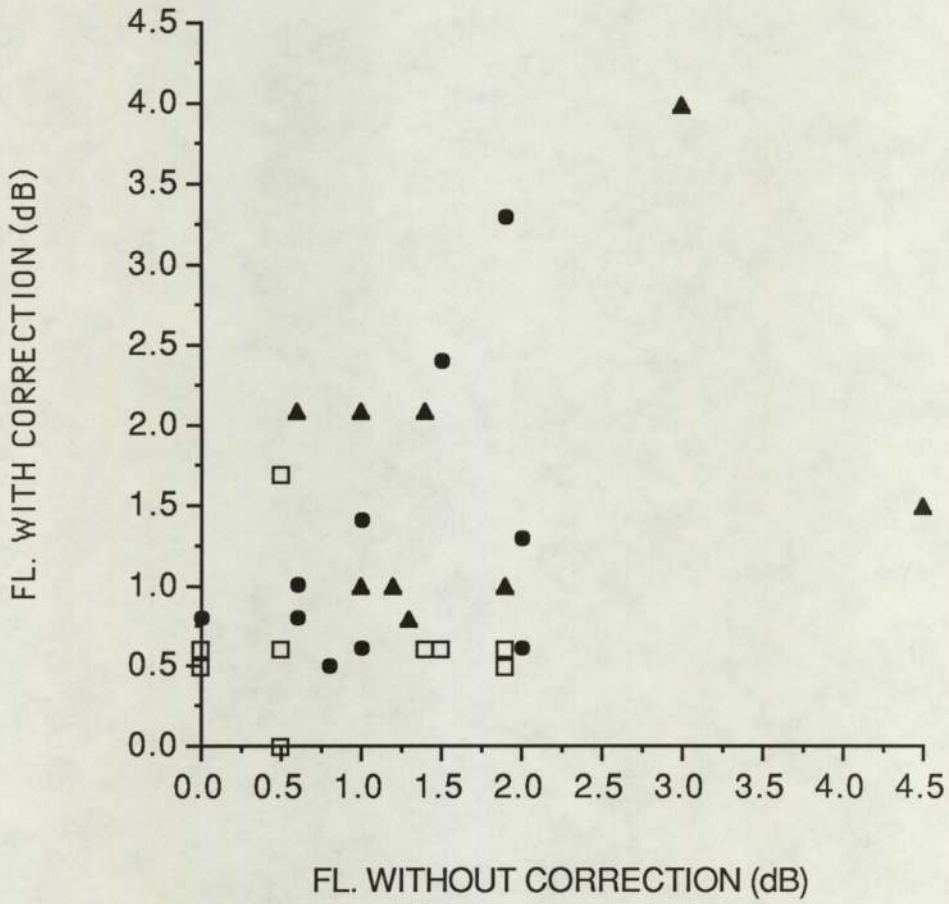


Fig 8.7 R.M.S. fluctuations in differential light sensitivity measured with correction of the refractive error against without correction of the refractive error for stimulus size III at eccentricities of 0° (filled circles), 20° (open squares) and 40° (filled triangles) along the nasal meridian recorded with the Octopus 201 automated perimeter.

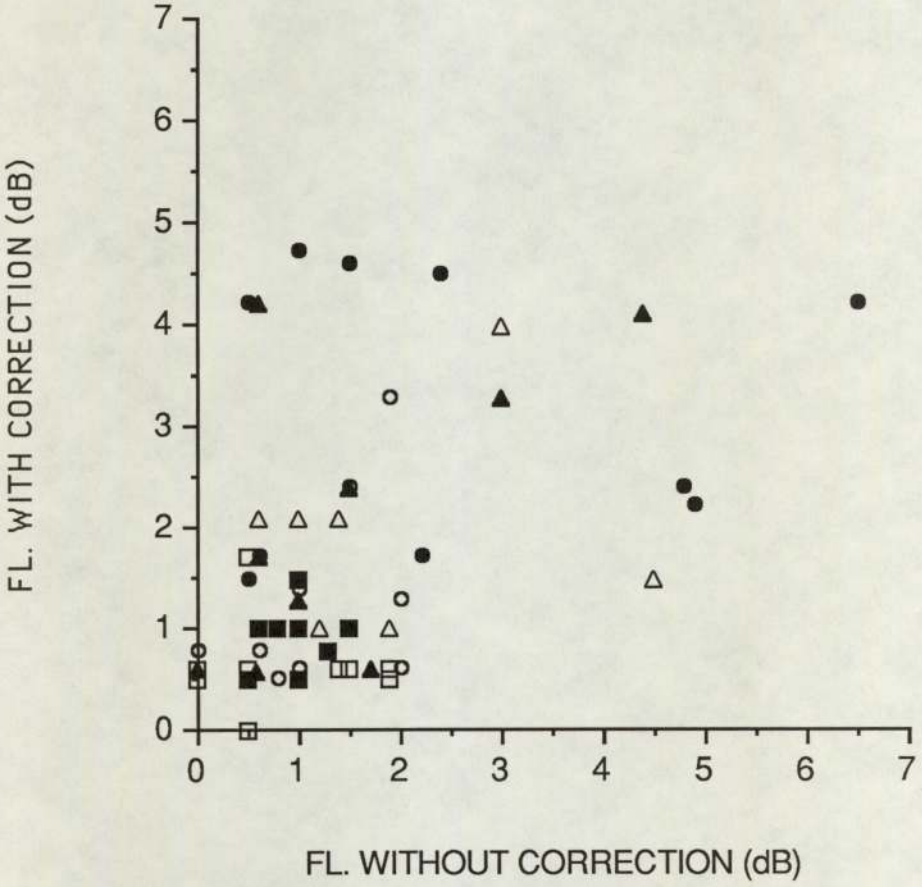


Fig 8.8 R.M.S. fluctuations in differential light sensitivity measured with correction of the refractive error against without correction of the refractive error for stimulus size 0 at eccentricities of 0° (filled circles), 20° (filled squares) and 40° (filled triangles) and for stimulus size III at eccentricities of 0° (open circles), 20° (open squares) and 40° (open triangles) along the nasal meridian recorded with the Octopus 201 automated perimeter.

Source	SS	DF	MS	F	Significance Level
Eccentricity (A)	28.408	2	14.204	14.11	p<0.001
AS	18.128	18	1.007		
Stimulus Size (B)	14.7	1	14.7	13.626	p<0.005
BS	9.715	9	1.079		
AB	10.362	2	5.181	3.442	NS
ABS	27.097	18	1.505		
Correction (C)	0.192	1	0.192	0.237	NS
CS	7.266	9	0.807		
AC	1.255	2	0.627	0.646	NS
ACS	17.491	18	0.971		
BC	0.867	1	0.867	0.848	NS
BCS	9.207	9	1.023		
ABC	0.276	2	0.138	0.149	NS
ABCS	16.653	18	0.925		
Subjects (S)	27.142	9	3.015	3.259	
TOTAL	188.764	119			

Table 8.5 Four - way analysis of variance with fluctuations in perimetric sensitivity as the dependent variable.

regions (Weinreb and Perlman 1986). Interestingly, McBrien and Millodot (1985) reported that for cylinders < 0.75 D, the axis recorded with the Canon can differ by as much as 37° compared to that determined subjectively.

Correction of peripheral astigmatism has no significant influence on either perimetric sensitivity or fluctuations in perimetric sensitivity (Table 8.4; 8.5) for either stimulus size. These findings are in contrast to those of Fankhauser and Enoch (1962) and Ronchi (1971) who both demonstrated that perimetric sensitivity at peripheral stimulus locations could be improved by correction of peripheral refractive error. Interestingly, the electrophysiological results of Ikeda and Wright (1972) demonstrated that the peripheral retinal ganglion cells in the cat are insensitive to optical blur whereas those cells within the central 5° are not. This finding suggests that the peripheral retina is less sensitive to refractive blur than the central regions. Interpolation from the cat to the human visual system must, however, be treated with caution. Furthermore, as stated in section 3.6.4, Jennings and Charman (1981a) suggested that the mid - peripheral image quality was more than adequate, despite the substantial oblique astigmatism.

It is possible that the lenses used to correct the peripheral astigmatism may have been slightly off the visual axis thus introducing prismatic effects. Atchison and Johnston (1979) reported, however, that within the central 30° - 40°, the prismatic effects of corrective ophthalmic lenses on static perimetric thresholds can be ignored for powers less than +/- 10 D. Since none of the lenses in the study exceeded these limits, it was felt that prismatic effects had little influence on the findings.

8.8 Conclusions

The correction of refractive error has no significant influence on either the magnitude of, or the fluctuations associated with, differential light sensitivity measured with small and relatively large stimuli at the peripheral locations measured in the study. Within the central regions, however, correction of refraction depressed sensitivity by a mean value of -1.48 dB for stimulus size 0, this was considered surprising since the subjects were considered to be centrally emmetropic.

9. THE INFLUENCE OF PUPIL SIZE ON THE PERIMETRIC PROFILE

9.1 Introduction

The pupil can either enhance or degrade retinal image quality by controlling the dioptrics of the eye and diffraction; it also modifies the quantity of light reaching the retina (Leibowitz 1952; Graham 1965; Davson 1980). Variations in the size of the pupil are therefore likely to influence the processing of perimetric stimuli (Tate 1985). During a single perimetric examination fluctuations occur in the size of the pupil, the control of which is thought to originate at the third nucleus (Campbell et al 1959); pupil size additionally varies with change in the adaptation level (Greve 1973; Davson 1980).

The retinal illumination depends upon the surface area of the pupil in addition to the magnification and transmission by the optical media of the eye (Davson 1980). Assuming that the distance from the nodal point of the eye to the retina is 16.7 mm, retinal illumination (D) may be expressed as:

$$D = 0.36\, t_{\lambda}.\, S.\, L$$

where S is the surface area of the pupil in cm^2 and L is the luminance of the stimulus. The transmission factor (t_{λ}) varies between 0.1 and 0.7 depending upon the wavelength of the stimulus (Dawson 1962). This formula is an approximation, however, because of the directional sensitivity of the retinal cones (Stiles - Crawford Effect) such that the subjective brightness of peripheral rays is only 15% that of the central rays (Stiles and Crawford 1934). Furthermore, as described in section 1.7.3, the efficacy of the pupil in facilitating light entry to the peripheral retina is reduced at oblique angles, however, the reduced retinal image projection compensates for this effect (Drasdo and Fowler 1974; Holden et al 1987), so that retinal illumination is approximately constant out to an eccentricity of 80° (Bedell and Katz 1982; Koojiman 1983).

In addition to limiting retinal illuminance, the pupil also modifies optical aberrations and diffraction and thus has a major influence on the image quality of the eye (Graham 1965). The degrading effects of spherical and chromatic aberrations become greater with increasing pupil size, whilst the effects of diffraction are minimized. Conversely, when the pupil diameter decreases below 2.4 mm in diameter, the diffraction effect becomes significant and is the limiting factor for resolution (Campbell and Gubish 1966). The pupil diameter also effectively limits the diameter of the blur circle on the retina; a decrease in pupil diameter reduces the size of the blur circle which increases the depth - of - focus of the eye (Campbell 1957; Ogle and Schwartz 1959; Tucker and Charman 1975; Charman and Whitefoot 1977). The tolerance to defocus, however, decreases more slowly with increasing pupil diameter (greater than or equal to 2 mm) than would be predicted from theoretical calculations of diffraction - limited systems. It has been suggested that this discrepancy may arise as a consequence of the apodizing effect of the Stiles - Crawford effect (Metcalf 1965) and the presence of ocular aberrations at the edge of large pupils (Charman and Whitefoot 1977; Charman 1979).

9.2 Influence of pupil size on visual function

Leibowitz (1952) using grating targets, demonstrated that an increase in pupil diameter resulted in a concomitant increase in visual acuity which peaked for a pupil diameter of 2.77 mm and then decreased for the larger pupil diameters. This is in general agreement with the findings of Campbell and Green (1965) who demonstrated that an increase in pupil diameter greater than 2 mm depressed contrast sensitivity, particularly at high spatial frequencies. In contrast, Kay and Morrison (1987) reported that changes in pupil diameter (between 2 - 8 mm) without correction for the change in retinal illumination, had no significant effect on contrast sensitivity, except at spatial frequencies of 0.5 cycles deg^{-1} and 1 cycle deg^{-1} when a significant reduction occurred with a 2 mm diameter pupil. Furthermore, it has been reported that the naturally occurring pupil diameter is optimal for visual resolution (Campbell and Gregory 1960) and that the optimum diameter decreases with increase in ambient illumination (Leibowitz 1952; Woodhouse 1975).

Alpern and Spencer (1953) reported that critical flicker fusion frequency (C.F.F.) was higher at the fovea than at the periphery for fixed pupils (the size of the pupils was not specified), whereas for natural pupils C.F.F. increased in the periphery. These results were explained in terms of changes in the retinal illumination. Pupil size also has an effect on the colour stereoscopic phenomenon. Sundet (1972) reported that with small pupils subjects perceived a red field to be behind a green field, whereas for large pupils the reverse effect was found. Interestingly, pupil size was not found to be a significant parameter in the measurement of the P.E.R.G. (Karpe and Wulfing 1969; Holder and Huber 1984) or the flash V.E.P. (Skalka and Holman 1986) although miosis was found to increase the latency and reduce the amplitude of the pattern V.E.P. (Hawkes and Stow 1981).

9.3 Influence of pupil size on perimetric thresholds

Empirical clinical observations with manual perimetry on normal eyes have suggested that the inter - individual differences in pupil size have a negligible effect on the kinetic visual field threshold (Drance, Berry and Hughes 1967; Williams 1983; McCluskey et al 1986). Similarly, using static automated perimetry, it has been demonstrated that in normal eyes, inter - subject differences in pupil size do not significantly influence mean sensitivity (Brenton and Phelps 1986) nor the magnitude of the short - term fluctuations (Flammer, Drance, Fankhauser and Augustiny 1984).

Drug induced miosis produces isopter contraction measured with manual kinetic perimetry out to an eccentricity of 30° (Day and Scheie 1953) and also across the full field (Engel 1942; Kolker and Hetherington 1976; Harrington 1981; Shields 1982). Furthermore, pupillary constriction has been shown to induce defects which simulate glaucomatous field loss and to increase the area of existing glaucomatous field damage by effectively reducing retinal illumination (Engel 1942; Forbes 1966). The effect of miosis induced by 2% pilocarpine was quantified by McCluskey et al (1986) who demonstrated that a reduction in pupillary area (for subjects who develop a pupillary miosis of less than 2.4 mm) was significantly correlated to the reduction in kinetic isopter area. These workers also stated that the effect of pupillary miosis on perimetric sensitivity was of greatest magnitude for the smaller stimuli such as the Goldmann $I_{2e,}$ which is in agreement with earlier findings (Feree et

al 1934; Traquair 1938).

Greve (1973) using the Friedmann Visual Field Analyser (F.V.F.A. I) demonstrated that a reduction in pupil diameter from 6 mm to 2 mm, modified by illuminating the non - examined contralateral eye, depressed the sensitivity profile out to an eccentricity of 25° by approximately 0.2 log units. Similarly, Bedwell and Davies (1977) using the F.V.F.A. I reported that a change in pupil diameter of between 3.5 mm and 9.5 mm, induced by 0.2% thymoxamine and 5% ephedrine respectively, produced a maximum change in sensitivity of 0.14 log units. Induced pupillary constriction has also been shown to produce a reduction in sensitivity out to an eccentricity of 30° using the Goldmann III projection stimuli of the Octopus automated perimeter: Fankhauser (1979) reported a 0.2 log unit depression in the mean threshold with 3% pilocarpine induced miosis, whilst Mikelberg et al (In press) found a good correlation between pupil area (modified by thymoxamine 0.5%) and mean sensitivity.

Several workers have proposed that the isopter constriction resulting from pupillary miosis arises as a direct consequence of reduced retinal illumination (Scott 1957 Forbes 1966). The visibility of perimetric stimuli is believed, however, to be dependent upon Weber's law, where the ratio between the stimulus luminance, ΔL, and the background luminance, L, is a constant (Aulhorn and Harms 1972; Greve 1973). From Weber's law it is predicted that if pupil size is varied, even though both the stimulus and the background luminance will change, the Weber ratio will be maintained; hence the differential light sensitivity should remain unaltered. Thus unless the retinal illumination levels fall within the mesopic range, where Weber's law is no longer operative, changes in retinal illumination due to variations in pupillary size should not affect perimetric sensitivity. McCluskey et al (1986), however, have conjectured that factors such as diffraction may reduce perimetric sensitivity when the pupil is miotic.

9.4 Aim of the investigation

The absence of quantitative data relating change in pupil size to perimetric sensitivity mitigates against the use of normative data for comparison purposes for patients whose pupil size lies outside the normal range. Furthermore, the use of serial field analysis to monitor visual field retention and hence the efficacy of treatment is confounded if pupil size variations are introduced. Such circumstances may arise if topical medication is altered or if the period between drug instillation and field examination varies and can also occur in patients taking systemic medications which modify the pupil size or in whom ocular disorders have compromised the motor or neuronal function of the eye.

The main purpose of the investigation was to quantify the influence of change in pupil size on perimetric sensitivity as a function of eccentricity. The influence of pupil size on the fluctuations in sensitivity measurements at a given location was further investigated to determine whether natural variations in pupil size contribute to the variation in perimetric response at a given location measured during a single examination.

9.5 Experimental work

The Dicon AP3000, described in section 4.7.1 was selected to assess the effect of pupil size on perimetric sensitivity since it provides the facility to vary bowl luminance. Bowl luminance was varied in order to test the hypothesis that the effect of pupil size on perimetric sensitivity is independent of background luminance (Aulhorn and Harms 1972; Greve 1973).

9.5.1 Materials and methods

The sample comprised 10 clinically normal, emmetropic subjects (mean age 23.45 years, S.D. 2.84 years; 3 females, 7 males). The subjects were free from any ocular or systemic medication and were experienced observers in automated perimetric routines and in psychophysical techniques of

measurement in general.

The pupil size of each eye was modified using one drop of 0.5% thymoxamine for miosis and one drop of 10% phenylephrine for mydriasis; 0.9% saline was used as the control solution. Thymoxamine and phenylephrine both act on alpha adrenoreceptors present on the smooth muscle of the dilator pupillae. In addition, both agents act on the ciliary body vasculature but interference with ciliary muscle function is, for young subjects, unlikely to affect the sustained accommodative response (Mordi, Lyle and Mousa 1986) required for fixation at the perimetric viewing distance of 33 cm. Thymoxamine induces pupillary miosis as a result of antagonist action on alpha receptors; phenylephrine induces pupil mydriasis as a result of agonist action on alpha receptors. All drugs employed in the investigation were obtained from Smith and Nephew single - dose applicators ("minims"). The instillations were made with a precision micro - pipette such that each instillation comprised 25 µl of drug. Prior to the administration of the drug, one drop of benoxinate HCl 0.4% was instilled into each eye to inhibit reflex tear formation. Benoxinate also facilitates penetration of ophthalmic agents used subsequently due to it's effect on the lipid barrier anterior to the corneal epithelium (O'Connor Davies 1981). The increased access of phenylephrine and thymoxamine into the ocular tissues had the effect of reducing their action times, such that the effect of the drugs reached a maximum within 30 minutes. To check that the action of the drugs was constant, the pupil diameter was monitored throughout the investigation; the maximum levels of dilation and constriction remained constant.

Perimetry was undertaken 30 minutes after instillation of benoxinate HCl. Perimetric sensitivity was determined for each of two bowl luminances, 10 asb and 45 asb, at eccentricities of 10°, 12.5°, 20°, 30°, 35°, 40° and 50° along the 265° meridian of the inferior visual field of the right eye using the Meridional Threshold Program and at eccentricities of 0°, 1°, 3° and 5° along the vertical meridian of the inferior field of the right eye using the Macular Threshold Program. Sensitivity at each location was measured three times and was represented as the mean of these measurements. The stimulus duration was 100 ms and the inter - stimulus duration 1 s. The order of bowl luminance and of perimetric program at a given bowl luminance was randomized throughout the sample. Each

subject underwent an adaptation period of 10 minutes to the appropriate bowl luminance. The head was steadied with the head rest and chin bar of the instrument and fixation was monitored throughout the examination via the video monitor.

Each subject attended a total of three sessions within a maximum period of three weeks. At each session one drop of benoxinate HCl was instilled into each eye followed by the instillation of one of the two active agents or the control solution; the period between the two instillations was five minutes. The washout period between each session was a minimum of two days. The order of the drug instillation was randomized for each subject and a double blind protocol was employed such that neither the examiner nor the subject were aware of which agent had been used.

Pupil size was measured immediately prior to perimetric examination and thereafter at five minute intervals using the scaled axes on the video monitor of the perimeter. The pupil size could be measured to an accuracy of 0.5 mm. The value for pupil diameter was represented as the mean of the measurements taken throughout the examination; the duration of the perimetric examination was approximately 30 minutes.

9.5.2 Results

Table 9.1 indicates the group mean pupil size and standard deviation for each combination of drug and adaptation level.

The relationship between group mean perimetric sensitivity and eccentricity for each drug is illustrated at the 10 asb (Figure 9.1a) and 45 asb (Figure 9.1b) adaptation levels. Perimetric sensitivity decreased with increase in eccentricity for all drug conditions at both adaptation levels. The standard deviations ranged from 0.35 dB to 3.5 dB and were, on average, 2 dB. They were fairly constant out to an eccentricity approaching 12.5° beyond which the magnitude increased with increase in eccentricity for each drug condition.

Adaptation Level	Phenylephrine 10%	Saline 0.9%	Thymoxamine 0.5%
10 asb	6.85	4.65	3.18
	(0.67)	(0.62)	(0.56)
45 asb	6.37	3.65	2.59
	(0.55)	(0.55)	(0.34)

Table 9.1 Group mean and one standard deviation values for pupil size (mm) modified by phenylephrine 10%, saline 0.9% and thymoxamine 0.5% for the 10 asb and 45 asb bowl luminances.

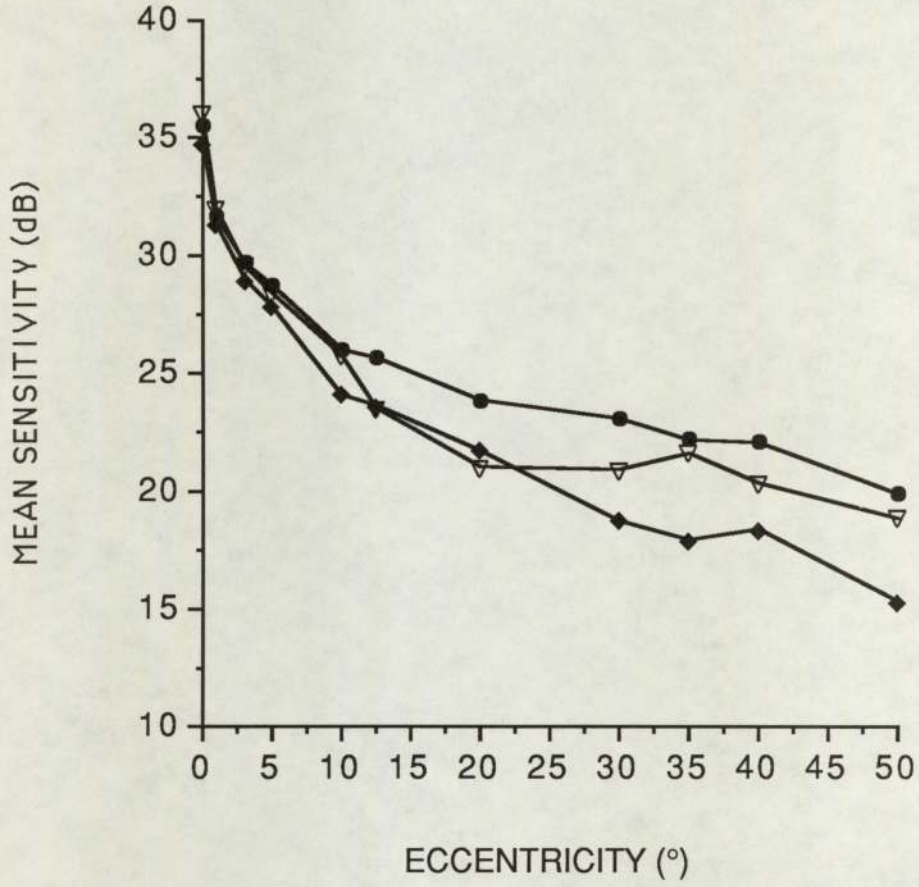


Fig. 9.1a Group mean perimetric sensitivity against eccentricity measured along the inferior meridian of the right eye as a function of pupil size modified by thymoxamine 0.5% (filled diamonds), phenylephrine 10% (filled circles) and saline 0.9% (open inverted triangles) at the 10 asb background luminance recorded with the Dicon AP3000 autoperimeter.

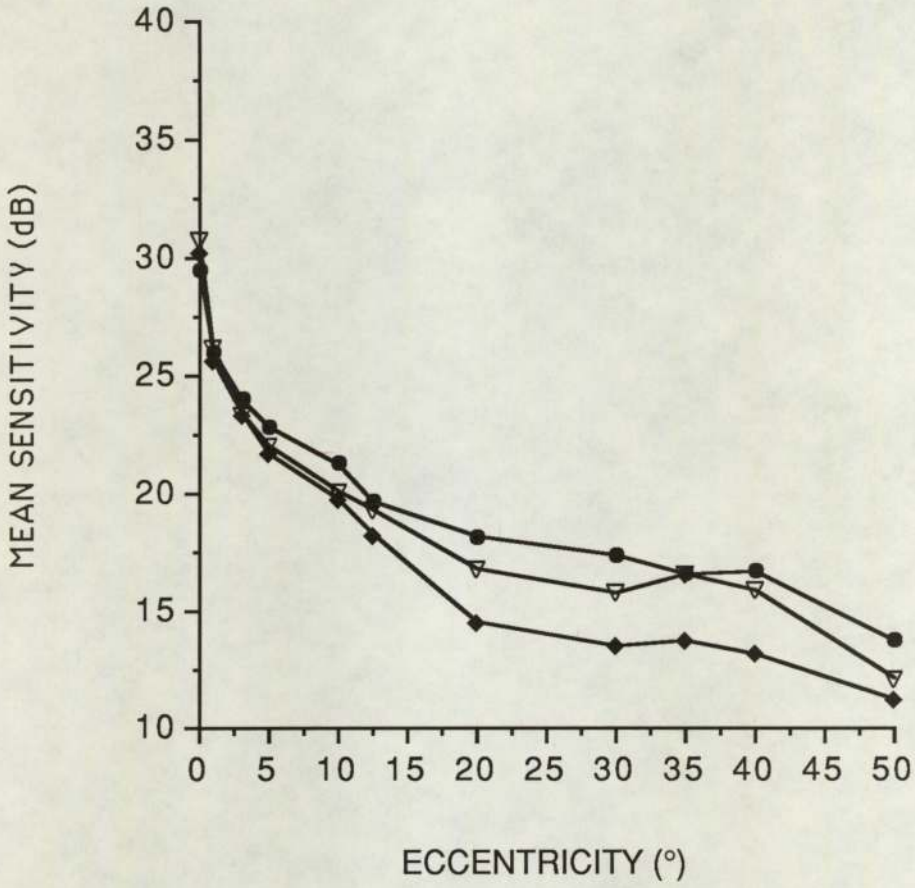


Fig. 9.1b Group mean perimetric sensitivity against eccentricity measured along the inferior meridian of the right eye as a function of pupil size modified by thymoxamine 0.5% (filled diamonds), phenylephrine 10% (filled circles) and saline 0.9% (open inverted triangles) at the 45 asb background luminance recorded with the Dicon AP3000 autoperimeter.

The relationship between group mean sensitivity and pupil size for each drug is illustrated at the 10 asb (Figure 9.2a) and 45 asb (Figure 9.2b) adaptation levels as a function of eccentricity. Sensitivity increases with increase in pupil size.

Group mean proportionate change in perimetric sensitivity relative to the saline control for each drug is illustrated at the 10 asb (Figure 9.3a) and 45 asb (Figure 9.3b) adaptation levels. Proportionate change in sensitivity with increase in eccentricity at both adaptation levels decreases for thymoxamine and increases with phenylephrine. The proportionate change in sensitivity for any drug condition reaches a maximum value of approximately 7 dB for a pupil size difference of 3.7 mm.

Table 9.2 shows the linear regression characteristics of group mean proportionate change in sensitivity against group mean proportionate change in pupil area relative to the saline control at the 10 asb and 45 asb adaptation levels as a function of eccentricity. At both adaptation levels, the relationship exhibited an increasing gradient with increase in peripheral angle. The magnitude of the correlation coefficient generally increased in a similar manner with the values being statistically significant beyond approximately 30° eccentricity. Second order regression analysis gave similar results.

An estimate of the influence of pupil size on the short - term fluctuations in perimetric sensitivity may be derived by plotting the group mean range of sensitivity values. These, given the software limitations of the Dicon AP3000 autoperimeter system, are an indication of the short - term fluctuations in perimetric sensitivity and are plotted as a function of eccentricity for each drug at the 10 asb (Figure 9.4a) and 45 asb (Figure 9.4b) adaptation levels. The range increases with increase in peripheral angle for both adaptation levels and with decrease in pupil size.

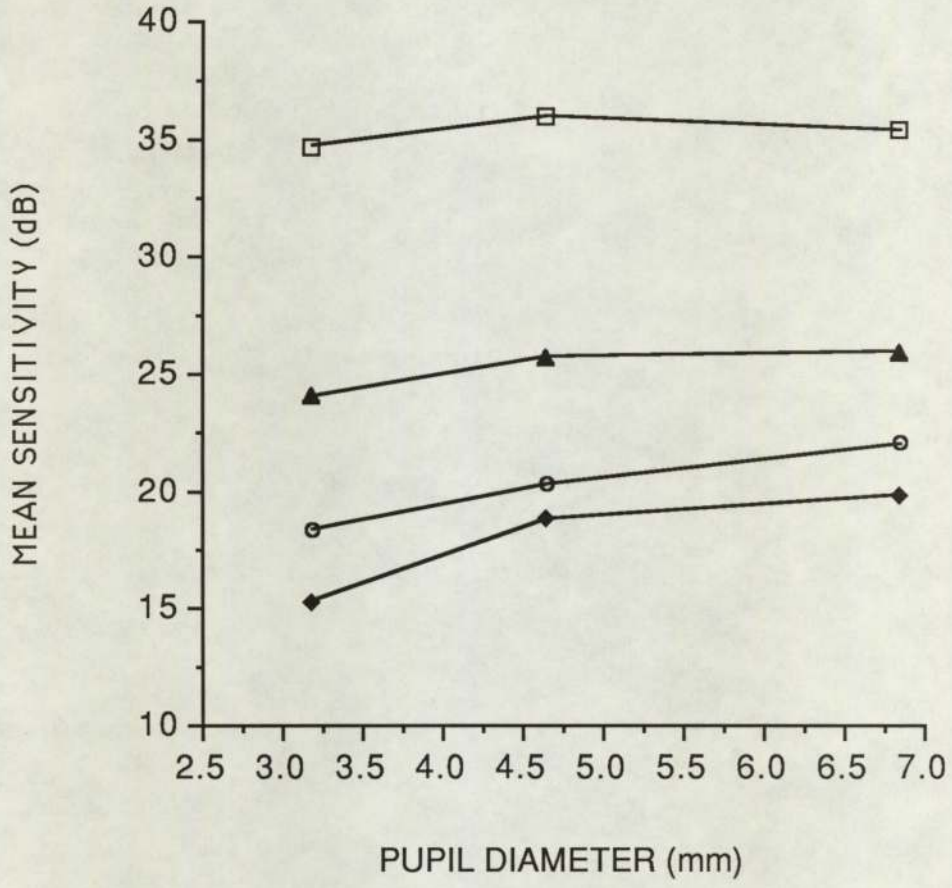


Fig. 9.2a Group mean perimetric sensitivity against pupil size modified by thymoxamine 0.5% and phenylephrine 10% at eccentricities of 0° (open squares), 10° (filled triangles), 40° (open circles) and 50° (filled diamonds) measured along the inferior meridian of the right eye for the 10 asb background luminance recorded with the Dicon AP3000 autoperimeter.

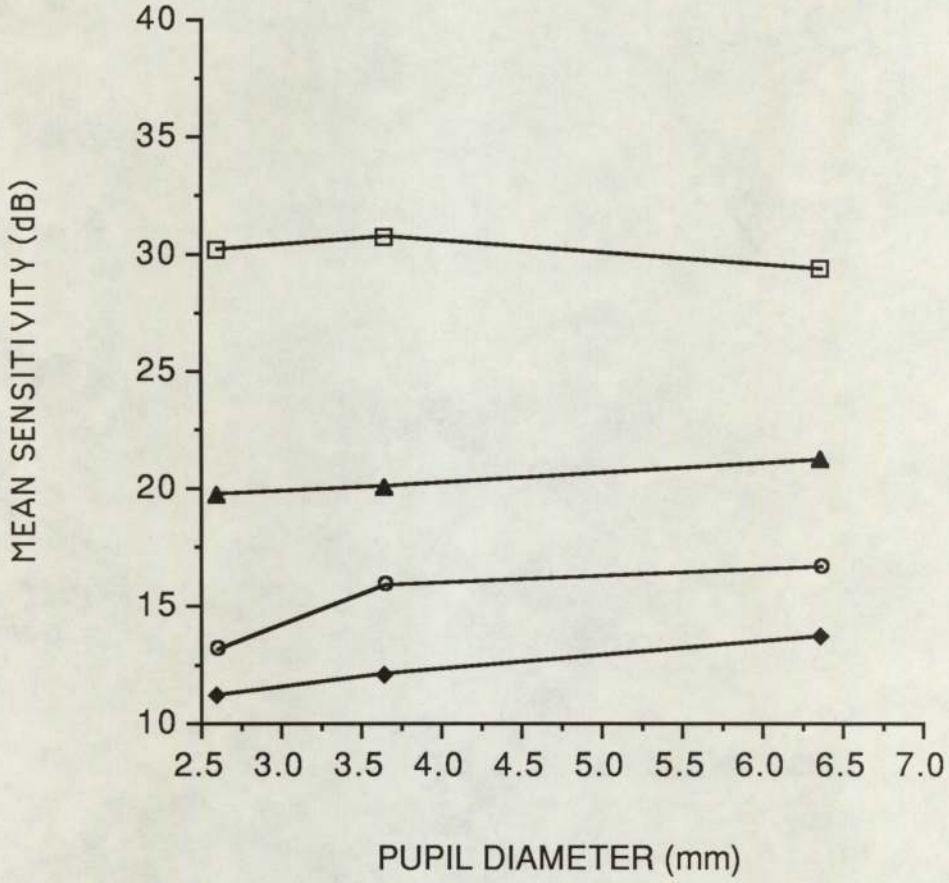


Fig. 9.2b Group mean perimetric sensitivity against pupil size modified by thymoxamine 0.5% and phenylephrine 10% at eccentricities of 0° (open squares), 10° (filled triangles), 40° (open circles) and 50° (filled diamonds) measured along the inferior meridian of the right eye for the 45 asb background luminance recorded with the Dicon AP3000 autoperimeter.

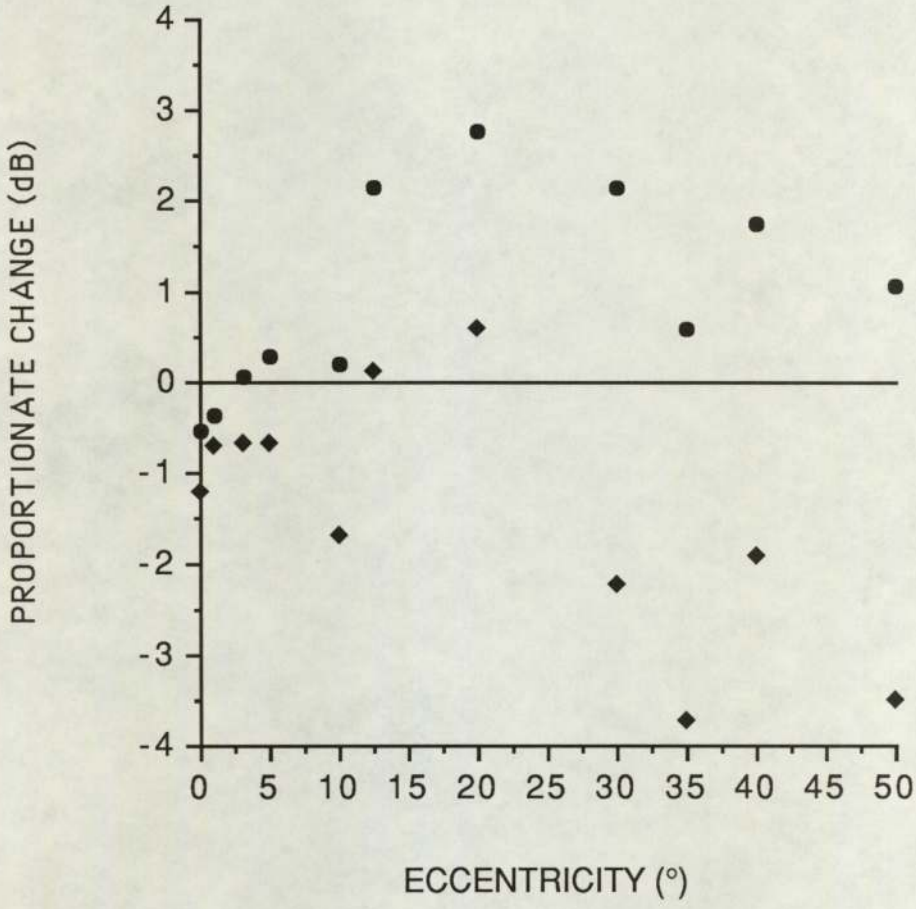


Fig. 9.3a Group mean proportionate change in sensitivity measured along the inferior meridian of the right eye relative to the saline control for thymoxamine 0.5% (filled diamonds) and for phenylephrine 10% (filled circles) at the 10 asb background luminance against eccentricity recorded with the Dicon AP3000 autoperimeter.

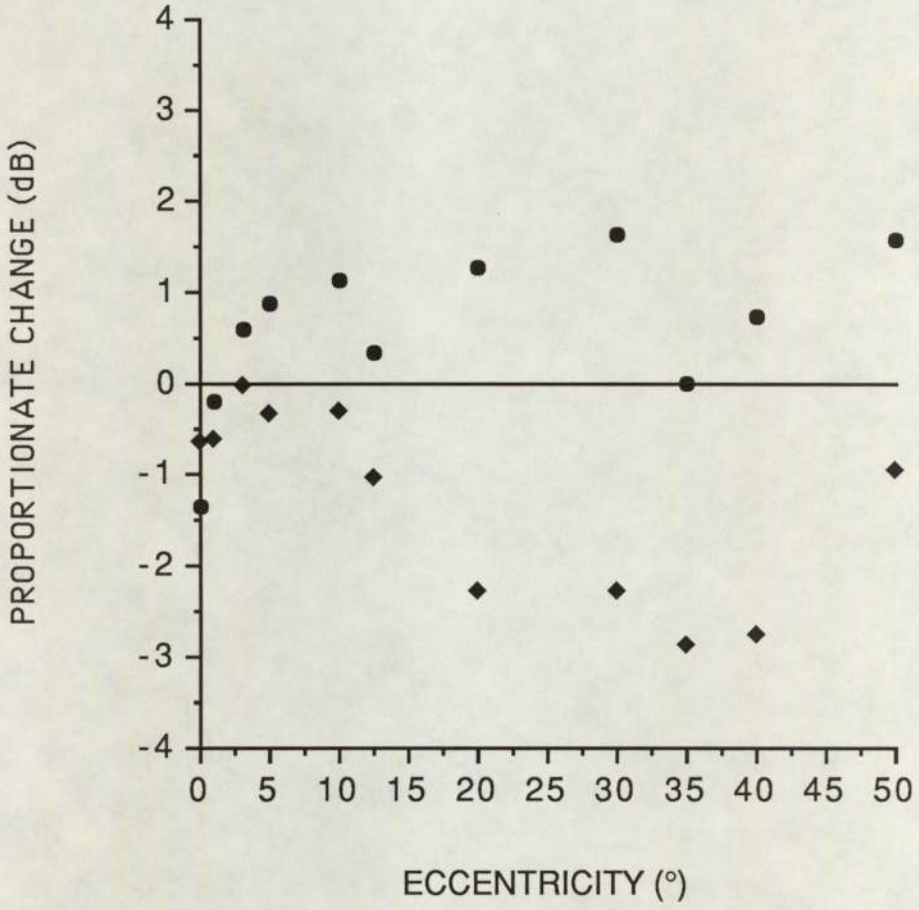


Fig. 9.3b Group mean proportionate change in sensitivity measured along the inferior meridian of the right eye relative to the saline control for thymoxamine 0.5% (filled diamonds) and for phenylephrine 10% (filled circles) at the 45 asb background luminance against eccentricity recorded with the Dicon AP3000 autoperimeter.

	Eccentricity (°)	Slope	Intercept	Correlation Coefficient	Probability
	0	0.02	-0.96	0.19	NS
	1	0.01	-0.58	0.11	NS
	3	0.03	-0.47	0.37	NS
	5	0.025	-0.34	0.25	NS
	10	0.07	-1.13	0.40	NS
10 asb	12.5	0.07	0.73	0.49	p<0.05
	20	0.06	1.33	0.30	NS
	30	0.14	-0.84	0.63	p<0.025
	35	0.13	-2.33	0.45	p<0.05
	40	0.10	-0.65	0.50	p<0.05
	50	0.12	-1.90	0.40	NS
	0	-0.03	-0.78	0.14	NS
	1	0.02	-0.53	0.12	NS
	3	0.02	0.125	0.20	NS
	5	0.05	-0.13	0.46	p<0.05
	10	0.05	-0.02	0.45	p<0.05
45 asb	12.5	0.04	-0.71	0.26	NS
	20	0.13	-1.62	0.59	p<0.01
	30	0.13	-1.41	0.58	p<0.01
	35	0.09	-2.15	0.46	p<0.05
	40	0.12	-1.98	0.59	p<0.01
	50	0.11	-0.60	0.51	p<0.025

Table 9.2 The linear regression of the group mean proportionate change in sensitivity with group mean proportionate change in pupil area relative to the saline control at the 10 asb and 45 asb bowl luminances as a function of eccentricity.

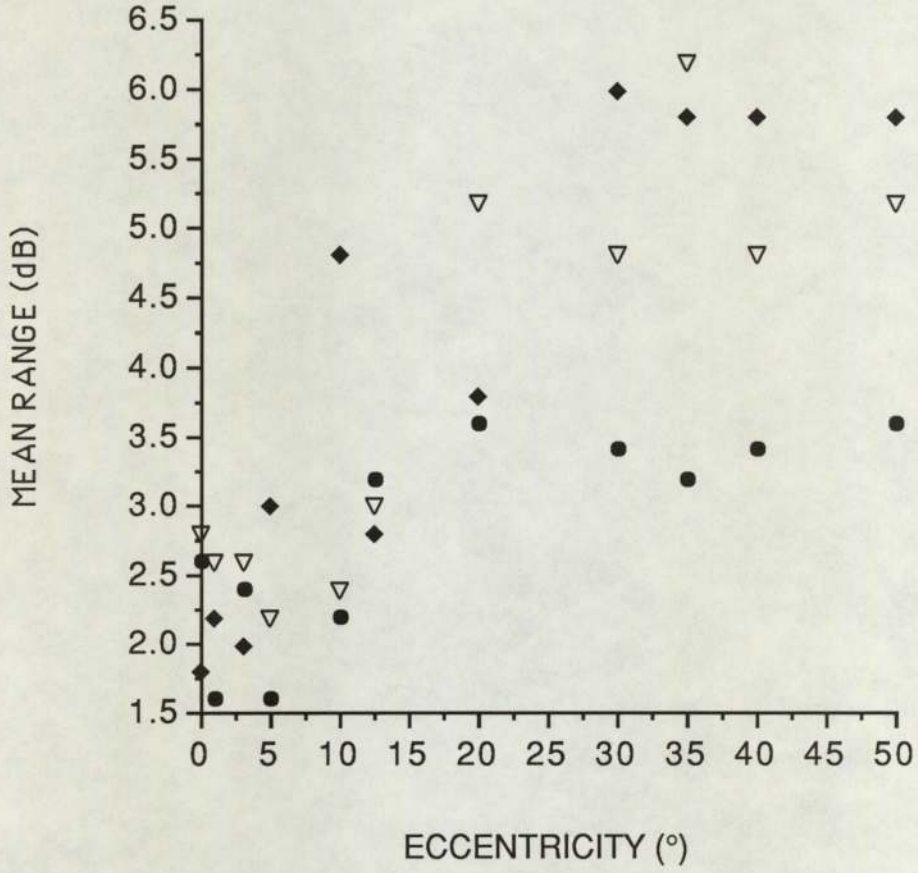


Fig 9.4a Group mean range of sensitivity against eccentricity measured along the inferior meridian of the right eye as a function of pupil size modified by thymoxamine 0.5% (filled diamonds), phenylephrine 10% (filled circles) and saline 0.9% (open inverted triangles) for the 10 asb background luminance recorded with the Dicon AP3000 autoperimeter.

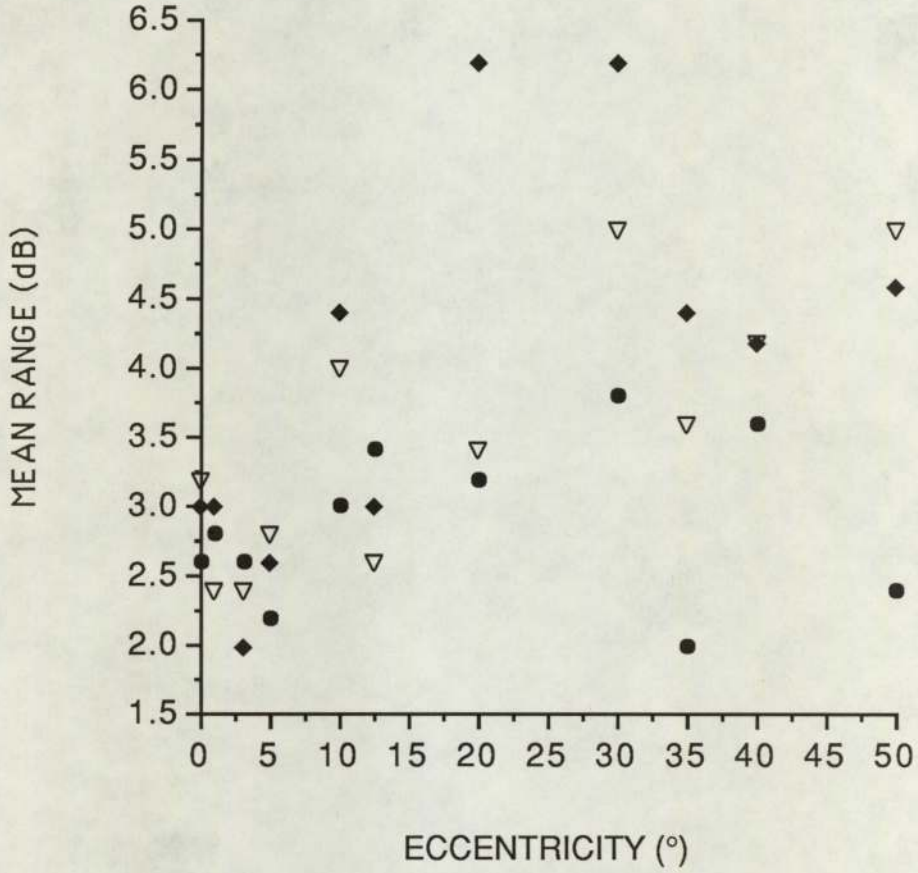


Fig 9.4b Group mean range of sensitivity against eccentricity measured along the inferior meridian of the right eye as a function of pupil size modified by thymoxamine 0.5% (filled diamonds), phenylephrine 10% (filled circles) and saline 0.9% (open inverted triangles) for the 45 asb background luminance recorded with the Dicon AP3000 autoperimeter.

9.5.3 Discussion

The decrease in sensitivity with increase in eccentricity (Figures 9.1a; 9.1b) is in accord with previous findings obtained with manual (Fankhauser and Schimdt 1960; Aulhorn and Harms 1972; Johnson et al 1978) and automated static projection (sections 3.6; 3.8) and LED (section 4.7) perimetry. The increase in variance with increase in peripheral angle is in accord with that demonstrated for automated projection (sections 3.6; 3.8) and LED (section 4.7) perimetry.

Increase in pupil size (Figures 9.1a; 9.1b) has the effect of reducing the rate of decay in sensitivity with increase in peripheral angle, i.e., a flattening of the sensitivity profile, such that the sensitivity of the more peripheral regions is elevated with respect to that obtained with the smaller pupil size. The reason for this finding is unclear. Flattening of the sensitivity profile has been reported in automated perimetry with increase in size of projected stimuli at adaptation levels both of 4 asb and 31.5 asb (sections 3.6; 3.8) and with LED stimuli for decrease in adaptation level (section 4.7) and for increase in intraocular light scatter (section 6.9). The steepening of the profile has been demonstrated with projected stimuli for increase in age (Jaffe et al 1986) and for increase in intraocular light scatter (section 6.9) .

The eccentricity - dependent alteration to the profiles is further illustrated in Figures 9.2a and 9.2b. A 4 - way ANOVA (Table 9.3) indicated that eccentricity ($p<0.05$) and drug ($p<0.001$) both significantly affected proportionate change in sensitivity. At both adaptation levels, there is a small decrease in sensitivity for both active drugs relative to the control out to an eccentricity of 10° (Figures 9.3a; 9.3b). This finding may indicate that the natural pupil is optimum for differential light sensitivity, measured centrally with LED stimuli. At eccentricities greater than 10°, however, an increase in pupil size produces an increase in sensitivity. With smaller pupils, sensitivity decreased beyond a peripheral angle of 10°. The eccentricity - dependent change in sensitivity may relate to the fact that the effective illumination for all stimuli is reduced with increasing peripheral angle, however, as described in section 1.7.3, retinal illumination is approximately constant out to an eccentricity of 80° due to concomitant changes in the retinal image projection with eccentricity

Source	SS	DF	MS	F	Significance Level
Eccentricity (A)	137.615	10	13.761	2.204	p<0.05
AS	562.007	90	6.244		
Luminance (B)	0.909	1	0.909	0.135	NS
BS	60.419	9	6.713		
AB	121.199	10	12.119	1.947	p<0.05
ABS	560.216	90	6.224		
Drug (C)	480.909	1	480.909	50.163	p<0.001
CS	86.287	9	9.59		
AC	221.95	10	22.195	6.811	P<0.001
ACS	293.418	90	3.26		
BC	5.636	1	5.636	1.512	NS
BCS	33.358	9	3.728		
ABC	22.012	10	2.201	0.921	NS
ABCS	215.005	90	2.388		
Subjects (S)	587.148	9	65.238	27.308	p<0.001
TOTAL	3388.29	439			

Table 9.3 Four - way analysis of variance with perimetric sensitivity as the dependent variable.

(Bedell and Katz 1982; Koojiman 1983). Alternatively, it can be argued that the increase in peripheral sensitivity with increase in pupil size may arise because the larger pupil aperture permits more peripheral aberrations which increases the intraocular light scatter. The greater capacity for spatial summation of the peripheral regions relative to the central regions will allow this scattered light to be harnessed and thus may facilitate the increased peripheral sensitivity. Furthermore, the eccentricity - effect may also in part arise from the difference in the fixation target employed in the two programs. The Meridional Threshold Program utilizes the standard green LED fixation target whilst the fixation target for the Macular Threshold Program is a smaller aperture at the apparent centre of 4 red illuminated LEDs. This latter target may require greater sustained accommodation.

The influence of pupil size change on perimetric sensitivity is similar at both adaptation levels ($p<0.75$) which is in contrast to the findings of Baldwin and Smith (In press) who demonstrated that the reduction in retinal illuminance (using neutral density filters) produced a greater depression in perimetric sensitivity at a bowl luminance of 3.15 asb compared to that of 31.5 asb. They attributed this result to changes in Weber's fraction at the lower luminances; pupil size, however, was not controlled in this study.

It has been recently suggested that perimetry undertaken at an adaptation level of 315 asb facilitates the detection of early glaucomatous and neuro - ophthalmological lesions (Paige 1985). In addition, dark - and light - adapted automated perimetry has been shown to facilitate the separation of patients with retinitis pigmentosa into sub - groups (Jacobson et al 1986). Indeed, it has been suggested that the use of perimetric examinations over a range of adaptation levels provides the opportunity to examine differential sensitivity over a further dimension (Barnes et al 1985). The results from this investigation demonstrate that the effects of proportionate change in pupil size induced by such large changes in adaptation level must be controlled in order that meaningful results may be obtained.

Mikelberg et al (In Press) using Program G1 of the Octopus automated perimeter have reported that reduction in pupil diameter induced by thymoxamine 0.5% showed no statistically significant

change in the visual field indices (Flammer et al 1985) such as mean sensitivity and mean defect. Highly significant positive relationships were found, however, between change in both proportionate pupil diameter and area and proportionate change in mean sensitivity. The use of the mean sensitivity index, however, provides a measure of the overall sensitivity of the field which is independent of stimulus location and also of short - term fluctuation. The index will thus mask any eccentricity - effect; moreover Octopus Program G1 only determines threshold out to an eccentricity of 26°.

Some indication of the short - term fluctuation in perimetric sensitivity can be obtained from the group mean range of sensitivity at each eccentricity (Figures 9.4a; 9.4b). The range increases with increase in peripheral angle for both adaptation levels and with decrease in pupil size. This finding is in contrast to that of Flammer, Drance, Fankhauser and Augustiny (1984) who found that pupil size did not influence the magnitude of the short - term fluctuation obtained in normal subjects for the larger projected Goldmann III stimulus of the Octopus. These workers did report, however, that a decrease in pupil size increased the magnitude of the short - term fluctuations in a series of glaucomatous subjects.

9.6 Conclusions

The effect of pupil size, modified by thymoxamine 0.5% and phenylephrine 10%, on perimetric sensitivity and on a measure of the accompanying fluctuations at the two adaptation levels of 10 asb and 45 asb is greatest at peripheral angles greater than 10°. The magnitude of the effect reaches a maximum value of 7 dB for a pupil size difference of 3.7 mm. Within the normal range of pupil size, the effects of pupil size on clinical perimetry may thus be discounted. This variable must, however, be considered in those patients whose pupil size lies outside the normal range or in the serial visual field analysis of patients whose therapeutic regime produces a significant modification of pupil diameter.

10. THE INFLUENCE OF ACCOMMODATIVE MICROFLUCTUATIONS ON THE PERIMETRIC PROFILE

10.1 Introduction

The steady - state accommodation response to a visual stimulus exhibits microfluctuations (Campbell et al 1959; Campbell and Westheimer 1960; Bour 1981; Denieul 1982). The amplitude of these accommodative microfluctuations is approximately 0.10 D with a frequency bandwidth ranging from 0 to 6 Hz (Campbell et al 1959; Denieul 1982). Accommodative microfluctuations are not considered to be a product of muscular noise (Campbell 1960) but are thought to be under central nervous control, with the purpose of continuously monitoring the quality of the retinal image (Millodot 1968; Charman and Tucker 1978).

Studies have reported that microfluctuations in accommodation increase with increasing accommodative effort (Campbell et al 1959; Denieul 1982; Johnson et al 1984; Bullimore et al 1986), in the presence of small pupils (Campbell et al 1959) and when the image quality is poor (Arnulf and Dupuy 1980; Denieul 1982).

10.2 Influence of transient defocus on perimetric thresholds

The influence of sustained defocus on perimetric sensitivity is well documented and is described in section 8.4, however, little is known about the influence of accommodative microfluctuations on perimetric sensitivity. The relationship between transient defocus, arising from variations in accommodative response, and perimetric sensitivity has, however, been discussed by several workers. Tate (1985) stated that accommodative spasm and fatigue can depress foveal sensitivity, the former being common in young uncorrected hyperopes and the latter in undercorrected presbyopes. Greve (1973) reported that accommodative fatigue can induce progressively decreasing

differential light sensitivity which is manifested in a spiralling kinetic visual field and increased variation in threshold measurements. Miotics have also been reported to depress perimetric sensitivity by virtue of the myopia - inducing accommodation spasm (Greve 1973). Following the administration of 2% pilocarpine, Greve (1973) reported a depression in perimetric sensitivity of 0.6 log units at fixation and 0.4 - 0.5 log units at 20° eccentricity, however, details of the experimental protocol for these investigations was not given.

10.3 Aim of the investigation

It was hypothesized that microfluctuations in accommodation, which occur during the sustained fixation of the central fixation target during perimetric examination, may induce transient defocus of the perimetric spot stimuli. The effect of this transient defocus on the format of the perimetric sensitivity profile and on the variability of the perimetric response at a given location measured during a single examination is, however, unknown.

The aims of the investigation were therefore twofold: firstly, to investigate whether the transient defocus of the perimetric stimuli due to accommodative microfluctuations influences perimetric sensitivity and secondly, to assess whether these accommodative microfluctuations contribute to the variability of the threshold response at a given location measured during a single examination.

10.4 Experimental work

The Dicon AP3000 which is described in section 4.7.1. was selected since it has, in common with many other automated perimeters, a bowl radius of 33 cm, which requires a relatively high level of accommodation to be sustained throughout the examination. The LED stimuli subtend a visual angle approximately equivalent to that of the Goldmann II stimuli and may be more sensitive to optical degradation than the standard Goldmann stimulus III used in automated projection perimeters. These properties facilitate investigation of accommodative microfluctuations since the magnitude of the microfluctuations increases in proportion to the accommodation exerted (Campbell

et al 1959; Denieul 1982; Johnson et al 1984; Bullimore et al 1986).

The accommodation response was assessed prior to visual field examination using the Canon Autoref R - 1 (described in section 8.7).

10.4.1 Materials and methods

The sample for the investigation consisted of 10 clinically normal, emmetropes (mean age 23.72 years, S.D. 3.53 years; 3 females, 7 males) with visual acuity of 6/5 or better. All subjects were free from any ocular or systemic medication and were experienced observers in automated perimetry and in other psychophysical techniques of investigation.

The ciliary smooth muscle activity was modified on separate occasions with either cyclopentolate HCl 1% or phenylephrine HCl 10%; saline 0.9% was employed as the control solution. Cyclopentolate is a muscarinic antagonist which produces marked cycloplegia and attenuation of the accommodative microfluctuations (Campbell et al 1959; Johnson et al 1984) together with mydriasis and abolition of the direct and indirect pupillary light responses. Phenylephrine acts on alpha adrenoreceptors present on the smooth muscle of the dilator pupillae leaving both the direct and indirect pupillary light response relatively unaffected. The latter drug was employed to match the pupillary mydriasis of cyclopentolate without markedly affecting the sustained accommodative response. In this way, the influence of accommodative microfluctuations on perimetric sensitivity could be separated from the influence of changes in pupil size.

Each subject attended a total of three experimental sessions within a maximum period of three weeks. At the beginning of each session one drop of benoxinate HCl was instilled into each eye to inhibit reflex tearing and facilitate the penetration of the ophthalmic drugs used subsequently (as described in section 9.5.1). This was followed by two 25 µl instillations, each made with a precision micro - pipette, of either one of the two active agents or of the control solution; the period between the two instillations within a given session was five minutes. All drugs employed

in the investigation were obtained from Smith and Nephew single - dose applicators ("minims"). The wash - out period between sessions was a minimum of 2 days. The order of instillation of the active drug and of the control drug was randomized for each subject.

Twenty five minutes following the instillation of the benoxinate HCl, the monocular amplitude of accommodation was measured under normal room illumination using the RAF rule, a standard clinical technique. The measurement was repeated at the end of the session, immediately following the perimetric examination. The marked cycloplegic effect produced by cyclopentolate necessitated the use of a +3 D auxiliary lens to measure the amplitude of accommodation.

Further evaluation of the action of the active drugs was made by the assessment of the accommodative response to a target placed at a stimulus vergence of -3 D. This was measured using the Canon Autoref R - 1 following the initial measurement of the amplitude of accommodation and immediately prior to the perimetric investigation. The target consisted of a matrix of numbers equivalent to N5 positioned at 33 cm from the subject, who was instructed to focus on the central number within the matrix whilst a series of 30 consecutive readings were taken under normal room illumination. The standard deviation of the measured accommodative response is considered to be an index of the magnitude of the microfluctuations of accommodation but not a measure of their absolute amplitude (Johnson et al 1984; Bullimore et al 1986).

Perimetry was undertaken 30 minutes following instillation of the benoxinate HCl. The differential light sensitivity of the right eye was measured at eccentricities of 0°, 1°, 3° and 5° along the vertical meridian of the inferior field using the Macular Threshold Program and at eccentricities of 7.5°, 10°, 15°, 20°, 25° and 27.5° along the 265° meridian of the inferior field using the Meridional Threshold Program. The order of perimetric program was randomized throughout the sample. Stimulus duration was 100 ms with an inter - stimulus duration of 1 s. Each subject underwent a 10 minute adaptation period to the bowl luminance of 10 asb. A bowl luminance of 10 asb was used since this provides the greatest dynamic range with which to assess sensitivity. The threshold for each stimulus location was measured five times in order to obtain a measure of the variability of the

threshold perimetric response during a single session. During the cyclopentolate session, a +3 D lens was suspended in front of the eye using the lens holder of the perimeter. The head was steadied with the head rest and chin bar of the instrument and fixation was monitored throughout the examination via the video monitor.

The size of the pupil was measured immediately prior to perimetric examination and thereafter at 5 minute intervals using the scaled axes on the video monitor of the perimeter. Pupil size could be measured to an accuracy of 0.5 mm. The value for pupil diameter was represented as the mean of the measurements taken during the examination; the duration of the perimetric examination was of the order of 30 minutes.

10.4.2 Results

Table 10.1 indicates the group mean and one standard deviation for the various aspects of accommodative function investigated. The results for the accommodative response to a -3 D target are representative of 30 measurements per subject. Data relating to pupil size indicates that the mydriatic responses to cyclopentolate and phenylephrine were similar. The microfluctuations in accommodative response are represented in terms of the group range of standard deviations of the accommodative response obtained for each drug. A 50% reduction in the accommodative microfluctuations was obtained with cyclopentolate compared to that for phenylephrine and saline.

Figure 10.1 illustrates the relationship between group mean perimetric sensitivity and eccentricity for each drug. Sensitivity decreases with increase in eccentricity for all trials and is consistent with the results of section 9.5. The standard deviations ranged from 0.95 dB to 2.66 dB and were on average 2.0 dB. They were fairly constant out to an eccentricity approaching 12.5° beyond which the magnitude increased with increasing eccentricity for each drug trial, in agreement with the findings of section 9.5.

Figure 10.2 illustrates the group mean proportionate change in perimetric sensitivity with

		Cyclopentolate 1%	Phenylephrine 10%	Saline 0.9%
Amplitude of accommodation (D)	(mean)	1.06	8.10	9.60
	(S.D.)	0.58	1.22	1.72
Accommodative response (-3D) stimulus (D)	(mean)	0.16	2.49	2.52
	(S.D.)	0.48	0.12	0.17
Accommodative microfluctuations (D)	(range)	0.05-0.11	0.10-0.20	0.13-0.21
Pupil size (mm)	(mean)	7.48	7.25	4.87
	(S.D.)	0.47	0.55	0.72

Table 10.1 Group mean and one standard deviation of the amplitude of accommodation, the level of accommodation in response to a -3 D target, group mean pupil diameter and the group mean range in the standard deviations of the accommodative response for each drug.

eccentricity for each drug relative to the saline control. For eccentricities less than 5°, proportionate sensitivity decreased for both active drugs; beyond this eccentricity both drugs induced an increase in proportionate sensitivity.

Figure 10.3 shows the relationship between the group mean perimetric sensitivity and group mean pupil diameter as a function of eccentricity. There is a small increase in sensitivity with increase in pupil diameter at the more peripheral locations, whereas at fixation, there is a small decrease in sensitivity as pupil size increases; for a pupil size of 7.5 mm there is a reduction in sensitivity at all eccentricities.

The group mean range of sensitivity values (an indication of the short - term fluctuation in perimetric sensitivity) are illustrated as a function of eccentricity for each drug (Figure 10.4). A reduction in the range in sensitivity values was observed with both of the active drugs relative to the control. The mean range of perimetric sensitivity was of least magnitude for the cyclopentolate trial. In general, there is a decrease in mean range in perimetric sensitivity with eccentricity for the cyclopentolate trial, and an increase in the mean range in perimetric sensitivity with increase in eccentricity both for the phenylephrine and saline trials. Paracentrally, there is a dip in the mean range in perimetric sensitivity for all trials. The large mean range of perimetric sensitivity values at 7.5° for the saline trial were not found in the results of section 9.5 in which the subject group was taken from the same population; the reason for this finding is unclear.

10.4.3 Discussion

The monocular amplitude of accommodation measured with the RAF rule was relatively unaffected by either saline or phenylephrine, but was profoundly reduced by cyclopentolate in all subjects (Table 10.1). This finding is in agreement with previous reports (Garner et al 1983; Ward and Charman 1986; Mordi, Tucker and Charman 1986). The accommodative response to a -3 D target was also depressed by cyclopentolate in all subjects, relative to the saline trial (Table 10.1). Interestingly, although the effect of phenylephrine on the accommodation response was small

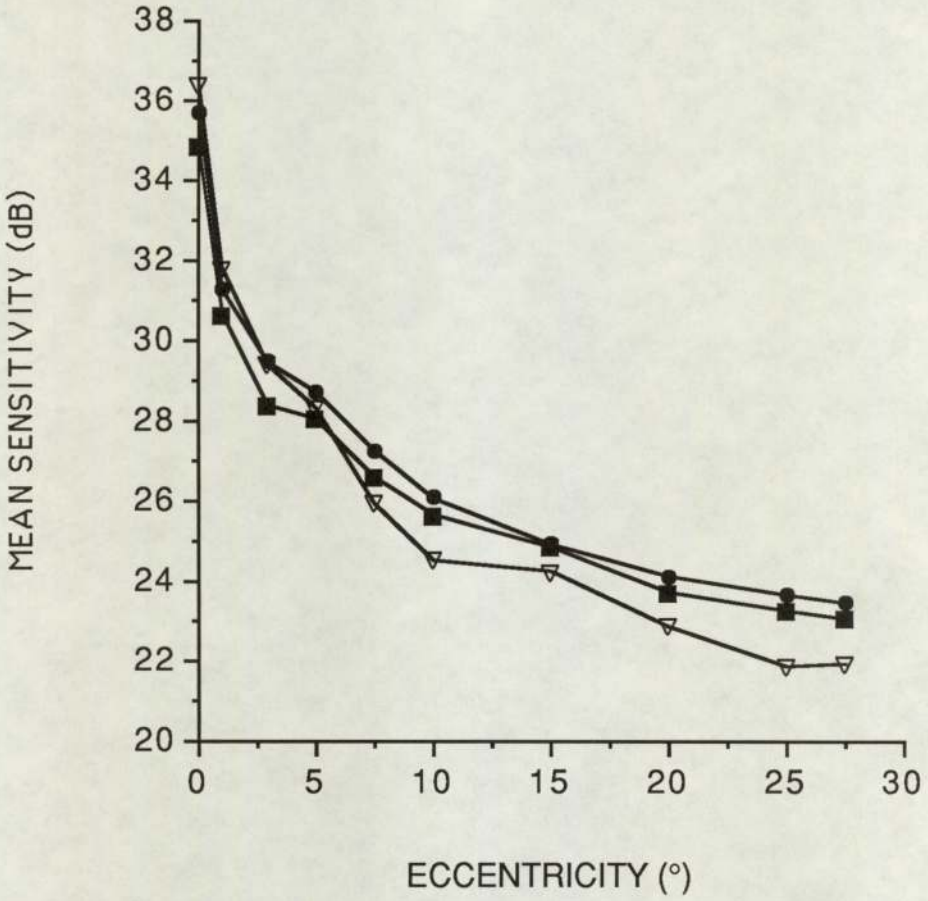


Fig. 10.1 Group mean perimetric sensitivity against eccentricity along the inferior meridian of the right eye for phenylephrine 10% (filled circles), cyclopentolate 1% (filled squares) and saline 0.9% (open inverted triangles) recorded with the Dicon AP3000 autoperimeter.

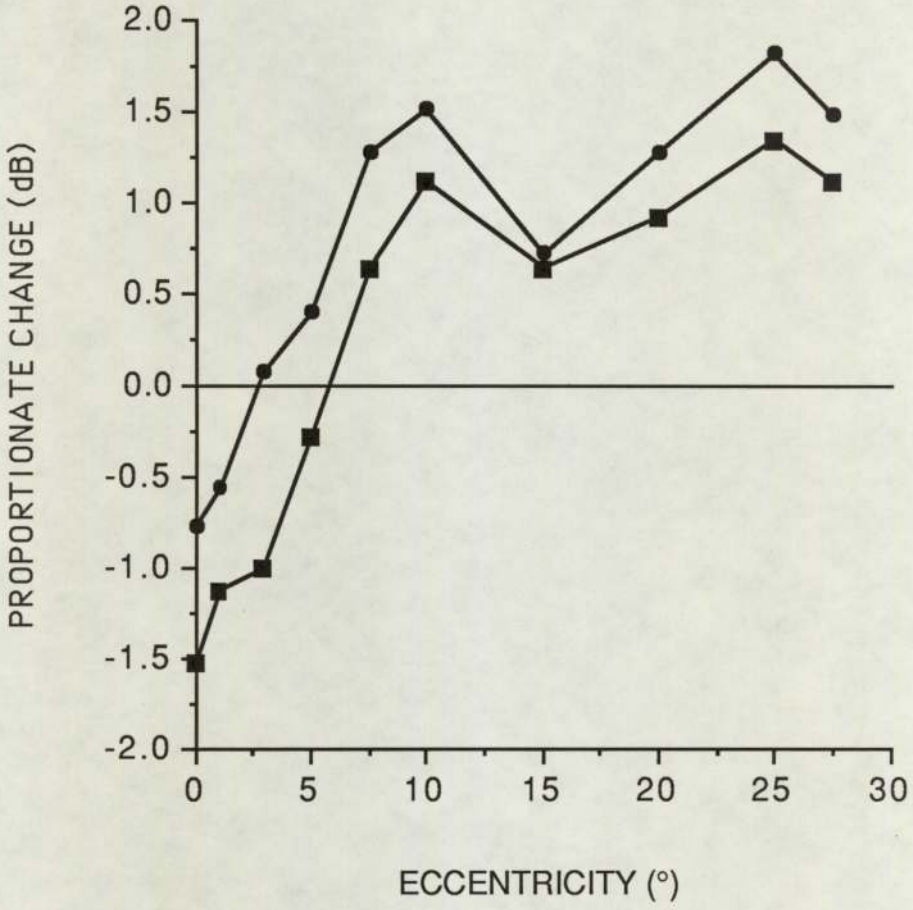


Fig. 10.2 Group mean proportionate change in perimetric sensitivity relative to the saline control against eccentricity along the inferior meridian of the right eye for phenylephrine 10% (filled circles) and cyclopentolate 1% (filled squares) recorded with the Dicon AP3000 autoperimeter.

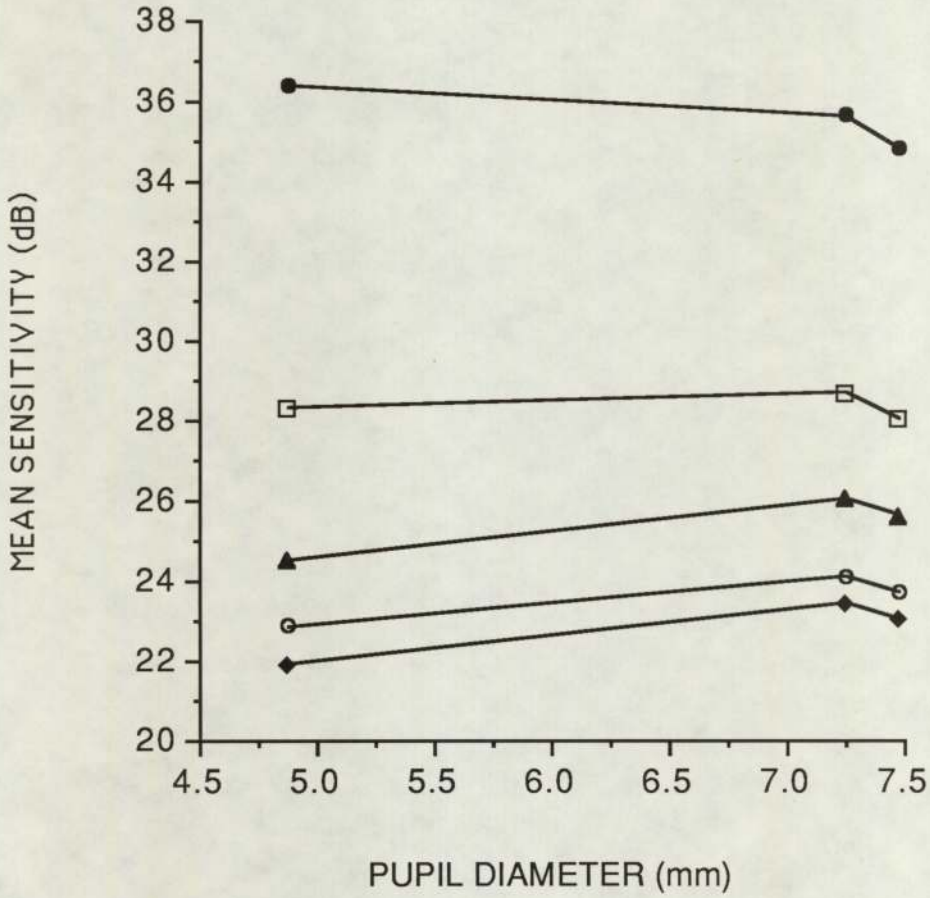


Fig. 10.3 Group mean perimetric sensitivity along the inferior meridian of the right eye against group mean pupil diameter at 0° (filled circles), 5° (open squares), 10° (filled triangles), 20° (open circles) and 27.5° (filled diamonds) recorded with the Dicon AP3000 autoperimeter.

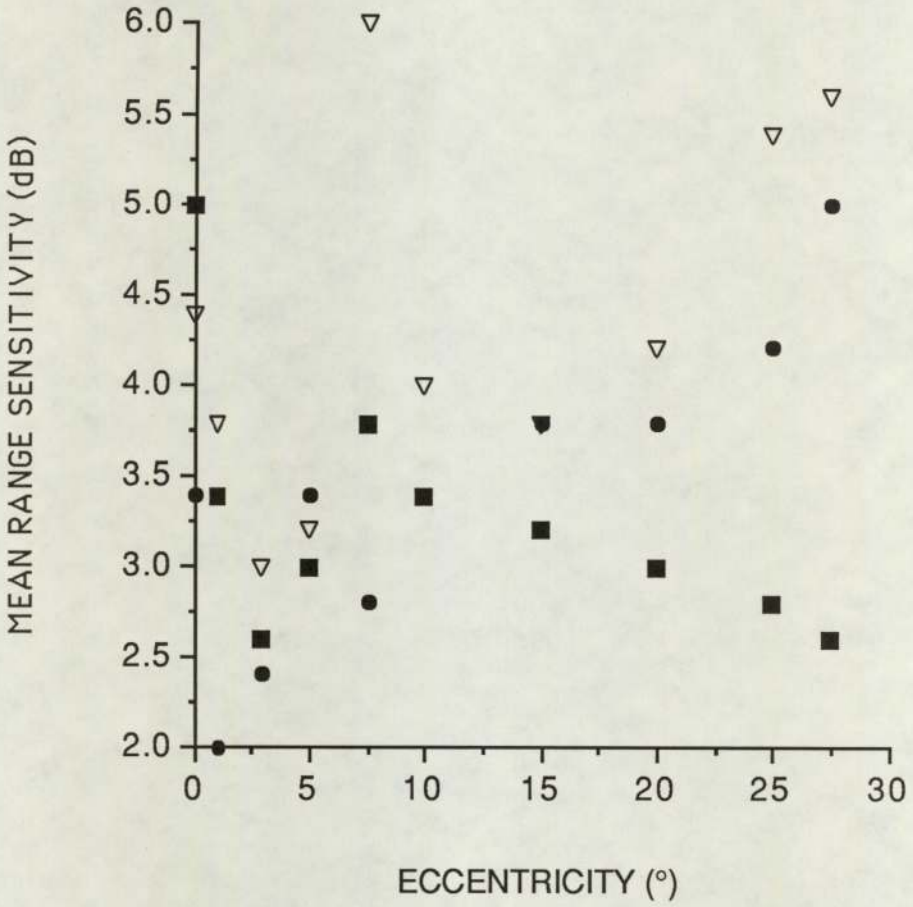


Fig. 10.4 Group mean range in perimetric sensitivity values along the inferior meridian of the right eye measured at a single location against eccentricity for phenylephrine 10% (filled circles), cyclopentolate 1% (filled squares) and saline 0.9% (open inverted triangles) recorded with the Dicon AP3000 autoperimeter.

compared with that of cyclopentolate, it did reduce accommodation slightly which is in accord with the findings of Garner et al (1983) and Mordi, Tucker and Charman (1986). The apparent accommodative microfluctuations present with cyclopentolate can be attributed to the measurement error of the Canon Autoref R - 1.

The group mean pupil size for the 3 experimental conditions (Table 10.1) demonstrates that the effect on pupil size is very similar for both phenylephrine and cyclopentolate. This permits studies of the accommodative response.

The decrease in perimetric sensitivity with increasing eccentricity (Figure 10.1) is in accord with the findings for automated projection (sections 3.6; 3.8) and LED (sections 4.7; 9.5) perimetry.

A 3 - way ANOVA (Table 10.2) indicated that eccentricity ($p<0.001$) but not drug, significantly affected proportionate change in sensitivity. Indeed, Figure 10.2 (where proportionate change in sensitivity relative to saline is plotted against eccentricity) reveals that sensitivity for both cyclopentolate and phenylephrine is depressed relative to the saline trial for eccentricities out to 5°, and has a maximum depression of 1.5 dB and 0.75 dB respectively, at fixation. Interestingly, proportionate sensitivity for both phenylephrine 10% and thymoxamine 0.5% was also shown to be depressed relative to saline 0.9% within the central regions in section 9.5, where pupil size alone was varied.

The elevation in sensitivity for saline within the central 5° relative to cyclopentolate and phenylephrine, may arise because accommodative microfluctuations, maintained in the saline run, are a necessary prerequisite for the sustained accommodation required in a perimetric examination of 30 minutes. This is in accord with the hypothesis that the purpose of accommodative microfluctuations is to continuously monitor the optical quality of the eye (Millodot 1968; Charman and Tucker 1978). The finding that the accommodative microfluctuations were only slightly reduced in the phenylephrine trial, however, (Table 10.1) invalidates this hypothesis. The main difference between the saline trial and the cyclopentolate and phenylephrine trials was the size

Source	SS	DF	MS	F	Significance Level
Eccentricity (A)	173.728	9	19.303	5.472	p<0.001
AS	285.706	81	3.527		1
Drug (B)	14.472	1	14.472	1.905	NS
BS	68.369	9	7.596		
AB	3.361	9	0.373	0.321	NS
ABS	93.977	81	1.16		
Subjects (S)	224.256	9	24.917	21.476	p<0.001
TOTAL	863.871	199			

Table 10.2 Three - way analysis of variance with perimetric sensitivity as the dependent variable.

of the pupil, it therefore seems probable that the results pertain to this change in pupil size. Indeed, the findings of section 9.5, in which pupil size was varied whilst accommodation was relatively unaffected, suggested that the natural pupil was optimum for differential light sensitivity measured out to an eccentricity of 5° with LED stimuli.

The elevation of proportionate sensitivity for both cyclopentolate and phenylephrine between eccentricities of 5° and 27.5° (Figure 10.2), may be an indication of the relative insensitivity of the peripheral regions to optical defocus (Ikeda and Wright 1972), but is more likely to pertain to the eccentricity - dependent increase in sensitivity with increase in pupil size as illustrated in Figure 10.3. Interestingly, although the mean pupil size for cyclopentolate is slightly larger than that for phenylephrine (7.48 mm compared to 7.25 mm), the sensitivity with the latter drug is greater, although this effect is not significant (Table 10.2). This may arise because of the discomfort experienced by the observers resulting from the reduction in amplitude of accommodation following instillation of cyclopentolate. In addition, the use of a auxiliary lens for perimetry in the cyclopentolate trial may have resulted in a depression in sensitivity due to the reduction in light transmission and to the prismatic effects induced by the ophthalmic lens. The prismatic effects of ophthalmic lenses can be ignored during static perimetry for lens powers up to ±10 D, whilst the light transmission of ophthalmic lenses is of the order of 92% (Atchison and Johnston 1979).

The value of the mean range of perimetric sensitivity (which is a correlate of the short - term fluctuation) recorded at each location (Figure 10.4) is greatest for saline and least for cyclopentolate. Indeed, the mean range in sensitivity is attenuated by cyclopentolate for stimulus locations beyond 5°. This difference may arise because of differences in pupil size (section 9.5) in which the mean range in sensitivity increased with decrease in pupil size. The greater mean range in sensitivity for the phenylephrine trial relative to the cyclopentolate trial, where pupil size with the two drugs is very similar, would, however, tend to discount this explanation. It is possible that the reduction in accommodative microfluctuations due to the cyclopentolate may account for the reduction in the mean range of perimetric sensitivity. The mean range in sensitivity is greatest at stimulus locations beyond 5° for all three trials. This may arise, as in section 9.5, because the fixation target employed

for the Meridional Threshold Program requires less accurate accommodation than for the supplementary fixation target of the Macula Threshold Program due to their relative differences in angular subtense.

10.5 Conclusions

The findings suggest that although accommodative microfluctuations play a minor role in determining the magnitude of perimetric sensitivity within the central 5°, their importance in the periphery is superseded by factors such as the pupil size modified by the drugs used in the investigation. Nevertheless, the range in perimetric sensitivity values measured at a specific location, were in general reduced when accommodative fluctuations were minimized. This suggests that when relatively high levels of accommodation must be sustained, as for the Dicon AP3000 autoperimeter, accommodative microfluctuations are a minor component of the short - term fluctuations in perimetric sensitivity. In clinical perimetry these effects can largely be discounted.

11. GENERAL DISCUSSION

11.1 Summary of results

The major findings of the study are given in summary form as follows:

1 A) The process of M - scaling applied to spatial stimulus parameters alone, whereby stimulus size at each location in the visual field is scaled in inverse proportion to the square root of ganglion cell receptive field density, did not result in isosensitivity profiles using the conventional spot stimuli employed in the Octopus and Humphrey automated perimeters.

B) Theoretical isosensitive profiles may be obtained by presenting the standard Goldmann stimuli at eccentricities which were determined by interpolation from the actual profiles measured with the Octopus and Humphrey automated perimeters. The particular eccentricities varied with meridian.

C) Larger stimuli, such as the standard Goldmann stimulus size III used in automated perimetry, saturated the foveal regions at low photopic luminances of 4 asb and 31.5 asb.

D) Subsidiary peaks of enhanced sensitivity were found at 15° nasally and at 21.2° inferio - temporally. The magnitude of the peaks was stimulus size dependent, being greatest for stimulus sizes I and V and of least magnitude for stimulus size III. The presence of the peaks was validated in separate investigations using separate groups of subjects, although the spatial location and the magnitude of the peaks was found to vary between investigations.

2. A) A good relationship was found between log ganglion cell receptive field density and

perimetric sensitivity; the relationship was linear for the projected stimulus size 0 and became non - linear for stimuli larger than size 0. The relationship between log ganglion cell receptive field density and perimetric sensitivity measured with LED stimuli (Goldmann size II equivalent) was non - linear, as predicted from the results for projected stimuli of an equivalent size. Adaptation level (10, 31.5 and 45 asb) had no influence on the format of this relationship.

B) The relationship between log rod density and perimetric sensitivity measured with projected stimuli was linear for stimulus sizes 0 and I ; for stimulus sizes larger than this, the relationship became non - linear. The relationship between log rod density and perimetric sensitivity measured with LED stimuli (Goldmann stimulus size II equivalent) was non - linear at all the adaptation levels measured. This finding was not unexpected since the relationship was also non - linear for the stimulus size II projected stimuli. The format of this relationship was not influenced by adaptation level (10, 31.5 and 45 asb).

C) The relationship between log cone density and perimetric sensitivity was non - linear for projected and for LED stimuli for all the stimulus sizes and adaptation levels measured.

3. A) Patients with retinitis pigmentosa (R.P.) responded atypically over the dynamic range in both the spatial and temporal domain. Some patients exhibited enhanced sensitivity to short compared to long duration stimuli and, within the constraints of the experimental design, displayed enhanced spatial sensitivity across the residual islands of vision within the field.

B) All 7 patients with R.P. who were specifically investigated for stato - kinetic dissociation, exhibited this phenomenon, whereby perimetric sensitivity was increased when measured with kinetic stimuli compared to static stimuli.

C) Visual loss in the R.P. patients was more extensive in the superior compared to the inferior regions of the visual field.

4. A) A good relationship was found between perimetric attenuation (measured with the Octopus and Dicon automated perimeters) and the intraocular light scattering factor, both in normal subjects in whom intraocular light scatter was simulated using cells containing various concentrations of latex beads and in those patients with opacities of the crystalline lens.

   B) For both experimental samples, perimetric attenuation was greatest in the periphery with the Goldmann size III projected stimulus, whereas, for LED stimuli perimetric attenuation was greatest centrally.

   C) Perimetric attenuation was of greatest magnitude when measured at the lower adaptation level of 10 asb compared to that of 45 asb.

5. A) Perimetric sensitivity measured with the Octopus perimeter improved heterogeneously across the visual field with serial examination in eight of ten observers.

   B) Three patterns of learning were demonstrated: Type 1 observers who exhibited a large increase in sensitivity at the second session which then plateaued over the subsequent sessions; Type 2 observers who exhibited a gradual increase in sensitivity over each of the five sessions and Type 3 observers in whom no obvious improvement in sensitivity was demonstrated.

   C) The learning - effect was of greatest magnitude beyond an eccentricity of 30°, particularly in the superior visual field.

6. A) Correction of the central/peripheral refractive error, in observers who were centrally emmetropic, had no significant effect on perimetric thresholds measured with the small (size 0) or large (size III) projected stimuli of the Octopus.

7. A) The effect of changes in pupil size on perimetric sensitivity measured with the LED stimuli of the Dicon, was of greatest magnitude at peripheral angles larger than 10°. The magnitude of this effect reached a maximum of 7 dB for a pupil size difference of 3.7 mm, whereby an increase in pupil size produced a corresponding increase in perimetric sensitivity.

8. A) Accommodative microfluctuations had little effect on the level of perimetric sensitivity measured with the LED stimuli of the Dicon, however, they did contribute to the fluctuations in sensitivity measured during a single examination.

11.2 Discussion of results

The finding that isosensitivity profiles did not result from M - scaling of the spatial parameters of conventional perimetric stimuli and that the relationship between log ganglion cell receptive field density was linear for stimulus size 0 only, indicated that the spatial summation characteristics of ganglion cells, in addition to their density, have a role in determining the format of the normal perimetric profile. This conclusion was further supported by the finding that the fovea was saturated by the larger stimulus sizes used in conventional perimetry (at adaptation levels of 4 asb and 31.5 asb). Indeed, it is likely that this central saturation, which renders the fovea relatively less sensitive to small changes in light intensity, accounts for the finding that the perimetric attenuation arising from intraocular light scatter, was least centrally when measured with stimulus size III. The LED stimuli, however, by virtue of their smaller size (equivalent to Goldmann stimulus size II) did not saturate the fovea, thus the perimetric sensitivity of the central regions was attenuated to a greater extent by intraocular light scatter than that of the peripheral regions of the visual field.

The subsidiary peaks of enhanced sensitivity at 15° nasally and 21.2° inferio - temporally were demonstrated in 3 separate samples of subjects using 3 different programs on the Octopus; the magnitude and the exact spatial location of peaks varied, however, between the groups. It was conjectured that the peak of sensitivity measured with stimulus size I may be a product of the increased fluctuations in perimetric sensitivity recorded around this region for this stimulus size.

The subsidiary peaks measured with stimulus V were not accompanied by an increase in perimetric fluctuations and corresponded to areas of increased ganglion cell and rod density; it was further conjectured that the peaks may arise due to an increase in the density of rod - driven ganglion cells.

The finding of stato - kinetic dissociation (S.K.D.) in patients with R.P. poses problems in interpretation, since S.K.D. is a characteristic of neurological conditions (Riddoch 1917; Safran and Glaser 1980) and is explained in terms of cortical processing. It is possible, however, that the S.K.D. may relate to the finding that some patients with R.P. also exhibit increased sensitivity to short rather than to long duration perimetric stimuli.

The enhanced spatial summation over the islands of peripheral vision exhibited by the R.P. patients was considered with caution, since it was felt that the experimental technique was particularly influenced by the short - and the long - term fluctuations inherent in the measurement of perimetric sensitivity.

The model describing the relationship between perimetric attenuation and intraocular light scatter compared well with the results for patients with non - nuclear lens opacities and suggested that this technique may be of value in separating the depression in perimetric sensitivity arising due to optical attenuation from that arising due to neural attenuation. In addition, the finding that the relationship between perimetric attenuation and light scatter in central nuclear lens opacities differed from that in non - nuclear opacities, together with the increased glare problems experienced by patients with posterior subcapsular cataracts indicates that the plane of the opacity as well as the degree of forward light scatter it produces determines the resultant perimetric attenuation.

The increase in differential light sensitivity exhibited with serial examination was not considered to arise wholly as a result of a change in the subjects response criteria since the change in sensitivity was heterogeneously distributed across the visual field. The large increase in sensitivity in the peripheral regions at eccentricities greater than 30° confirmed previous concepts of the peripheral retina as an unpractised sensory area. Furthermore, the increase in sensitivity in the superior field

relative to the inferior field may arise because the former is utilized to a lesser extent in the normal visual environment and thus may have the greatest potential for improvement. Indeed, this is in accord with a hypothesis of Mayer (1983), which stated that contrast sensitivity measured at fixation with oblique rather than vertical or horizontal gratings exhibits an improvement with practise because oblique patterns are less encountered in normal vision.

The presence of a learning - effect in automated perimetry has several implications in monitoring the progression of field defects in diseased eyes. For subjects of the Type 1 group, discarding the results of the first visual field examination may negate the effects of practise, however, for Type 2 subjects the learning - effect would still be apparent.

The investigation of the effect of pupil size on perimetric sensitivity demonstrated, for subjects who are not taking ocular medication, and in whom the intraocular musculature is intact, that pupil size did not significantly modify the level of the perimetric response. In those patients, however, whose pupil size lies outside the normal range, or in the serial field analysis of patients whose ocular medications produce a significant modification of the pupil diameter, the role of pupil size should be considered, particularly at peripheral angles greater than 10°.

Similarly, microfluctuations in the accommodative response which occur during the sustained fixation of the central fixation target in perimetric examination, do not influence the magnitude of perimetric sensitivity. Accommodative microfluctuations, which are present during perimetric examinations, do, however, contribute to the fluctuations in sensitivity measured during a single examination. Interestingly, in both the investigation of the effect of pupil size and of the accommodative microfluctuations on perimetric sensitivity, the natural pupillary and accommodative state was found to be optimal for stimuli presented out to an eccentricity of 5° in the visual field. This finding is in accord with previous reports which state that the naturally occurring pupil diameter is optimal for visual resolution (Campbell and Gregory 1960; Leibowitz 1952; Woodhouse 1975).

11.3 Future work

Areas for future work can be divided into 5 categories which develop and expand the investigations undertaken during the period of the study.

11.3.1 Cortical representation of the perimetric profile

It is proposed that the subsidiary peaks of perimetric sensitivity at 15° nasally and 21.21° inferio - temporally should be validated in a normal sample either with a second Octopus perimeter or with an instrument whose stimulus parameters match those of the Octopus as closely as possible. Once validated, the characteristics of the subsidiary peaks should be investigated in a larger population in order to establish clinical normals in term of magnitude, spatial location and repeatability. In addition, the parametric adjustment would be varied to determine how background luminance, stimulus size, colour and duration influence the configuration of the peaks. Such data should provide some indication of the mechanisms underlying the presence of the peaks in sensitivity. It is envisaged that having established the format of the subsidiary peaks in normal subjects, the characteristics would be determined in a series of diseased eyes, in particular those with glaucoma. Indeed if the hypothesis developed in the original study is correct, namely that the subsidiary peaks are a function of ganglion cell characteristics, then in a disease such as glaucoma, where a primary feature is ganglion cell damage, the peaks should reflect early onset of such damage.

A further objective of the future work would be to design perimetric routines which incorporate different stimulus sizes based upon the coverage factor of retinal ganglion cells, such that larger stimuli are presented peripherally and smaller stimuli centrally. The stimuli would be scaled in the periphery in proportion to the decreased representation at the cortex compared to the more central areas (thus avoiding saturation) and would result in isosensitive profiles (since stimulation of the cortex is equivalent across the field) in the normal eye.

11.3.2 Retinitis pigmentosa

Further studies would investigate the temporal perimetric characteristics of R.P. patients. The influence of adaptation level and stimulus size on the temporal summation of these patients would also be investigated to determine whether the abnormal temporal characteristics reach a maximum at a particular state of parametric adjustment. Such anomalous behavior could then be evaluated as a potential diagnostic indication of early R.P. The characteristics of S.K.D. and spatial summation should, as the technology becomes available, also be studied using an automated perimeter which permits perimetric investigation both using kinetic and static stimuli under the same states of parametric adjustment. The influence of adaptation level on the magnitude of the S.K.D. would also be determined. The spatial characteristics of summation would be investigated using a perimetric program which incorporates several stimulus sizes within a single examination. Although not currently available, such a program would improve the accuracy with which spatial summation could be calculated, since the larger the range of stimulus sizes examined, the more accurate the result. Furthermore, the use of such a program would obviate the problem of long - term fluctuations confounding the analysis of spatial summation. Adaptation level and the temporal characteristics of the stimuli would again be varied to determine the state of parametric adjustment at which the abnormal spatial characteristics were most evident. The results would also be examined to determine whether the different genetic typings of R.P. exhibit different spatial and temporal responses.

11.3.3 Intraocular light scatter

The influence of induced intraocular light scatter on perimetric sensitivity in patients with concomitant ocular diseases such as glaucoma would be investigated. The purpose of this investigation would be, primarily, to determine whether the presence of scotomatous regions in the visual field may be reduced in size by intraocular light scatter. In addition, the investigation would determine whether abnormal retinal areas resulting from, for example, the pigmentary changes in R.P. constitute another source of light scatter. It is envisaged that the investigation would be

undertaken using the simulating cells and the experimental procedures as described in section 6.9.2.

It is proposed that the apparatus for the assessment of intraocular light scatter in the patient sample should be modified in order to decrease the level of illumination of the glare sources since some patients with high degrees of media opacification, and also with posterior subcapsular cataracts, could not be assessed with the original apparatus.

In addition, it is proposed that the relationship between perimetric attenuation and intraocular light scatter should be investigated in a series of subjects with media opacities at sites other than the crystalline lens. These would include corneal and vitreous opacities of varying aetiologies and would provide a further insight on how the position of the source of intraocular light scatter affects the format of the perimetric profiles.

11.3.4 The learning - effect

It is envisaged that the learning - effect in automated perimetry would be further investigated in a larger sample of subjects covering a series of age groups to determine how age influences the learning curve. The objective of the future work would also be to develop a practical means of determining the learning potential, with respect to perimetric responses, of a particular subject. This may constitute a program executed prior to the main perimetric examination which assesses the rate of change in perimetric sensitivity with repeated measurement, at a limited number of locations across the visual field. Such a result would then have to be correlated with the eventual outcome of the examination.

Furthermore, it is proposed that investigation of the learning - effect in subjects with existing ocular disease, such as glaucoma, would provide practical clinical information for serial field examinations and in addition, would indicate whether the learning - effect is a result of retinal or cortical changes or of a criterion change independent of the level of sensitivity. Indeed, if the learning - effect was the same in patients with ocular pathology and in age - matched normal

subjects it would indicate that the learning - effect arises from a criterion change, whereas if the learning - effect differed between the 2 groups the reverse would be concluded.

11.3.5 The effect of pupil size

To supplement the results pertaining to the effect of pupil size on perimetric sensitivity it is proposed that the effects of pupil size on perimetric sensitivity measured with projection stimuli should be evaluated, in particular to determine the influence of stimulus size, commensurate with the isosensitive profiles. These results together with those from the original study, would permit a correction factor to be calculated to take into account the size of the pupil in perimetric assessment.

11.3.6 General considerations

Consideration of the results achieved in the study and the perimetric literature as a whole suggests that the future work is innovative and of particular current interest.

The findings of the study and the subsequent proposals for future work are broadly divided into 3 sections:

1) Investigation of the influence of patient specific variables on conventional automated perimetric profiles and the derivation of the appropriate correction factors.

2) The utilization of perimetry as a means of measuring spatial and temporal summation and stato - kinetic dissociation and the application of these phenomena as diagnostic tools.

3) The development of the concept of isosensitive profiles for perimetric examination based upon the coverage factor of the retinal ganglion cells.

Worldwide perimetric research is currently being directed towards the application of correction

factors for patients specific variables; nevertheless the work is currently at a formative stage. The investigation of the spatial and temporal visual processing of patients beyond that normally employed in perimetry, particularly with R.P., has been the subject of recent research (Temme et al 1985; Greenstein and Hood 1986; Taylor 1987). The isolated findings documented in such studies, and the lack of understanding of the mechanisms underlying these phenomena, indicates that the study of temporal and spatial characteristics will provide an important contribution to the understanding of perimetric processing and consequently the early diagnosis of abnormality. The possible existence of a relationship between perimetric sensitivity and retinal ganglion cells has been acknowledged by some workers, however, the concept of isosensitive profiles based upon cortical representation is an innovation yet to be investigated by other researchers.

The development of automated perimetry has revolutionized the role of visual field investigation in the diagnostic procedure. The current approach, namely, using a standard parametric adjustment within one stimulus program will eventually be refined. Automated perimetry will not, however, replace the other standard psychophysical techniques available to the clinician.

APPENDIX 1

A1. THE INFLUENCE OF STIMULUS CONFIGURATION ON THE PERIMETRIC PROFILE

A1.1 Introduction

It was recognized that the LED stimuli of the Dicon AP3000, which do not incorporate a device to mask the apertures in which they are situated, and which have been consequently termed "black hole" stimuli (Heijl 1985), may produce a unique measurement of differential light sensitivity. The potential problems incurred with the use of these "black hole" stimuli include: variations in local retinal adaptation and incorrect assessment of the Weber fraction, in that the intensity of the stimulus when lit, is not added to an even background (Heijl 1985). In clinical terms, the various types of stimuli (either LED or projection) are undoubtedly effective in facilitating the detection of early visual field loss, but the mechanisms underlying the responses may be quite different.

It was therefore decided to examine the validity of the "black hole" LED stimuli of the Dicon in assessing perimetric sensitivity. This was achieved by comparison of the response elicited by the Dicon AP3000 with that of the Topcon SBP1000. The latter perimeter employs LED stimuli the luminance of which are matched to that of the surrounding bowl luminance.

A1.2 Experimental work

A1.2.1 Topcon SBP1000

Hardware

The Topcon SBP1000 is a single unit LED automated perimeter, consisting of a hemispheric bowl, LEDs and a computer system. The perimeter bowl has a radius of 33 cm, and has a luminance of

31.5 asb which is automatically regulated. Two hundred and fifty seven LEDs are mounted into the bowl. The LEDs are yellow (wavelength 585 nm) and have a diameter of 2 mm. To obtain a diffuse background adaptation, all LEDs emit light at a luminance equivalent to that of the 31.5 asb level of the bowl. The dynamic range of the instrument is 25 dB in 1 dB increments with a maximum stimulus luminance of 425 asb. Both stimulus duration and interval can be varied within the range of 0.2 - 3.2 s. Fixation is checked via a monitor, such that when the patient loses fixation, the examiner can interrupt the examination, a procedure which also cancels the two stimulus locations measured directly prior to this. In addition, the fixation is automatically checked by the Heijl - Krakau method of monitoring. If the patient responds to a stimulus which falls within the blindspot, the 5 preceding stimulus locations are rechecked.

Software

This perimeter offers both suprathreshold and threshold strategies; the threshold strategy was most appropriate for the investigation. The thresholding strategy is a 4 - 2 - 1 treble staircase with a genuine 1 dB increment at the final crossing. The stimulus presentation is pseudo - random in terms of both staircase and stimulus position and is controlled by the microcomputer.

A1.2.2 Materials and methods

The sample for the investigation comprised 22 clinically normal, emmetropes (mean age 22.01 years; S.D. 2.39 years; 14 males, 8 females) who were free of ocular and systemic medication. Visual acuity was 6/5 or better and the subjects were experienced observers in perimetry and in other psychophysical techniques of measurement in general. Mean pupil diameter with the Topcon was 5.41 mm (S.D. 0.74 mm) and with the Dicon 5.52 mm (S.D. 0.77 mm).

The differential light threshold of the right eye was measured with the Topcon along the 15° - 195° meridian at eccentricities of 0°, 1°, 2.5°, 5°, 7.5°, 10°, 15°, 20°, 25° and 30° using the Threshold

Program. Similarly, the differential light threshold of the right eye was determined with the Dicon along the 15° meridian of the temporal field and the 195° meridian of the nasal field at eccentricities of 5°, 10°, 12.5°, 15°, 20°, 25° and 30° using the Meridional Threshold Profile Program and at eccentricities of 0°, 1°, 2° and 4° along the horizontal meridian using the Macular Threshold Program. The default bowl luminance of 31.5 asb for the Dicon was used in order to match that of the Topcon. The stimulus presentation time for both instruments was set at 200 ms and that of inter - stimulus duration at 800 ms. The head was steadied with the chin bar and head rest of the instrument and fixation was constantly recorded using the video screen and blindspot monitoring techniques of the two perimeters.

The subjects underwent a 10 minute adaptation period to the bowl luminance and received a short familiarization period to the particular perimeter, prior to commencement of each examination. The two perimetric investigations were both undertaken at the same session; the order of program for the Dicon and the order of examination between the two instruments were randomized.

A1.2.3 Results

The group mean sensitivity profiles for the Dicon and for the Topcon, expressed in dB, are shown in Figure A1.1. The variance corresponding to the two types of LED stimuli ranged from 0.7 dB to 2.2 dB but was approximately constant between the two stimuli types and across the field. At all stimulus locations measured, the Dicon exhibits a higher level of sensitivity (measured in dBs) compared to the Topcon. For both perimeters sensitivity decreases with increase in peripheral angle for both perimeters, although the gradient is steeper centrally with the Dicon.

The relationship between perimetric sensitivity and increase in eccentricity, as a function of the type of LED used for measurement, is illustrated in Figure A1.2 with sensitivity expressed in terms of log apostilibs ($1/asb.10^{-3}$) rather than dBs. The Topcon evoked a greater sensitivity than the Dicon at all stimulus locations measured. The decline in sensitivity for the Dicon with increase in peripheral angle is similar to or slightly steeper than that for the Topcon out to an eccentricity of

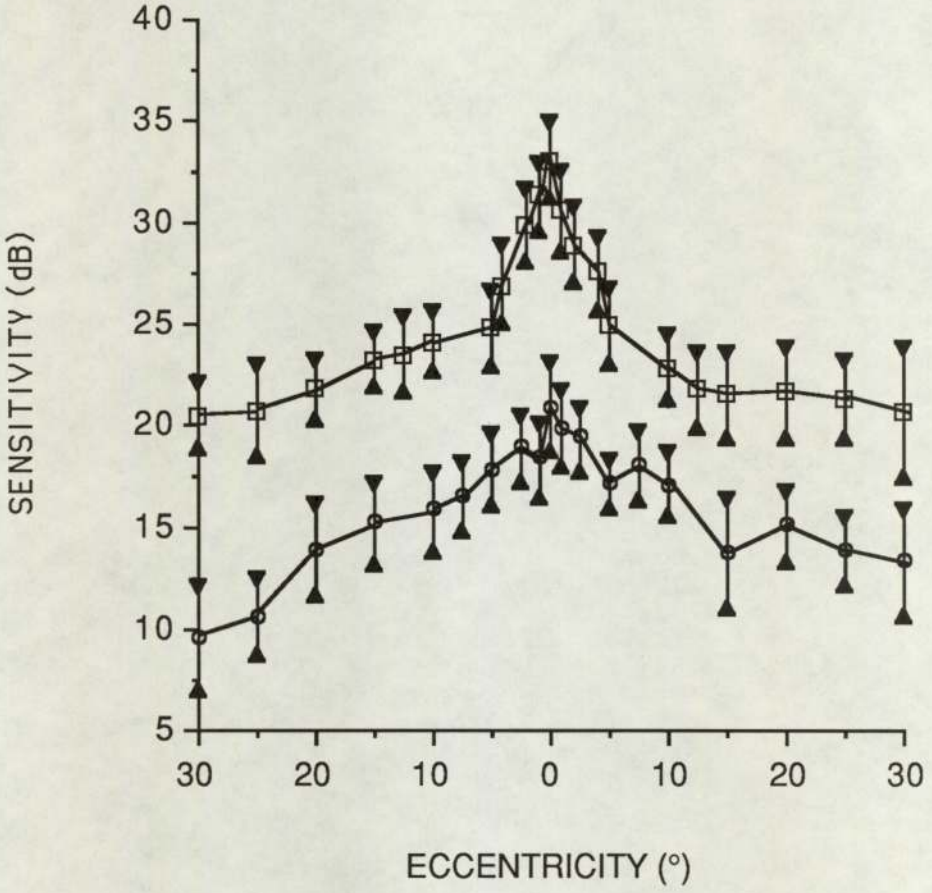


Fig. A1.1 Group mean differential light sensitivity (dB) against eccentricity along the nasal (left) - temporal (right) meridian for the "black hole" LED stimuli of the Dicon AP3000 autoperimeter (open squares) and the back lit LED stimuli of the Topcon SBP1000 autoperimeter (open circles) plotted for comparison. Note the sensitivity scale for the Dicon is referenced to 10,000 asb whilst that of the Topcon is referenced to 425 asb. The error bars denote one standard deviation from the mean.

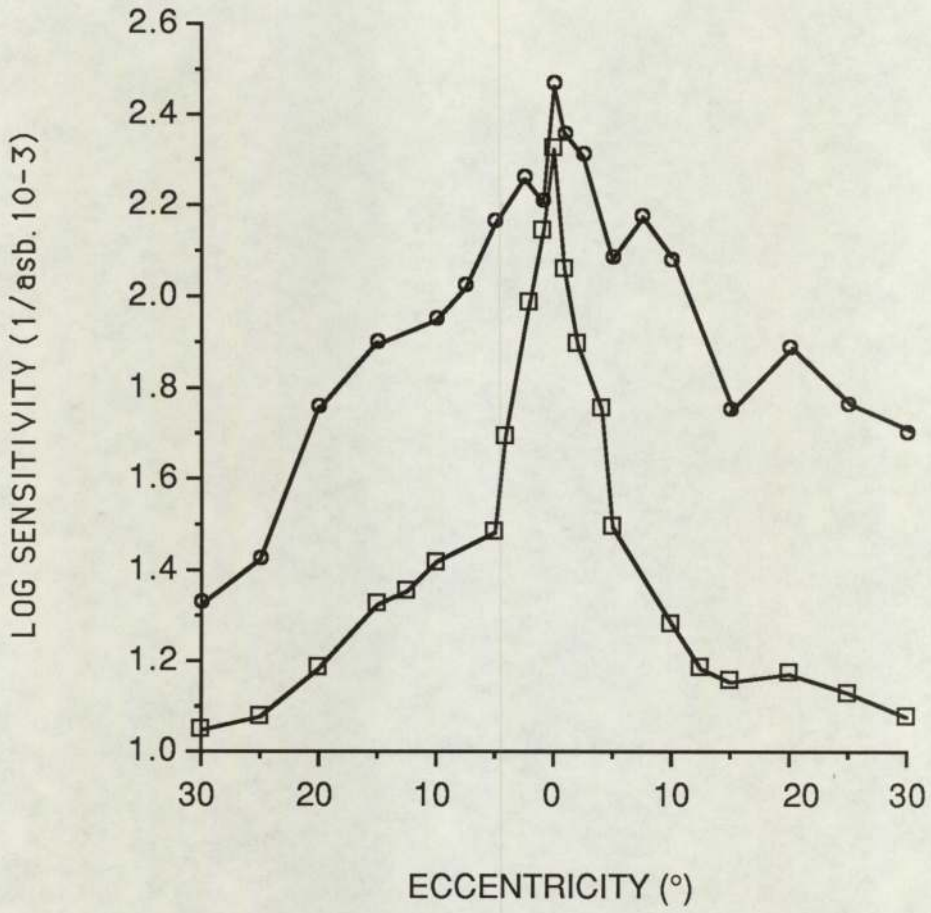


Fig A1.2 Log relative sensitivity (1/asb) with eccentricity along the nasal (left) - temporal (right) meridian for the "black hole" LED stimuli of the Dicon AP3000 autoperimeter (open squares) and the back lit LED stimuli of the Topcon SBP1000 autoperimeter (open circles).

5°, but beyond this eccentricity the Topcon gradient is steeper than that of the Dicon.

A1.2.4 Discussion

The Topcon appeared to exhibit a lower dynamic range of sensitivity than that of the Dicon (Figure A1.1). The comparison of sensitivity data between automated perimeters is confounded, however, by the fact that the measurement in dB is a logarithmic representation of stimulus luminance referenced to a maximum value, the magnitude of which varies between instruments. The sensitivity scale of the Dicon is referenced to a maximum stimulus luminance of 10,000 asb whilst that of the Topcon is referenced to a maximum luminance of 425 asb. Comparison between these instruments is further confounded as an effective (ΔL) is measured for the LEDs of the Topcon whilst a unique threshold, associated with the "black holes", is obtained for the Dicon. In addition, the value of sensitivity for the Dicon (which has the facility to vary adaptation level) is the absolute luminance of the LED regardless of the adaptation level. To permit meaningful comparison between the two perimeters, the data is therefore represented as the reciprocal of the threshold value measured in asb (Figure A1.2).

The differences in both the level and the shape of the sensitivity profiles for the Dicon and Topcon perimeters expressed in asbs, may arise due to the differences in the stimulus configuration and to the thresholding strategy of the two instruments. The larger stimulus size of the Topcon (2 mm) compared with that of the Dicon (1.613 mm) would be expected to elicit a greater sensitivity due to the increasing involvement of spatial summation. This does not, however, fully account for the differences in the slopes of the two profiles. The peak wavelength of the Topcon LEDs is 585 nm whilst that of the Dicon is 570 nm. An increase in spectral sensitivity has been reported between 560 nm and 600 nm at 10° eccentricity nasally for stimuli subtending 0.68° and 2.3° respectively and at 20° nasally for stimuli subtending 2.3° and 5.5° (Johnson and Massoff 1982). The stimuli in this investigation subtend 0.35° (Topcon) and 0.28° (Dicon) and therefore the chromatic explanation must be treated with caution; nevertheless, it may account for the increased peripheral sensitivity of the Topcon profile. The mountings of the LEDs in both instruments are flush to the surface of the

bowl and the LED stimulus luminances are calibrated on this assumption. The differences between the two profiles may also be due to the "black hole" effect of the Dicon producing variations in local retinal adaptation (Heijl 1985) and a potentially greater stimulus to accommodation, although the effect of this with increasing eccentricity is unknown. Interestingly, Britt and Mills (1987) using a modified Dicon autoperimeter, compared the threshold response elicited by the "black hole" LED stimuli with that of identical stimuli over which diffusing covers had been placed. Although the variance measured with the "black hole" stimuli was higher than that measured with the modified stimuli, the magnitude of the differential light threshold was unaffected; Britt and Mills (1987) stated that the differences were of marginal clinical significance only.

Moreover, despite careful selection of the stimulus parameters in order to minimize the inter - instrument differences certain disparities still remain. The most obvious of these is the thresholding strategy. The Topcon thresholding strategy is a 4 - 2 - 1 treble staircase with a genuine 1dB increment at the final crossing and the stimulus presentation is truly pseudo - random in terms of both staircase and stimulus position. The Dicon, however, employs a 4 - 2 heuristic ascending method of limits for the full threshold strategy and performs the complete threshold determination for a given location before proceeding to the next stimulus location; although the selection of the stimulus position is pseudo - random. In addition, the profile for the Dicon was generated by use of the Macular Threshold Program with locations along the horizontal meridian and by use of the Meridional Threshold Program with locations along the 15° - 195° meridian.

A1.3 Conclusions

The results demonstrate that the characteristics in addition to the spatial component of the stimulus influence the sensitivity profile in the normal eye. The implication is that the measurement of the perimetric differential light threshold involves a variety of neural processes and that a particular stimulus configuration may preferentially investigate specific neural aspects of the visual field. Furthermore, it would seem that the use of a range of different stimulus configurations could, in any given condition, provide additional information to that of a particular stimulus type.

Ultimately, the choice of stimulus size, colour, background luminance, background colour and the temporal characteristics of the stimulus presentation may vary according to the suspected ocular and/or neuro - ophthalmological condition.

APPENDIX 2

A2. SUPPORTING PUBLICATIONS

1. Wild J.M., **Wood J.M.,** Flanagan J.G. and Crews S.J. (1986) The interpretation of the differential threshold in the central visual field. Documenta Ophthalmologica. 62: 191-202.

2. **Wood J.M.,** Wild J.M., Drasdo, N. and Crews S.J. (1986) Perimetric profiles and cortical representation. Ophthalmic Research 18: 301-308.

3. Wild J.M., **Wood J.M.** and Barnes D.A. (1986) The cortical representation of gradient - adapted multiple - stimulus perimetry. Ophthalmic and Physiological Optics 6: 401-405.

4. **Wood J.M.,** Wild J.M., Good P.A. and Crews S.J. (1986) Stimulus investigative range in the perimetry of retinitis pigmentosa: some preliminary findings. Documenta Ophthalmologica 63: 287-302.

5. **Wood J.M.,** Wild J.M., Drasdo N. and Crews S.J. (1987) Isolation of the mechanisms determining the normal perimetric differential light threshold. In: Fiorentini, A., Guyton, D.L. and Siegel, I.M. (eds.) Advances in Diagnostic Visual Optics. Proceedings of the Third International Conference of Visual optics, Pisa, Italy, May 1986. Springer - Verlag, Berlin. pp 141-145.

6. **Wood J.M.,** Wild J.M., Hussey M.K. and Crews S.J. (1987) Serial examination of the normal visual field using Octopus automated projection perimetry: evidence for a learning effect. Acta Ophthalmologica 65: 326-333.

7. **Wood J.M.,** Wild J.M., Smerdon, D.L. and Crews S.J. (In press) The role of intra - ocular light scatter in the attenuation of the perimetric response. In: Transactions of the 7th International Visual Field Symposium, Amsterdam, Holland, September 1986. Documenta Ophthalmologica Proceedings Series.

8. Wild J.M., **Wood J.M.,** Hussey M.K. and Crews S.J. (In Press) The quantification of the visual field in computer assisted threshold perimetry. In: Transactions of the 7th International Visual Field Symposium, Amsterdam, Holland, September 1986. Documenta Ophthalmologica Proceedings Series.

9. Wild J.M., **Wood J.M.,** Worthington F.M. and Crews S.J. (In Press) Some concepts on the use of three - dimensional isometric plots for the representation of differential sensitivity. Documenta Ophthalmologica.

10. Wild J.M., **Wood J.M.** and Flanagan J.G. (In Press) Spatial summation and the cortical magnification of perimetric profiles. Ophthalmologica.

11. **Wood J.M.,** Wild J.M. and Crews S.J. (In Press) Induced intraocular light scatter and the sensitivity gradient of the normal visual field. Graefe's Archive for Clinical and Experimental Ophthalmology.

12. **Wood J.M.,** Wild J.M., Bullimore M.A. and Gilmartin B. (In press) Factors affecting the normal perimetric profile derived by computer - assisted static threshold light emitting diode perimetry. I. Pupil size. Ophthalmic and Physiological Optics.

13. **Wood J.M.,** Bullimore M.A., Wild J.M. and Gilmartin B. (In press) Factors affecting the normal perimetric profile derived by computer - assisted static threshold light emitting diode perimetry. II. Accommodative fluctuations. Ophthalmic and Physiological Optics.

Documenta Ophthalmologica 62, 191–202 (1986).

The interpretation of the differential threshold in the central visual field

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Abstract. Computer assisted perimetry has revolutionised the investigation of the visual field. Experience of central field assessment with the Octopus Automated Perimeter shows that sensitivity recorded with target size 3 across all age groups can frequently be greater than the published normative values. Use of the latter values can therefore provide a serious underestimation of field loss. Inter-individual variation in sensitivity is found within and between age groups. The limitations associated with the use of the measurement error to define abnormality and the additional problems of hypernormal thresholds and resolution of the blind spot are discussed. It is suggested that methods should be developed to evaluate sensitivity on an intra-individual basis.

Introduction

The introduction of computer assisted perimetry has enabled the rapid assessment of the visual field using test strategies and procedures hitherto considered impractical. The technology has increased the importance of the visual field examination as a diagnostic aid and is beginning to provide fresh insight into underlying disease mechanisms. At the same time, however, the technique is still in its relative infancy and much work is necessary before the next generation of perimeters can be developed. The purpose of this paper is to report some of our experiences associated with the interpretation of differential threshold visual field data derived by computer assisted perimetry. We illustrate these points with particular reference to central field assessment with the Octopus Automated Perimeter.

Method

The clinical material reported here was obtained at the Retina Department of the Birmingham and Midland Eye Hospital. It is based upon an expanding research data bank of over 200 patients of all ages with field loss resulting from a wide range of ocular and neurological pathology. All fields are obtained under controlled conditions (Flanagan et al., 1984 ab; Wild et al., 1984; Barnes et al., 1985). Patients adapt to the bowl luminance for a 10 min period prior to examination and natural pupils are used throughout. For central field examinations, patients wear the distance refractive correction and where necessary, the appropriate near correction. Clinically normal, age matched subjects are examined in the same manner in order to provide control data.

Table 1. Mean sensitivity and standard deviation with eccentricity for Program 31 along the horizontal meridian (top) and vertical meridian (bottom) for the sample of 15 normal observers compared with the normative values for the under 25 years age group

	Horizontal										
			Nasal					Temporal			
	30°	24°	18°	12°	6°	0°	6°	12°	18°	24°	30°
Mean (dBs)	33.0	35.1	35.4	35.1	34.9	35.9	35.1	33.3	17.4	35.5	34.6
SD	3.2	4.4	4.3	2.6	2.2	1.2	4.4	5.4	13.1	3.5	3.9
Normative values (dBs)	27	28	30	32	33	36	32	31	30	29	29
Difference	+6.0	+7.1	+5.4	+3.1	+1.9	−0.1	+3.1	+2.3	–	+6.5	+5.6
	Vertical										
			Superior					Inferior			
Mean (dBs)	29.6	31.7	32.4	34.0	34.5	35.9	34.8	34.8	34.6	33.9	33.7
SD	5.9	4.6	5.2	2.9	3.1	1.2	2.6	3.7	4.1	3.4	4.2
Normative values (dBs)	24	26	28	30	31	36	32	31	30	29	27
Difference	+5.6	+5.7	+4.4	+4.0	+3.5	−0.1	+2.8	+3.8	+4.6	+4.9	+6.7

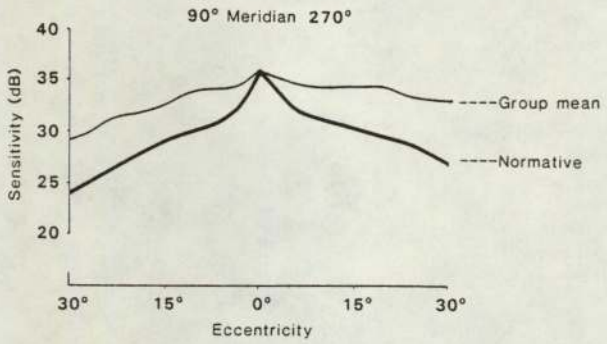

Figure 1. Mean sensitivity profile of the sample along the vertical meridian for Program 31 (target size 3) compared with normative profile for the under 25 years age group.

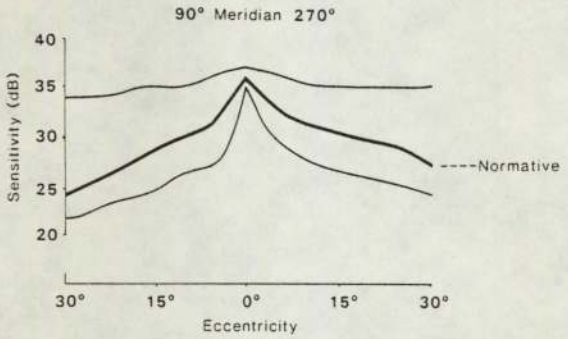

Figure 2. Program 31 (target size 3) sensitivity profiles along the vertical meridian for two normal 21 year olds from the sample compared with the normative profile for the under 25 years age group.

Results for the central 30° with 6° resolution (Program 31; target size 3) are presented for the right eye from a sample of 15 normal subjects and also for patients with cases of field loss. The normal sample (mean age 19.9 years; range 8.6 to 24.4 years) was chosen in order to match the age range of the under 25 Octopus normative values.

Results and discussion

The mean sensitivity profile based upon the 15 subjects along the 0–180° meridian exhibits an increased sensitivity compared with the normative curve. The enhanced sensitivity increases with eccentricity and is approximately 6 dBs higher at 18° eccentricity and beyond. A similar finding is present for the 90–270° meridian (Figure 1). Interestingly, however, the measured and specified values for the foveal point are identical. Variation is found between

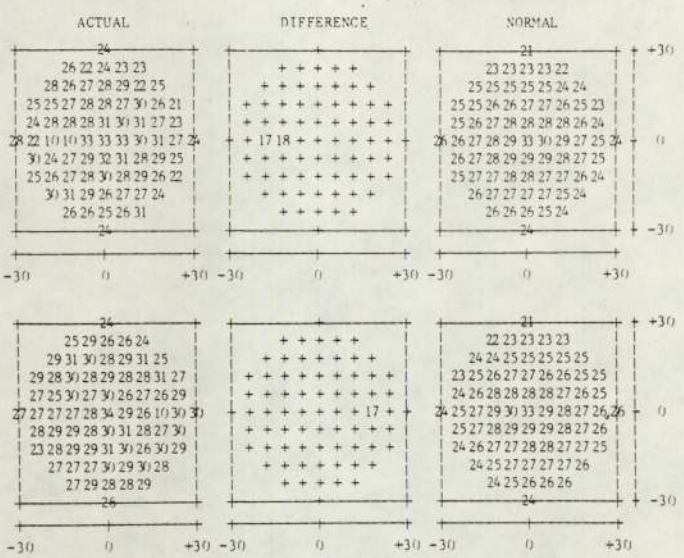

Figure 3. Program 31 (target size 3) CO printouts illustrating enhanced sensitivity relative to normative values. (Top) A 49 year old (left eye) with acromegaly (RMS value 1.7). (Bottom) A 54 year old (right eye) with ischaemic optic neuropathy (RMS value 1.5)

individuals within the age group in terms of both shape and height of the gradient with the greatest inter-individual difference occurring, as the SDs demonstrate, beyond 12° eccentricity. Two profiles with low RMS values illustrating variations in sensitivity are illustrated in Figure 2. The inter-individual variation in sensitivity can also be found in the presence of localised field loss and is also seemingly independent of the age group in question (Figure 3).

Possible explanations for the inter-individual variation may include, for example, differences in peripheral refraction, pupil size and intra-ocular light scatter, or may simply be variations in experience of, and ability to perform, perimetric tasks.

The literature is unequivocal as to the precise effect of peripheral refraction and aberration on the differential threshold. Closely associated with this phenomenon is that of pupil size. Indeed, it is apparent from observation of the video monitor that during any one examination pupil size is a dynamic entity, the fluctuations of which may possibly be associated with accommodative hysteresis. It is clear, however, from the work of Bedwell and Davies (1977) and Fankhauser (1979) that the variations in pupil size encountered in the sample were insufficient to materially alter the shape of the sensitivity gradient. The variation in sensitivity due to intra-ocular light scatter alone might, on a priori grounds, be expected to be greater with increasing age. The Octopus normative values, however, take little account of this possibility;

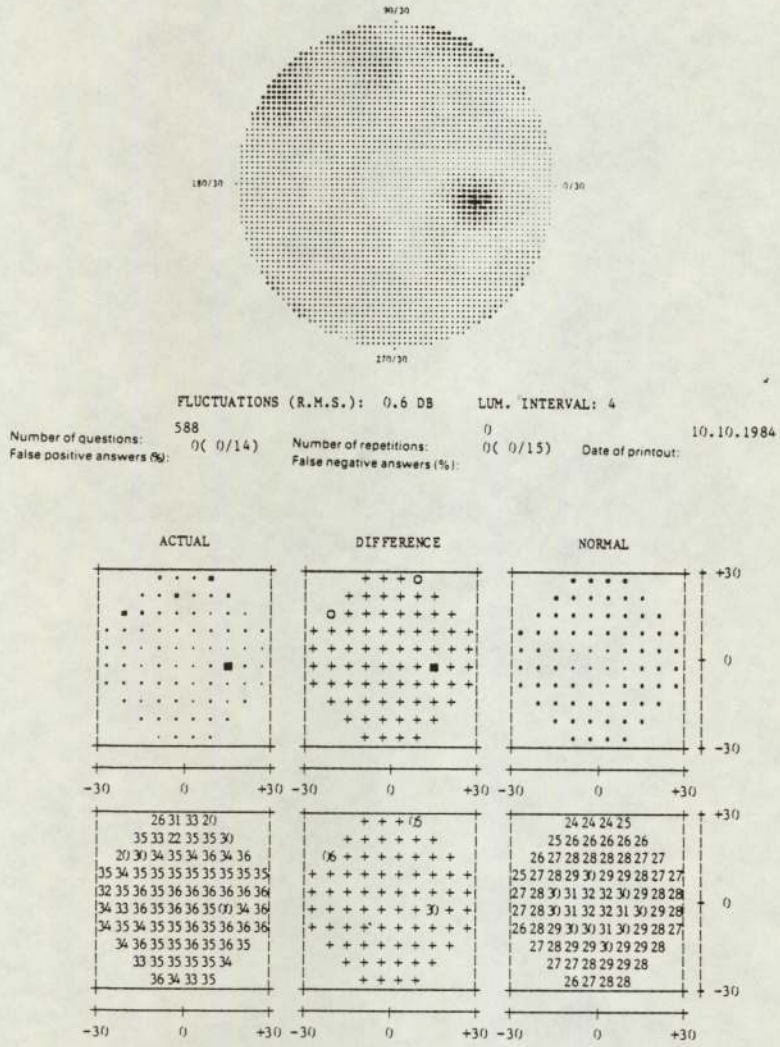

Figure 4. Program 32 (target size 3) results for the right eye of a normal 28 year old illustrating the high level of sensitivity relative to the normative values.

sensitivity at each point in the field decreases by 1 dB for every decade of life from 25 years of age, resulting in a 5 dB difference in sensitivity between the under 25 and over 65 age groups (Barnes et al., 1985).

A further explanation may be the initial height and the rate of change of the learning curve for the more peripheral points. The effect of learning on peripheral differential sensitivity is undefined in perimetry. It is of significance,

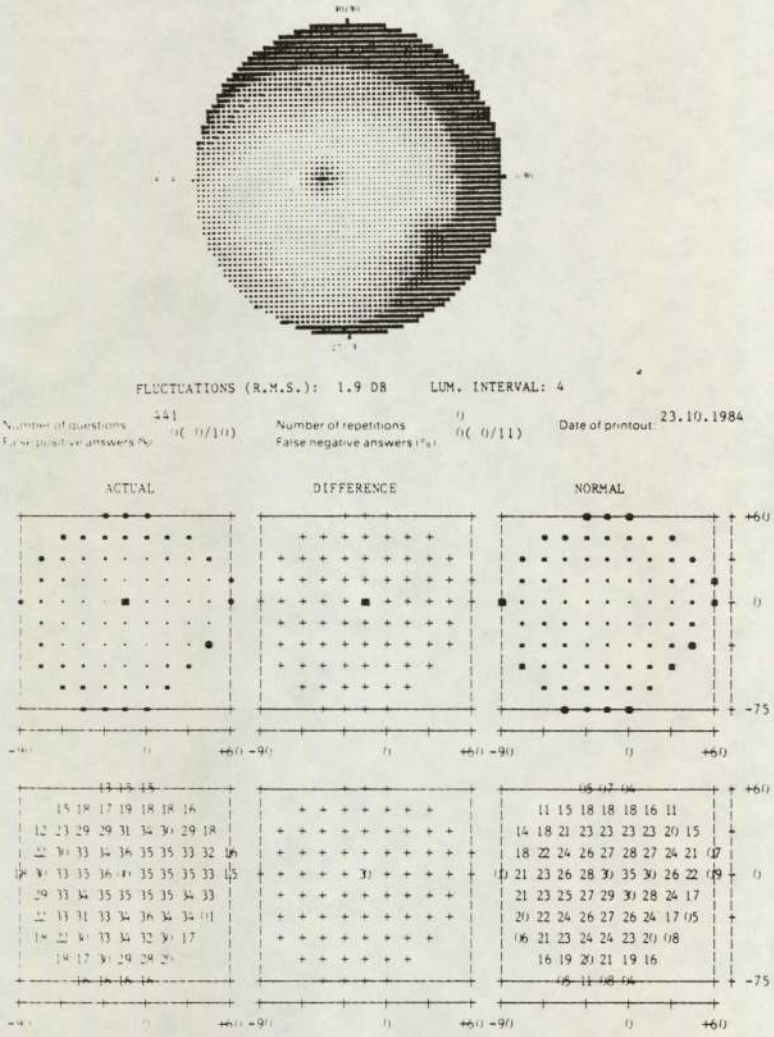

Figure 5. Program 21 (target size 3) results for the left eye of a normal 31 year old illustrating the high level of sensitivity relative to the normative values.

however, in peripheral motion thresholds (Low, 1946; Johnson and Leibowitz, 1974) and peripheral visual acuity (Low, 1951; Saugstad and Lie, 1964); the periphery being regarded as an unpractised sensory area. Inspection of the data, however, shows no apparent correlation between the number of prior examinations and either the height or shape of the gradient.

The intra-subject data is obviously subject to measurement error, namely

short-term fluctuations (SF) (Bebie et al., 1976) but the SF should be minimal as sensitivity is high and, more importantly, as the program covers the central 30°, stable between test locations (Flammer et al., 1984). Furthermore, our experience with different samples suggests that a similar discrepancy with the normative values occurs, not unexpectedly, with Program 32 (target size 3) (Figure 4), whilst the findings must also be placed in context with those reported for Program 21 (target size 3) by Barnes et al. (1985), an example of which is shown in Figure 5.

The inter-subject variability in Program 31 may have been overlooked by Heijl and Drance (1981) as they chose to ignore the points situated 25° at 30° from fixation on account of lens rim artefacts.

The enhanced sensitivity demonstrated by the group mean relative to the published normative data may be a function of the above factors, but it is also likely to be associated with the small sample and repetitive procedures used to obtain the normative values.

The increase in the SDs of the grouped data with increase in eccentricity can be compared with the findings of Parrish et al. (1984) obtained with the Perimetron along the 45° meridian using target size 2 and a bowl luminance of 31.5 asb. In their study, Parrish et al. report similar SDs between 24° and 30°. In our study the SDs increase from fixation indicating the wider variability in the form of the sensitivity gradient obtained at the lower bowl luminance of 4 asb.

The dynamic range of measurement in the central area using target size 3 combined with the 4 asb bowl luminance is clearly potentially greater than has been hitherto suggested and the increased sensitivity found, particularly in the pericentral areas, has clinical implications. Reliance cannot now be placed solely upon a comparison with the appropriate age-related normal values, in terms of Δ/σ and D/σ (where Δ is the criterion for sensitivity loss, σ is the measurement error and D is the true depth of sensitivity loss) without the possibility of either failing to detect or seriously underestimating both the area and depth of the reduction in sensitivity. This is particularly important, for example, in glaucoma where it has been shown that the earliest detectable field loss is usually found in the pericentral area (Aulhorn and Karmeyer, 1976; Furuno and Matsuo, 1979; Coughlan and Friedmann, 1981), and in early neuro-ophthalmological involvement. In addition, the findings also have important ramifications for the use of Program Delta which is based upon the normative values. The dynamic range at 30° eccentricity can be further extended by approximately 4 dBs, if required, with the aid of target size 5.

The use of the global Root Mean Square deviation (RMS) value for defining abnormality has, in itself, important limitations and, as Flammer et al. (1984) point out, a high value does not necessarily indicate poor subjective response. In addition, the SF can be expected to increase in situations such as those reported by Heijl (1977) and Heijl and Drance (1983) where sensitivity decreases with prolonged examination time. Nevertheless, the definition and

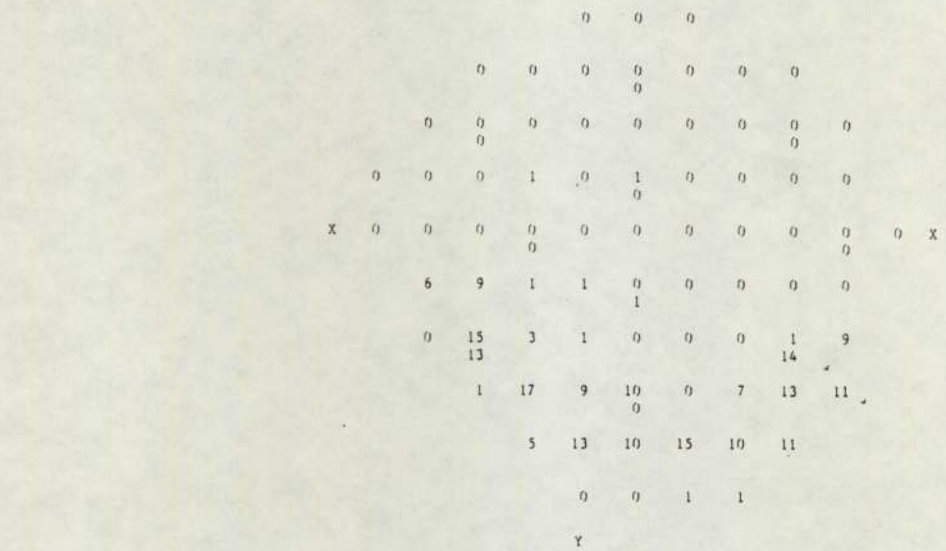

Figure 6. Program 21 (target size 3) VA printouts for a 34 year old patient with retinitis pigmentosa (top) and a 20 year old normal individual (bottom) showing the test-retest values and the resultant global RMS values.

detection of (shallow) depressions depends upon a minimal value for the global RMS. Furthermore the magnitude of the global value is governed by the sum of the squares of the difference between successive determinations for the various individual test locations. The calculation does not include points of zero sensitivity which exhibit perfect test-retest concordance and several points exhibiting large differences between test-retest thresholds exert greater influence on the global value than a large number of points exhibiting small differences (Figure 6). Indeed, since the isolated large differences frequently occur not unexpectedly in the periphery we feel it would be more meaningful to give greater weighting in the calculation of the RMS value to the more centrally located stimuli.

It is interesting to note in this context, however, that Heijl and Drance (1981) adopted abnormality criteria which were independent of the local and global RMS values and defined field loss in terms of the intra-individual variation in sensitivity. In particular, we feel that their comparison of points in the upper hemifield with the mirror image points in the lower field may have some merit over the central 30°, but consider that caution must be exercised in view of the finding by Flammer et al. (1984) that glaucoma patients exhibit a higher SF in the upper than lower fields. In addition, the neurophysiological evidence of gross assymetry in the electrophysiological and psychophysical responses recorded from the upper and lower fields (Michael and Halliday, 1971; Blumhardt and Halliday, 1979; Flanagan and Harding, 1985) suggests that a comparison of hemifields about the vertical axis would be more appropriate and, assuming constancy of the SF beyond 30°, would be valid for up to approximately 60° eccentricity (Figure 7).

A further problem which can frequently confound the interpretation of sensitivity and which is undoubtedly an extreme manifestation of the local measurement error, is the presence in some individuals of isolated points which exhibit apparent hyper-normal threshold values. Such thresholds must not be confused with the large range of sensitivities found across the whole

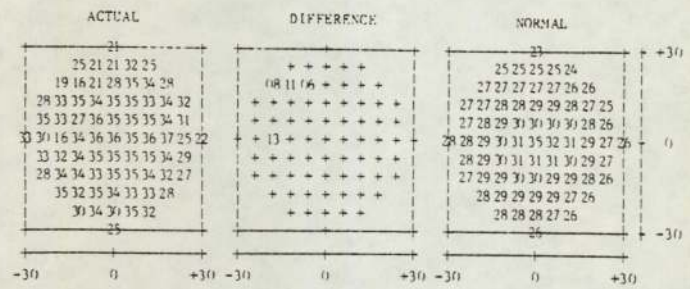

Figure 7. Program 31 (target size 3) of a 33 year old (left eye) with a cerebral tumour (RMS value 4.4). Defining abnormality in terms of the measurement error underestimates the upper temporal loss amidst the high sensitivity of the remaining field.

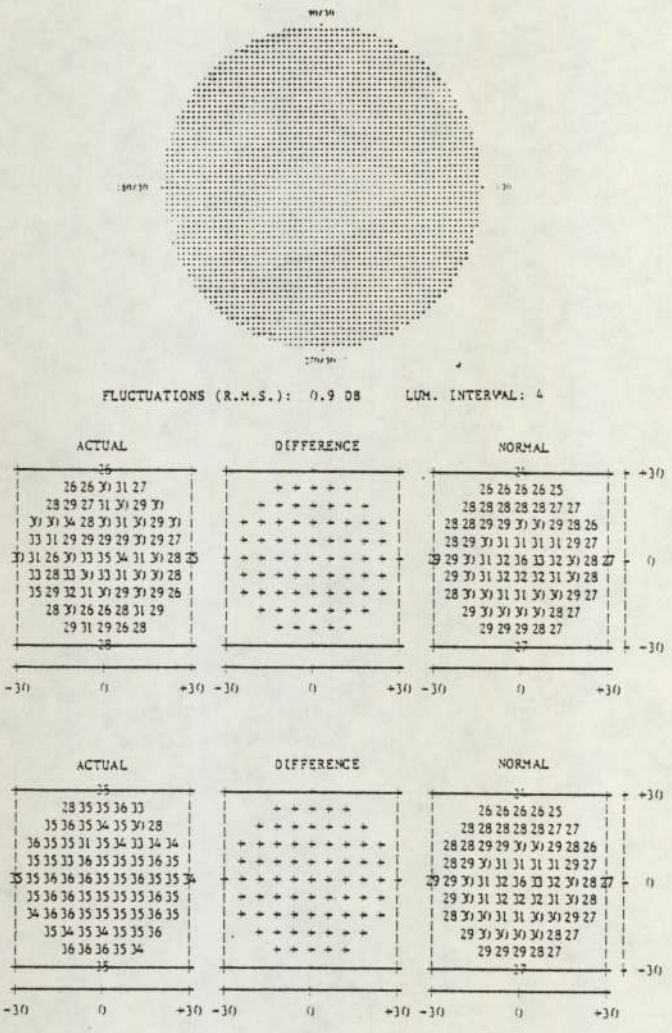

Figure 8. Program 31 (target size 3) printouts from the left eyes of two individuals demonstrating absence of the blind spot. (Top) A 16 year old with a history of papillitis (RMS value 0.9). (Bottom) A normal 20 year old (RMS value 1.8)

field in the case of a poor observer, nor with the more sensitive type of field discussed earlier. The points occur in both the normal and abnormal eye, are seemingly independent of ocular condition and are most frequently found with increased eccentricity. In certain instances such points can confuse the assessment of abnormality by simulating apparent reductions in sensitivity of adjacent points.

An additional problem lies in the variability of data involving the blind spot. It is normal for the point at 18° eccentricity temporally to exhibit a large reduction in sensitivity. Indeed, the probability of detecting scotoma of 4.2° diameter with a 6° square grid has been calculated to be 100% (Fankhauser and Bebie, 1978). Nevertheless, our experience suggests that it is not unusual for the blind spot to be completely overlooked using programs 31 or 32 (target size 3) (Figure 8) and thus doubt must be cast on this calculation at least when associated with the unique phenomenon of the blind spot. One possible explanation for this discrepancy may be that of stray light emanating from the stimulus (Frankhauser and Haeberlin, (1980).

Despite the apparent improvement of visual field assessment arising from the advent of computer assisted perimetry, the measurement of the differential threshold is still, nevertheless, a psychometric function subject to the usual subjective fluctuations (Haider and Dixon, 1961). Clearly, there is a need for abnormality to be defined in terms of the individual patient rather than by reference to a set of normative values. Further work is certainly necessary to elicit the components of the long term fluctuation (LF) described by Bebie et al. (1976), Flammer et al. (1984), Wilensky and Joondeph (1984). In particular, the need to separate neural sensitivity from attenuation due to intra ocular light scatter is also necessary (Barnes et al., 1985). Such information could then be weighted into the dynamic range equation for a given strategy and stimulus combinations. Such an approach would not only enable intra-individual evaluation of sensitivity, but would also permit inter-instrument standardization of visual field assessment.

Acknowledgement

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Perimetric Profiles and Cortical Representation

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Key Words. Cortical magnification · Spatial summation · Octopus automated perimeter · Differential light threshold

Abstract. The nature of the interaction between spatial summation and M-scaling was investigated by means of the Octopus automated perimeter. It was found that M-scaling of spatial stimulus parameters, alone, did not result in the expected isosensitivity profile. A clinically flat profile was, however, obtained within the central 30° along the horizontal meridian using a large uniform size target (size 3; projected diameter 0.431°). The eccentricities at which presentation of the standard Goldmann targets would result in an isosensitivity profile across the full extent of the visual field were calculated to further illustrate the overcompensation inherent in the current M-scaling equations.

Introduction

The threshold response to many types of retinal stimuli exhibits a linear function when plotted against increasing angular eccentricity from the fovea. This phenomenon was attributed to ganglion cell separation by Weymouth [1958] on the basis of the evidence then available. Subsequently it was reported that visual acuity and cortical magnification (M) were closely correlated and that M was proportional to the square root of ganglion cell receptive field density. M represents the extent, in millimetres, of striate cortex which corresponds to one degree of visual space and, for the central fovea, has been estimated to be 15.1 mm/° [Cowey and Rolls, 1974], 11.5 mm/° [Drasdo, 1977] and 7.99 mm/° [Rovamo and Virsu, 1979]. Several studies have indicated that stimuli which have equal projected cortical representation (M-scaled stimuli) possess identical sensitivities, therefore becoming independent of retinal location. These include contrast sensitivity [Virsu and Rovamo, 1979] detection of coherent motion for dynamic random on-off patterns [Van de Grind et al., 1983] motion and displacement thresholds [Wright and

Johnston, 1983] and lower thresholds for motion [Johnston and Wright, 1983].

Thresholds for some stimuli, however, appear to depart from the linear tendency of elevation with increasing peripheral angle. M-scaled CFF stimuli, for example, have been found to give different sensitivities across the visual field but can be equated by additionally adjusting the retinal illuminance [Rovamo and Raninen, 1984]. Such observations are not at variance with the underlying physiological theory since the ganglion cells are not homogeneous and exhibit varying types of receptive field properties. Indeed, studies of stimulus area and threshold luminance have demonstrated local variations in spatial summation characteristics [Sloan, 1961; Wilson, 1967, 1970; Scholtes and Bouman, 1977; Inui et al., 1981] which depend upon receptive field organisation and size.

The introduction of computer assisted perimetry has resulted in a convenient method for investigating spatial summation and differential sensitivity across the visual field. Thus the assumption that a further type of cortically equivalent stimulus will result in a flat sensitivity profile can now be investigated. From this study, additional insight into the interaction between receptive field properties and cortical representation can be gained.

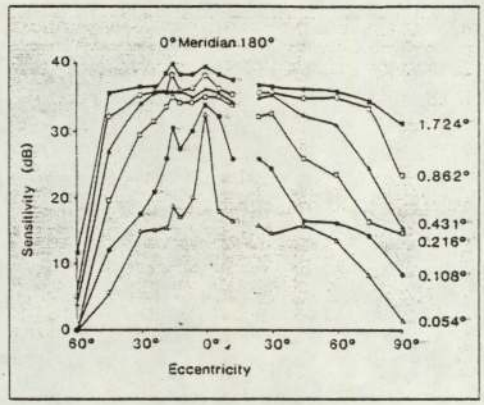

Fig. 1. Group mean differential light sensitivity along the horizontal meridian of the visual field of the right eye as a function of target size.

Method

The sample comprised 10 clinically normal, highly motivated emmetropes (mean age 21.4 years, SD 1.35 years) experienced in psychophysical tests. Visual acuity was 6/5 or better. The differential threshold for the visual field of the right eye was determined with the Octopus automated perimeter for six stimulus sizes (0.054°, 0.108°, 0.216°, 0.431°, 0.862° and 1.724° projected diameter). Stimuli were presented at 15° intervals over the full field (program 21) and at 6° intervals over the central 30° (program 31). Stimulus presentation time was 100 ms. The head was steadied with the head clamps and chin bar of the instrument and fixation was constantly monitored with the video camera. Natural pupils were used throughout; the mean pupil size was 7.03 mm (SD 0.71 mm). The subjects attended for seven sessions within a maximum period of 4 weeks. Each session consisted of a 10-min adaptation period to the perimeter bowl luminance (4 asb) followed by two test programs separated by a short rest period. The order, and combination of, program and stimulus size were randomised. The first session for each subject was used as a familiarisation period, the results of which were discarded prior to data analysis.

The equations for cortical representation proposed by Rovamo and Virsu [1979] were used to derive the cortical representation (M_e) at each eccentricity examined along the four principal meridians. The diameter of the retinal target (L_e) stimulating an equivalent cortical area to target size 0 (projected diameter 0.054°) at the fovea (L_o) was then calculated by $L_e = \frac{M_o}{M_e} \cdot L_o$ where $M_o = 7.99$ mm/°. By this means, the values of differential sensitivity for each eccentricity were obtained by graphical interpolation from the clinical data and plotted against peripheral angle. The equations of Rovamo and Virsu [1979] were selected since these

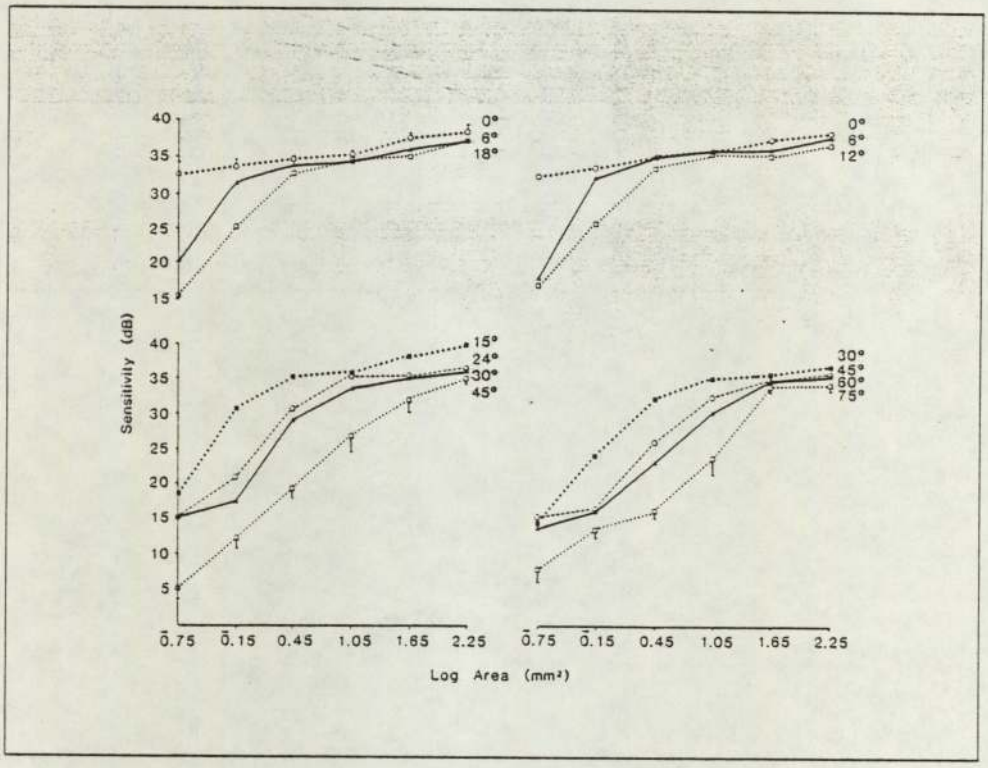

Fig. 2. Differential sensitivity against log target area as function of eccentricity for the nasal (left) and temporal (right) meridians of the visual field of the right eye illustrating the variation in spatial summation. The bars represent one standard error of the mean and illustrate the lowest (0° eccentricity) and highest (45° nasal and 75° temporal eccentricity) variance.

have previously been used in relation to the interaction of spatial summation with cortical magnification. The value of 0.054° was arbitrarily chosen to ensure that the M-scaled targets were kept within the stimulus range provided by the instrument.

Results

The group mean for differential sensitivity with increase in stimulus size along the 0–180° meridian of the visual field of the right eye, as a function of eccentricity, is shown in figure 1.

The level of spatial summation, manifested by the steepening gradient, as a function of eccentricity, along the 0–180° meridian is shown in figure 2.

The interpolated sensitivity values with peripheral angle for M-scaled stimuli, along the four principal meridians, corresponding to 0.146 mm^2 of striate cortex are shown in figure 3.

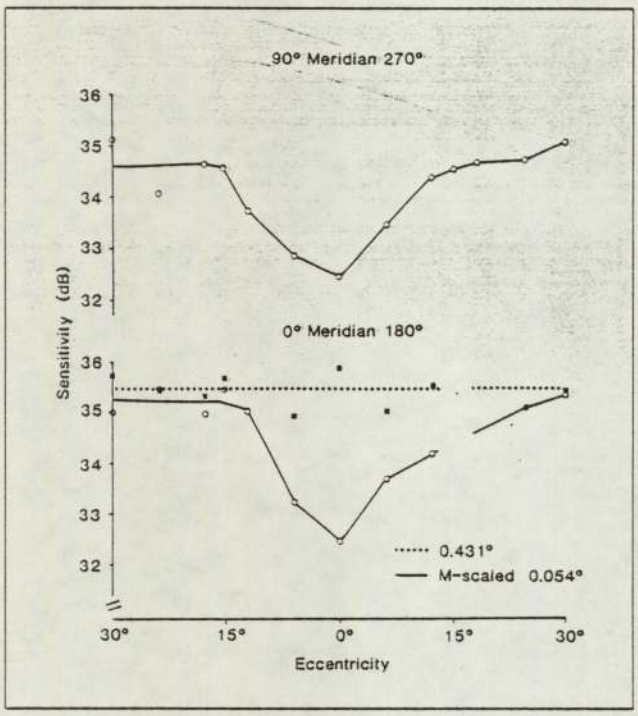

Fig. 3. M-scaled values (open circles) relative to the foveal value for target size 0 (projected diameter 0.054°) stimulating an equal area of cortex (0.146 mm²) which increase with eccentricity. Top: vertical meridian. Bottom: horizontal meridian of the visual field of the right eye. The clinically flat gradient obtained along the horizontal meridian of the same visual field with a large uniform target (size 3; projected diameter 0.431°) is shown for comparison (filled squares).

Discussion

The differential sensitivity data are in agreement with previous investigations [Sloan, 1961; Aulhorn and Harms, 1972; Johnson et al., 1978]. A steep sensitivity gradient is obtained for the smaller stimulus sizes which flattens with increase in stimulus size. A clinically flat profile is found within the central 30° along the 0–180° meridian for target size 3 (projected diameter 0.431°).

A region of enhanced sensitivity is seen between 15° and 18° eccentricity nasally for all stimulus sizes with the exception of stimulus size 3 (0.431°). Such a peak has previously been reported for scotopic [Wolf and Zigler, 1959; Wolf and Gardiner, 1963] and low photopic background luminances [Obstfeld, 1973].

In some states of parametric adjustment the sensitivity data reveals a marked nasotemporal asymmetry corresponding approximately to the reported differences in the densities of retinal elements in human [Vilter, 1954; Van Buren, 1963; Oppel, 1967; Stone and Johnston, 1981] and in primate [Van Essen et al., 1984]. As this tendency is unfortunately variable depending upon parametric adjustment, it would be difficult to establish a general mathematical relationship. The functional correspondence is most noticeable with the smaller target sizes and even appears to reflect certain marked local undulations in cell density for rods [Østerberg, 1935] and

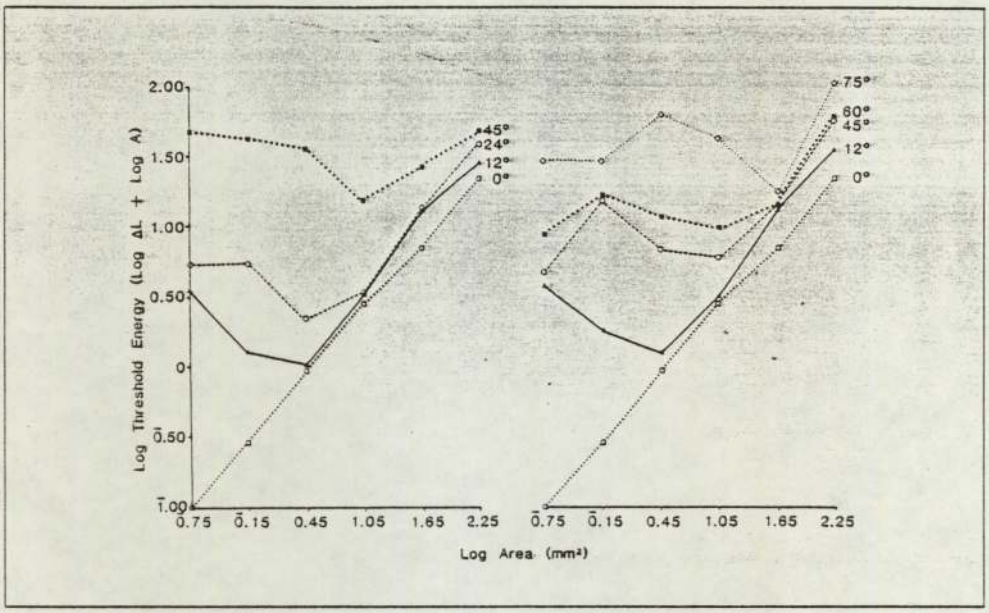

Fig. 4. Log threshold energy against log target area as a function of eccentricity for the nasal (left) and temporal (right) meridians of the visual field of the right eye illustrating the displacement of the minima to the right with increase in peripheral angle.

ganglion cells [Oppel, 1967]. The portrayal of the local topographical distribution of sensitivity encourages our belief that systematic studies of the variation of the stimulus parameters in visual field investigation might permit the matching of a perimetric profile corresponding to the neural elements.

The flattening of the peripheral response function with increasing target size is undoubtedly due, in part, to the increase in spatial summation exhibited by the peripheral retina. The lack of sensitivity exhibited peripherally for the smaller target sizes may arise as a direct consequence of reduced stimulus dynamic range. The differential threshold energy, calculated by log ΔL + log A, plotted against log A (fig. 4) reveals, however, that the minima for each eccentricity are displaced further to the right as peripheral angle is increased. This demonstrates that the optimum areal distribution of energy necessary to evoke a response increases with eccentricity and indicates that factors other than spatial summation are involved. This may be due to the fact that peripheral retinal images of small stimuli are more prone to degradation by oblique astigmatism than those of large stimuli [Jennings and Charman, 1978, 1981]. Indeed, it has been shown that the correction of peripheral oblique astigmatism significantly improves differential and absolute thresholds in the peripheral retina [Fankhauser and Enoch, 1962; Ronchi, 1971]. Alternatively, the distribution may reflect the

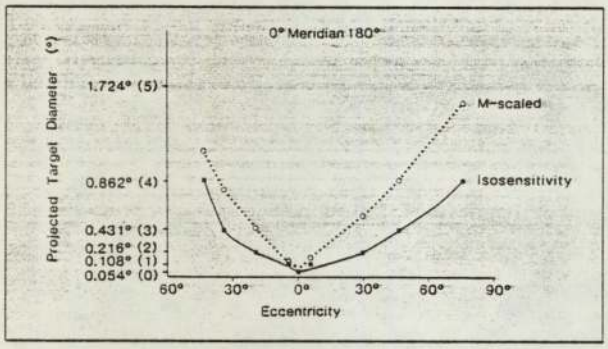

Fig. 5. Target size against eccentricity along the horizontal meridian of the visual field of the right eye demonstrating the eccentricities determined by interpolation at which standard Goldmann targets would produce a flat profile (filled squares) and the corresponding M-scaled values (open circles).

increase in receptive field size with eccentricity and relate to models which propose that spatial tuning may exist across the retina [Campbell and Robson, 1968]. Indeed, by correcting the width of a sine wave target for cortical representation, the peripheral retina has been shown to exhibit a similar sensitivity to the fovea for all spatial frequencies although the peak sensitivity shifts to lower spatial frequencies [Koenderink et al., 1978; Rovamo and Virsu, 1979]. The link between sine wave stimuli and spot targets must, however, be considered as tenuous.

The M-scaled data for all four meridians exhibit an increase in sensitivity with increase in peripheral angle relative to the theoretical flat profile through the foveal point. The difference rises to approximately 3 dB at 30°. It is thus apparent that M-scaling stimulus area alone does not result in sensitivities which are independent of retinal location.

The data points at greater than 15° eccentricity nasally and inferiorly exhibit scatter and for the purposes of illustration a straight line best fit relationship has been assumed. Clearly the spread may be attributable to variance in the data or may indicate that the M-scaling equations are not totally appropriate for clinical perimetry.

An interesting interpretation of the data can be seen if the eccentricities at which the standard Goldmann targets produce an isosensitivity profile relative to the foveal value for target size 0 (0.054°) are determined by interpolation and then compared with the estimated M-scaled stimulus values at the same eccentricities (fig. 5). The discrepancy between the two curves increases with peripheral angle and further demonstrates the over-compensation of the M-scaling equations. It would be expected that at greater background luminances this difference would diminish due to the decreasing spatial summation.

Currently some doubts have been expressed as to the degree of foveal enhancement of the human cortical magnification factor [Levi et al., 1985]. It is clear, however, that all the values recently reported involve greater foveal enhancement and steeper gradients than that of Rovamo and Virsu [1979]. These values inevitably further increase the incompatibility of M-scaled stimuli with a flat perimetric profile. This does not indicate that the recent data are less acceptable but emphasizes the inescapable need to consider the role of ganglion cell summation in the cortical representation of perimetric profiles.

These observations, together with the finding that a clinically flat profile occurs within the central 30° along the 0–180° meridian for a 0.431° projected diameter stimulus (fig. 1) indicates that the sensitivity to conventional perimetric targets depends upon an interaction between ganglion cell density and the spatial summation properties of the ganglion cells. These two quantities may be expressed as the coverage factor, defined anatomically as dendritic field area (mm^2) × cell density (cells/mm^2) and physiologically as receptive field area (mm^2) × cell density (cells/mm^2). Although Perry et al. [1984] have reported a remarkably constant coverage factor for the dendritic fields of the Pβ cells across the retina, Perry and Cowey [1985] have observed that this may not apply to receptive field size. These findings, in conjunction with the role of other types of ganglion cells, must account for the failure of M-scaling to produce a flat perimetric profile.

Conclusions

The process of M-scaling applied to spatial stimulus parameters, alone, does not result in a flat profile using spot targets. A flat profile may be obtained, however, using variable sized retinal stimuli at given eccentricities or large constant stimuli within the central 30°.

A flat profile representing the differential threshold, based upon the coverage factor, as opposed to large targets (which saturate central areas and are therefore less able to differentiate changes in sensitivity) is likely to be more appropriate for detecting changes occurring at any particular eccentricity. In perimetric terms this approach is highly desirable and could be used to facilitate multiple stimulus presentation and/or to permit maximum ease in identification and interpretation of abnormality. Implications at low photopic bowl luminance for perimetric program design incorporating varying stimulus sizes are far reaching.

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THE CORTICAL REPRESENTATION OF GRADIENT-ADAPTED MULTIPLE-STIMULUS PERIMETRY

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Abstract—Some stimuli, if scaled in proportion to the reciprocal of inter ganglion cell receptive field separation (*M*-scaled) exhibit an isosensitivity profile. Perimetric profiles which are isosensitive across the extent of the normal visual field facilitate multiple stimulus perimetry and provide a convenient method for the detection of abnormality. The purpose of the investigation was to establish whether the stimulus diameters necessary to produce an isosensitive perimetric profile were scaled in proportion to *M*. Sensitivity profiles for a sample of 15 age-matched observers were obtained with the Friedmann VFA Mk II. The stimulus aperture diameters were then measured under 100 × magnification. The observed elliptical apertures, corrected for obliquity of viewing, plate thickness and distance from the eye were represented as diameters of circles possessing an equivalent area to that of the ellipse. The apparent diameters were then *M*-scaled relative to stimulus pattern *h* using the equations of Rovamo and Virsu (1979). An overestimation of the *M*-scaled diameters relative to the apparent diameters was noted which increased with eccentricity for all four cardinal meridians by a factor of up to 3.5 times. It is suggested that the over compensation indicates that the cortical representation of perimetric spot targets at low photopic adaptation levels depends not only upon retinal ganglion cell density but also upon the variation of ganglion cell characteristics with eccentricity. The implications of this finding for perimetric instrument design are discussed.

INTRODUCTION

Suprathreshold gradient adapted static perimetry is generally considered to be the most sensitive strategy for the detection phase of the visual field examination (Greve, 1982). This procedure employs stimuli at constant and known levels above threshold: stimuli which increase in either intensity or size with increase in peripheral angle are used to compensate for the decline in sensitivity with eccentricity from the fovea. The former target design is present in computer-assisted perimeters such as the Peritest and the Dicon Auto-perimeter, which employ light emitting diode stimuli, whilst the latter is featured on the Friedmann Visual Field Analyser (VFA). Such approaches facilitate both single and multiple stimuli presentation and the shape of the normal gradient produced by a given instrument is a function of the interaction between the stimulus parameters afforded by the instrument.

The visual field is represented topographically across the primary visual cortex and varies as a function of peripheral angle, with the central areas having disproportionately greater representation (35 ×) than the periphery (Hubel and Wiesel, 1983). This representation can be defined by the cortical magnification factor (*M*) which describes the linear extent, in millimetres, of striate cortex corresponding to one degree of visual space. The value of *M* has been estimated in various studies to have a value at the fovea of 15.1 mm/° (Cowey and Rolls, 1974), 11.5 mm/° (Drasdo, 1977) and 7.99 mm/° (Rovamo and Virsu, 1979) and can be calculated for any eccentricity along the four cardinal meridians (Drasdo, 1977; Rovamo and Virsu, 1979).

Various visual functions have been made independent of retinal location by adjusting target size such that equivalent cortical areas are stimulated (*M*-scaling) thereby producing an isosensitivity profile. Verification of this relationship has been reported for contrast sensitivity (Virsu and Rovamo, 1979), detection of coherent motion for dynamic random on and off patterns (Van der Grind *et al.*, 1983), lower thresholds for motion (Johnston and Wright, 1983) and motion and displacement thresholds (Wright and Johnston, 1983). Thresholds for some visual functions cannot, however, be made independent of retinal location by *M*-scaling spatial stimulus parameters alone; these include CFF (Rovamo and Raninen, 1984), vernier acuity (Levi *et al.*, 1985) and the differential light threshold at a luminance of 4 asb (Wood *et al.*, in press).

By employing stimuli which increase in diameter with increasing peripheral angle, the Friedmann VFA produces a flat sensitivity gradient across the normal visual field out to an eccentricity of 25° when used in conjunction with a low photopic level of adaptation (1 asb, i.e. 0.318 cd m^{-2}) and a presentation time of 0.25 s. In the design of the instrument (Bedwell, 1982) the aperture diameters necessary to produce a flat profile were determined experimentally, relative to a standard solid angle at fixation, using a front plate with variable aperture sizes. The resultant values were then modified to allow for the effects of oblique viewing and a prototype front plate was produced with the estimated aperture diameters. These were subsequently further modified following additional clinical trials.

The aim of the study was to investigate whether the increase in stimulus diameter with increase in eccentricity, necessary to produce an isosensitive perimetric profile, was scaled in proportion to the reciprocal of ganglion cell receptive field separation with peripheral angle. The knowledge of such a relationship

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is important in providing further insight into the processing of perimetric stimuli and thus the design of the next generation of visual field instrumentation. The VFA II was used as the instrument for investigation.

METHODS

The sample consisted of 15 clinically normal age matched emmetropic observers (mean age 21.2 years, SD 1.25 years) experienced in visual field examination. The subjects were adapted to the screen luminance for a period of 10 min and natural pupils were used throughout. The Friedmann VFA Mk II was used in the threshold mode: the thresholding procedure was that of Barnes *et al.* (1985) whereby stimuli were presented in 0.2 log unit steps from an infraliminal level until each individual stimulus had been correctly identified on two out of three presentations at a given intensity setting. The stimuli lying on, and within 1.5° of, the cardinal meridians were used to create vertical and horizontal profiles (Fig. 1).

The stimulus aperture diameters were measured using a Nikon Shadowgraph Projector at a magnification of 100 × and were each represented as the mean of four separate measurements made on one occasion by one observer. The observed elliptical areas of the circular stimulus diameters resulting from obliquity of viewing at 33 cm were calculated taking into account eccentricity, front plate thickness and distance from the eye. The data for each stimulus aperture was then represented in terms of the diameter of the circle possessing the same area as that of the corresponding observed ellipse.

The *M*-scaling equations proposed by Rovamo and Virsu (1979) were used to derive, along the four principal meridians, the cortical representation (M_r) in mm/° at each aperture eccentricity. The derived aperture dimension at each eccentricity was then *M*-scaled to obtain the calculated dimension (L_E) which stimulated an equivalent area of cortex relative to the aperture diameter of pattern h (L_h) for the appropriate meridian using the equation:

$$L_E = \frac{M_h}{M_E} \cdot L_h.$$

The stimulus pattern h was selected since it was the central-most pattern to foveal fixation (see Fig. 1) and the use of the macular threshold aperture does not produce an isosensitivity profile. The value, M_h, defines the cortical representation at this location.

RESULTS

The group mean differential sensitivity, the derived stimulus diameters and the corresponding calculated *M*-scaled dimensions for the horizontal and vertical profiles are shown in Table 1. The results for the vertical meridian are represented graphically in Fig. 2.

DISCUSSION

The variation of the group mean differential sensitivity with increase in eccentricity along the four cardinal meridians does not describe an isosensitivity profile. Minor localized reductions in sensitivity occur between approximately 7° and 17° of approximately 0.1 log units. This reduction appears to be similar to that reported by Henson *et al.* (1984) which they attributed to angioscotoma. A more likely explanation is that of incorrect stimulus aperture diameters in this region

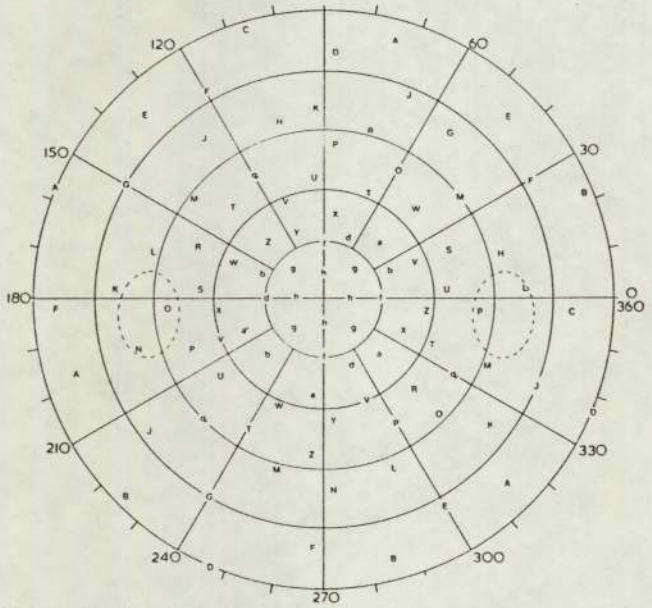

Fig. 1. Stimulus locations of the Friedmann VFA Mk. II. Stimuli *h'* lie closest to the centre of the field.

Table 1. Group mean and standard deviation sensitivity values (log units), equivalent diameters (mm) and *M*-scaled diameters (mm) for the stimulus locations lying within 1.5° of the vertical (top) and of the horizontal meridian (bottom)

	Superior							Inferior						
Stimulus location	D	K	P	U	X	f	h	h	f	a	Y	Z	N	F
Mean	2.33	2.35	2.27	2.29	2.21	2.27	2.31	2.32	2.31	2.24	2.24	2.15	2.36	2.39
SD	0.12	0.16	0.18	0.18	0.16	0.16	0.17	0.17	0.13	0.13	0.19	0.23	0.17	0.15
Equivalent diameter	2.11	2.02	2.15	1.78	1.49	1.43	1.28	1.31	1.43	1.50	1.51	1.56	1.98	2.07
M-scaled diameter	7.05	5.45	4.48	3.60	2.71	1.99	1.28	1.31	2.05	3.05	3.69	4.51	5.40	6.84
	Nasal							Temporal						
Stimulus location	F	k	O	S	X	d	h	h	f	Z	U	P	L	C
Mean	2.37	2.33	2.27	2.27	2.25	2.32	2.33	2.33	2.29	2.28	2.27	–	–	2.49
SD	0.13	0.14	0.19	0.19	0.16	0.17	0.16	0.16	0.15	0.17	0.18	–	–	0.12
Equivalent diameter	2.03	1.97	1.52	1.44	1.43	1.42	1.32	1.42	1.44	1.43	1.53	–	–	2.10
M-scaled diameter	6.91	5.46	4.23	3.45	3.02	1.99	1.32	1.42	2.10	2.57	3.49	–	–	6.12

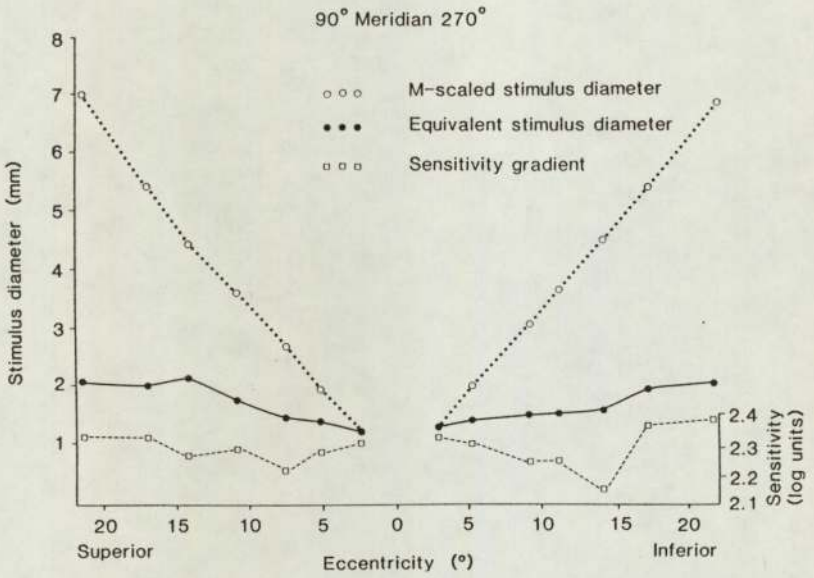

Fig. 2. Equivalent and *M*-scaled stimulus diameters (left hand axis) against eccentricity for the vertical meridian and group mean sensitivity (right hand axis) against eccentricity for the same meridian.

(Barnes *et al.*, 1985). The variation of the standard deviation with eccentricity shows no definite trend (Table 1) although there would appear to be a slight increase in the SD in the mid-peripheral region which decreases as the peripheral angle approaches 25°. Interestingly, however, an increase in SD with increase in eccentricity has been reported within the central 30° for the 45° meridian for the Perimetron, which employs a bowl luminance of 31.5 asb (Parrish *et al.*, 1984), and for the Octopus automated perimeter, which employs a bowl luminance of 4 asb (Wild *et al.*, 1986). The inter-subject variation in the shape of the gradient derived with the VFA (Greve, 1973; Wild *et al.*, in submission) may, however, mask such a trend. It is also possible that the absence of any particular pattern results from the gradient compensation of the VFA.

The increase in the equivalent diameter of the stimulus apertures with increase in peripheral angle is non-linear. The apparent aperture diameters between 11° and 17° eccentricity in the superior field were found to be up to 0.7 mm larger than those for the same eccentricity in the inferior field.

The *M*-scaled stimulus diameters increase linearly with increase in peripheral angle. The difference between the actual and predicted stimulus aperture diameters necessary to evoke an apparent isosensitivity profile increases with increase in eccentricity to a factor of 3.5 times. The use of other *M*-scaling equations, for

example those of Drasdo (1977), could have been used to analyse the data, but all would have produced a greater discrepancy between the derived and the *M*-scaled diameters than that described here. The differences could possibly be attributed to increasing off-axis optical effects. Indeed, Fankhauser and Enoch (1962) showed that the perimetric isopters varied with spherical blur out to an eccentricity of 30° although Jennings and Charman (1981) demonstrated that the mid-peripheral image quality is more than adequate despite the substantial oblique astigmatism. The discrepancy is more likely to imply that the sensitivity to perimetric spot targets across the visual field, at low photopic luminances, does not depend upon the density of retinal ganglion cells alone, and is in agreement with recent findings on the Octopus automated perimeter (Wood *et al.*, in press). The results are not entirely unexpected, as the characteristics of the ganglion cells are not uniform across the retina. Dendritic field size increases with eccentricity (Perry *et al.*, 1984) and this compensates for the decrease in ganglion cell density with the result that, for the Pβ cells, the dendritic coverage factor is fairly constant. Nevertheless, it has been reported that this constancy may not apply to receptive field coverage (Perry and Cowey, 1985). Thus the difference between the two profiles is therefore likely to arise, in part, as a result of spatial summation exhibited by the ganglion cells which increases with peripheral angle (Fankhauser and Schmidt, 1958, 1960; Gougnard, 1961; Sloan, 1961; Hallett, 1963; Wilson, 1967; Verriest and Ortiz-Olmedo, 1969; Dannheim and Drance, 1977) and decreases with increase in luminance levels (Fankhauser and Schmidt, 1960; Meur, 1965; Aulhorn and Harms, 1967). Alternatively it is possible that the current *M*-scaling equations misrepresent the visual field at the cortex. Indeed, Levi *et al.* (1985) suggested that the fovea was underestimated at the cortex although this was only of significance when tasks such as position acuities were *M*-scaled. They conjectured that this disparity may arise because position acuity is primarily limited by cortical processing, whilst tasks such as resolution or threshold in perimetry are limited by retinal factors, e.g. the blur function of the eye and the cone density (Westheimer, 1982; Barlow, 1979, 1981).

An isosensitive perimetric profile based upon the coverage factor of retinal ganglion cells would permit the utilization of the minimum stimulus diameter necessary to produce the required level of sensitivity at any eccentricity without oversaturating the visual system. The overriding clinical advantage of such a method would be the greater capability for differentiating local reductions in sensitivity. By varying the height of the isosensitive profile, the procedure could be further extended to investigate the response over a given dynamic range.

CONCLUSIONS

The findings imply that at the low photopic bowl luminances employed in conventional perimetry, the normal isosensitive perimetric profile is determined by factors in addition to the interganglion cell receptive field separation, the most notable of which is spatial summation. It is conjectured that from a knowledge of spatial summation at a given adaptation level and of retinal ganglion cell density it would be possible to calculate the stimulus diameters which would result in an isosensitivity profile. Such a profile, based upon the underlying physiology, could be applied at any background luminance across the entire field and would avoid the over saturation of the neural elements.

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Stimulus investigative range in the perimetry of retinitis pigmentosa: some preliminary findings

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Abstract. The manipulation of perimetric stimulus parameters over a given dynamic range has been reported to provide diagnostic information additional to that of changes in differential sensitivity. Preliminary studies (Flanagan et al., 1984a) have indicated that the perimetric response in retinitis pigmentosa behaves atypically over a range of stimulus combinations and strategies. The current study investigated the perimetric response of 17 retinitis pigmentosa patients of various genetic types over a range of stimulus parameters (target size, presentation time and background luminance) and test strategies (kinetic and threshold static) using the Octopus automated perimeter, the Goldmann and Tubinger bowl perimeters and the Dicon Autoperimeter 3000. Stato-kinetic dissociation was found to be present with large target sizes at 10 asb and 31.5 asb bowl luminances. Some patients demonstrated enhanced sensitivity to shorter stimulus presentations.

Introduction

It has been suggested over the years that different combinations of stimulus parameters presented by a given instrument can, in certain ocular and/or neurological disorders, be manipulated to provide diagnostic information additional to that obtained from the conventional perimetric examination.

Dubois-Poulsen (1952) and Dubois-Poulsen and Magis (1957) using kinetic perimetry at various stimulus sizes with the Goldmann bowl perimeter (adaptation level 31.5 asb) demonstrated abnormalities of spatial summation in certain disorders which they termed photometric dysharmony. They suggested that such disturbances could occur earlier, and be more pronounced, than the corresponding reduction in the differential threshold. They considered that photometric dysharmony resulted from oedema of the retina or optic nerve. This conclusion was not substantiated by Sloan (1961) and Sloan and Brown (1962) using static perimetry with the Goldmann perimeter. These authors demonstrated photometric dysharmony in achromatopsia but not in central serous retinopathy or in retinitis pigmentosa and concluded that photometric dysharmony occurred when the cone receptor mechanism was impaired. Wilson (1967) demonstrated, at an adaptation level of 674 asb, abnormalities of both spatial and temporal summation in lesions of the post-geniculate pathways and abnormalities of spatial summation, only, in pre-geniculate lesions.

Perimetry performed under various adaptation levels is also believed to provide additional diagnostic information. Greve, Bos and Bakker (1976) demonstrated with the Friedmann Visual Field Analyser that examination by means of comparative mesopic and photopic static perimetry aided the differential diagnosis of maculopathies and central neuropathies. In addition, Paige (1985) using the Humphrey Field Analyser suggested that the detection of 'subtle' visual field defects was enhanced at a high background luminance of 315 asb in suspected glaucoma, confirmed glaucoma and in neuro-ophthalmological lesions.

Stato-kinetic dissociation, whereby kinetic stimuli are visible in areas of the field where identical static stimuli are not visible, was demonstrated in occipital lesions by Riddoch (1917). The Riddoch phenomenon has subsequently been shown in optic tract lesions (Zappia et al., 1971), lesions of the optic radiations (Barbur, 1979) and tumours of the anterior optic pathways (Safran and Glaser, 1980).

In a study involving automated, semi-automated and manual perimetry of patients with a wide variety of ocular disorders, Flanagan, Wild, Barnes, Gilmartin, Good and Crews (1984a) suggested that the sensitivity gradient of some patients with retinitis pigmentosa behaved atypically over the dynamic range.

The advent of computer assisted perimetry permitting the rapid assessment of the visual field and the flexibility and ease of control over stimulus variables such as background luminance, target size, presentation time and test strategy, presents the opportunity for more detailed investigations of the earlier findings. Indeed, Barnes, Wild, Flanagan, Good and Crews (1985) using automated and semi-automated perimetry have recently demonstrated the potential for manipulation of the sensitivity gradient in identifying visual field loss.

The aim of the present investigation was to determine whether, in retinitis pigmentosa, additional diagnostic information is provided by varying the dynamic range of the major perimetric stimulus parameters, namely: target size, presentation time and bowl luminance.

Methods

The preliminary sample consisted of 10 patients with retinitis pigmentosa displaying varying degrees of visual field loss who were selected from previous hospital records on the criteria of possessing some peripheral residual field. The age of the sample ranged from 22 to 50 years (mean age 41.9; SD 9.3) and comprised 9 males and 1 female. The genetic typing included 5 recessive, 2 isolated, 2 dominant and 1 unknown. Details of scotopic and photopic ERG results and dark adaptation were available for each patient. The eye to be examined was selected on the premise of clearest media, best visual acuity and largest peripheral island of vision.

The patients each attended for 3 sessions. The first session consisted of kinetic perimetry with the Goldmann bowl perimeter (bowl luminance 31.5 asb; target sizes III and V; intensity 4e). The second and third sessions comprised examination with program 21 of the Octopus automated perimeter (bowl luminance 4 asb; target sizes 3 and 5; stimulus duration 100 msec) and static cuts along an arc and a meridian with the Tubinger perimeter (bowl luminance 10 asb; target sizes 3 and 5; stimulus durations 100 msec and 500 msec). The sequence of perimetry over the latter two visits, of target size within an examination and, in the case of the Tubinger, stimulus duration were all randomised. The examinations for a given patient were all carried out within a maximum period of 28 days.

Kinetic perimetry with the Goldmann perimeter was performed by one examiner to minimise inter-examiner variation (Berry et al., 1966; Ross et al., 1984) and to ensure standardisation of technique. For Tubinger perimetry, the meridian and arc were selected from the Goldmann results to cut through an area of high sensitivity in the peripheral field. Threshold was determined in 1 dB intervals by an ascending method of limits and was recorded as the mean of 3 determinations at each eccentricity. The Tubinger examinations were undertaken by a second clinician who had been instructed as to the appropriate location for investigation.

Prior to each examination, patients underwent 10 min adaptation to the bowl luminance. For perimetry inside the central 30°, patients wore the distance refraction together with the near correction, if necessary, for the appropriate viewing distance. Fixation was strictly monitored and natural pupils were used throughout. For Octopus perimetry, patients were instructed not to respond to the light flashes which filled the central bowl (Fankhauser and Haeberlin, 1980) and to ignore reflections in the fixation tube.

A qualitative comparative analysis of the field plots from the Octopus (numerical printout and gray scale) and Goldmann instruments was carried out using the level 4 analysis of Flanagan, Wild, Barnes, Gilmartin, Good and Crews (1984b). For a given patient, the field to a given stimulus combination was compared, in terms of type, shape, area, depth and location of field loss, to the field for a second stimulus combination which was designated as the reference field. The level of compatability between the comparison field and the reference field was ranked on a five-point scale where scores I+, I and I− represented levels of compatible fields and scores II and III represented levels of incompatible fields. The process was then repeated for all stimulus combinations with each instrument in turn providing the reference field. An example of the scoring system is shown in Figure 1. The results are listed in Table 1. A similar, but separate analysis, was carried out for the Tubinger (Table 2).

Results and discussion

Table 1a demonstrates the degree of compatability between the reference

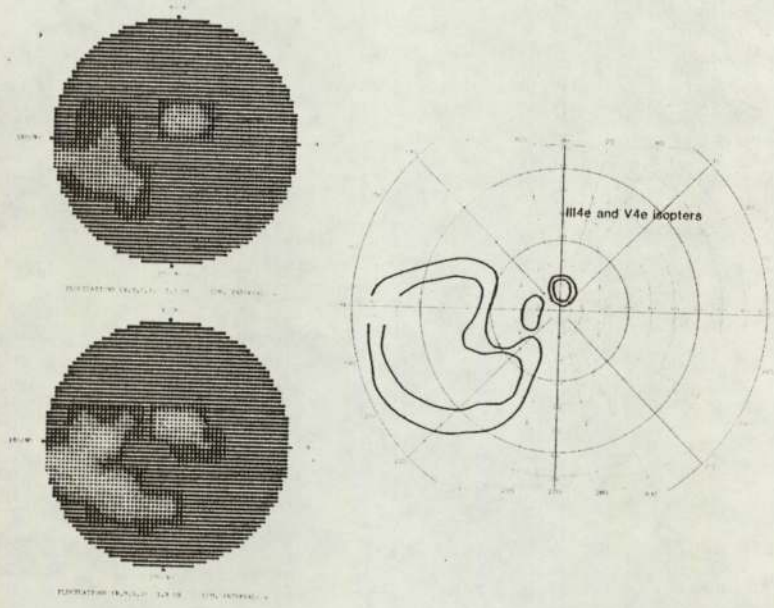


Figure 1. The qualitative scoring procedure used to compare the field plots in the study illustrated for the left eye of a 42 year old male with retinitis pigmentosa. Top left: gray scale printout of Octopus program 21 (target size 3) as reference field. Bottom left: gray scale printout of comparative field from Octopus program 21 (target size 5) scored as I– (less field loss). Right: comparative fields from Goldmann III4e and V4e kinetic isopters. III4e isopter scored as I (similar field loss); V4e scored as I– (less field loss).

field of Octopus target size 3 and the comparison fields of the Octopus target size 5 and the Goldmann target sizes III4e and V4e. Seven of the 10 kinetic target size III4e Goldmann fields exhibited a high degree of compatibility (Score I) with the static target size 3 on the Octopus. It would thus appear for the sample in question that the combination of static threshold presentation with target size 3 at a bowl luminance of 4 asb together with a 15° spatial resolution yields a similar level of areal field loss to that of a kinetic target size III4e at a bowl luminance of 31.5 asb. It is interesting to note in this context that Heijl (1985) considered that perimetry at low bowl luminances offered no diagnostic advantages over the conventional level of 31.5 asb.

The results also show that all 10 individuals showed less field loss (Score I–) with Octopus target size 5 when compared with target size 3 in terms of area and depth. Such findings are in accord with normal perimetric theory (Fankhauser, 1979) whereby a larger stimulus extends the dynamic range of measurement by virtue of spatial summation. Eight individuals demonstrated less areal field loss with the kinetic V4e Goldmann due to the gross suprathreshold nature of the stimulus .

Table 1a. Octopus target size 3 reference field

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Octopus 3)				
	I+ More	I Similar	I– Less	II Different field loss	III Normal
OCTOPUS 5	–	–	10	–	–
GOLDMANN III4e	1	7	2	–	–
GOLDMANN V4e	–	2	8	–	–

Table 1b. Octopus target size 5 reference field

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Octopus 5)				
	I+ More	I Similar	I– Less	II Different field loss	III Normal
OCTOPUS 3	10	–	–	–	–
GOLDMANN III4e	7	2	1	–	–
GOLDMANN V4e	1	3	6	–	–

Table 1c. Goldmann target size III4e reference field

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Goldmann III4e)				
	I+ More	I Similar	I– Less	II Different field loss	III Normal
OCTOPUS 3	2	7	1	–	–
OCTOPUS 5	1	2	7	–	–
GOLDMANN V4e	–	–	10	–	–

Table 1d. Goldmann target size V4e reference field

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Goldmann V4e)				
	I+ More	I Similar	I– Less	II Different field loss	III Normal
OCTOPUS 3	8	2	–	–	–
OCTOPUS 5	6	3	1	–	–
GOLDMANN III4e	10	–	–	–	–

When compared to Octopus target size 5 as the reference (Table 1b), 7 of the Goldmann III4e fields gave more loss (score I+) in terms of area whilst all 10 Octopus target size 3 plots also produced more loss in terms of both area and depth. The trend from Tables 1a–1d shows that the Octopus target size 5 yielded the greatest range of sensitivity. Within the limited numbers of the sample, the kinetic Goldmann III4e, by virtue of performance against Octopus target size 5, appeared to give a slightly greater areal investigative range than that of Octopus size 3. The Goldmann V4e produced the lowest range. The effect of the stimulus combinations is illustrated diagrammatically in Figure 2.

Table 2a. Tubinger target size 3: 100 msec reference field

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Tubinger 3:100)				
	I+ More	I Similar	I– Less	II Different field loss	III Normal
TUBINGER 5:100	–	1	8	–	–
TUBINGER 3:500	2	6	1	–	–
TUBINGER 5:500	–	2	7	–	–

Table 2b. Tubinger target size 3: 500 msec reference field

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Tubinger 3:500)				
	I+ More	I Similar	I– Less	II Different field loss	III Normal
TUBINGER 3:100	1	6	2	–	–
TUBINGER 5:100	–	2	7	–	–
TUBINGER 5:500	–	2	7	–	–

Table 2c. Tubinger target size 5: 100 msec reference field

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Tubinger 5:100)				
	I+ More	I Similar	I– Less	II Different field loss	III Normal
TUBINGER 3:100	8	1	–	–	–
TUBINGER 3:500	7	2	–	–	–
TUBINGER 5:500	4	5	–	–	–

Table 2d. Tubinger target size 5: 500 msec reference field

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Tubinger 5:500)				
	I+ More	I Similar	I– Less	II Different field loss	III Normal
TUBINGER 3:100	7	2	–	–	–
TUBINGER 3:500	7	2	–	–	–
TUBINGER 5:100	–	5	4	–	–

Table 2a shows that the Tubinger target size 5 at 100 msec produced less field loss in 8 of the 9 cases examined when compared to target size 3 at 100 msec as the reference field, thus obeying conventional perimetric theory. In contrast, target size 3 at 500 msec showed a similar result to the reference (target size 3 at 100 msec) in 6 cases. These findings, together with those in the remainder of the Table, demonstrate, that for the sample under study, increase in target size was more efficient in extending the dynamic range than increasing the stimulus duration from 100 to 500 msec.

The results reported for both the spatial and temporal characteristics may be influenced by extraneous stray light associated with the use of large targets

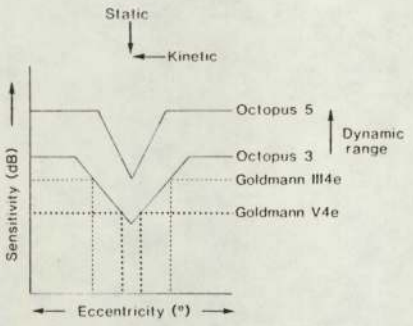


Figure 2. Schematic representation of the investigative range of the static threshold Octopus (target sizes 3 and 5) and kinetic Goldmann (target sizes III and V, intensity 4e) stimulus combinations in the detection of reduced sensitivity.

(Fankhauser and Haeberlin, 1980). Indeed, Wilson (1968) measured the thresholds for the detection of light scattered from stimuli presented in densely impaired regions of the visual field. He proposed various arbitrary limitations on the maximum permittable stimulus luminance to avoid light scatter. Such restrictions, however, were valid only for a stimulus duration of 1 second on a background luminance of greater than 75 cd/m^2 (236 asb). Weale and Wheeler (1977) concluded from their study on stray light with the Tubinger perimeter that both instrument design and observer and patient variability exclude the possibility of applying any but the crudest correction to perimetric measurements.

It was noted during both Goldmann and Tubinger perimetry, that patients frequently perceived a kinetic stimulus but reported an identical stationary stimulus as not seen. An additional study was undertaken to further investigate this stato-kinetic dissociation (SKD). The second sample consisted of 5 males and 2 females, (mean age 48.8 years; SD 8.8 years; range 38.9–65.7 years) and the genetic typing comprised 3 dominant, 1 X-linked and 3 unknown. The patients were examined with the Octopus program 21 (target sizes 3 and 5) and with the Goldmann perimeter performed in a static and kinetic mode using target sizes III and V. The kinetic examination was carried out as before at intensity 4e. The static investigation was undertaken along an arc in the middle of a region of preserved field; presentation time was 1 second and threshold was determined by a descending method of limits. In cases where the stimulus could not be seen at the maximum intensity (V4e) the presentation time was increased to between 3 and 5 seconds. Each patient attended for two sessions and the order of examination within and between instruments was randomized. The remaining protocol was as described for the first sample.

The kinetic Goldmann isopters and the static Octopus fields were analysed

Table 3a. Octopus target size 3 reference field

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Octopus 3)				
	I+ More	I Similar	I– Less	II Different field loss	III Normal
OCTOPUS 5	–	1	16	–	–
GOLDMANN III4e	1	11	5	–	–
GOLDMANN V4e	–	2	15	–	–

Table 3b. Octopus target size 5 reference field

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Octopus 5)				
	I+ More	I Similar	I– Less	II Different field loss	III Normal
OCTOPUS 3	16	1	–	–	–
GOLDMANN III4e	10	5	2	–	–
GOLDMANN V4e	2	4	11	–	–

Table 3c. Goldmann target size III4e reference field

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Goldmann III4e)				
	I+ More	I Similar	I– Less	II Different field loss	III Normal
OCTOPUS 3	5	11	1	–	–
OCTOPUS 5	2	5	10	–	–
GOLDMANN V4e	–	–	17	–	–

Table 3d. Goldmann target size V4e reference field

Comparison field	Number of patients and scoring level for comparison field relative to reference field (Goldmann V4e)				
	I+ More	I Similar	I– Less	II Different field loss	III Normal
OCTOPUS 3	15	2	–	–	–
OCTOPUS 5	11	4	2	–	–
GOLDMANN III4e	17	–	–	–	–

as previously. The results for the cumulative sample of 17 patients are summarised in Table 3 and support the original conclusions from the initial sample.

All 17 patients exhibited SKD showing an increased sensitivity in response to kinetic stimuli relative to static stimuli under the same set of stimulus conditions. The results further support those from the original sample which demonstrate SKD. The dissociation appeared to be of greater magnitude with target size 5. Three cases illustrating SKD are shown in Figures 3, 4 and 5. A minor SKD has also been reported in some normals (McColgin, 1960; Safran and Glaser, 1980) where static thresholds were slightly higher than kinetic

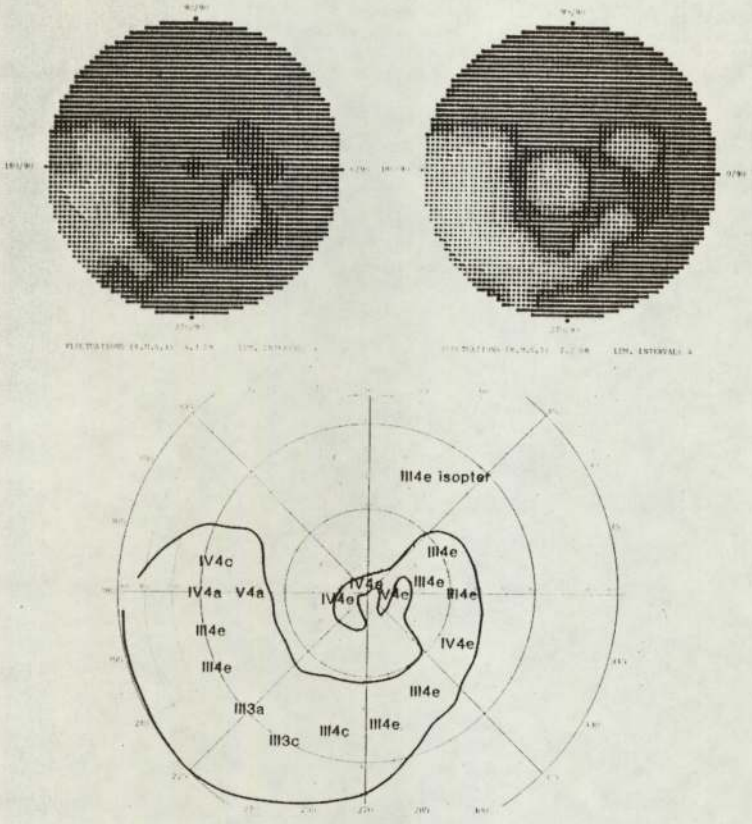


Figure 3. A case of stato-kinetic dissociation in the left eye of a 41 year old male with retinitis pigmentosa: (top left) Octopus target size 3 plot; (top right) Octopus target size 5 plot; (bottom) Goldmann III4e isopter and accompanying static thresholds.

thresholds peripherally, but lower centrally (Fankhauser and Schmidt, 1960). Greve (1973) attributed this physiological SKD to the phenomenon of successive lateral spatial summation and demonstrated that it accounted for a difference of 0.2 log units for the Goldmann size 1 at a speed of 1°/sec. The differences reported here are greater than that of Greve although the stimulus sizes used are larger.

Interestingly, Table 2c shows that, when compared to target size 5 at 100 msec, 4 of the 9 patients showed more field loss with the same target at a presentation time of 500 msec. Such a finding clearly runs contrary to conventional perimetric theory, whereby the dynamic range can be extended by increasing the presentation time. Nevertheless, it is in accordance with the finding of SKD; a stationary target (infinitely long presentation time) yields

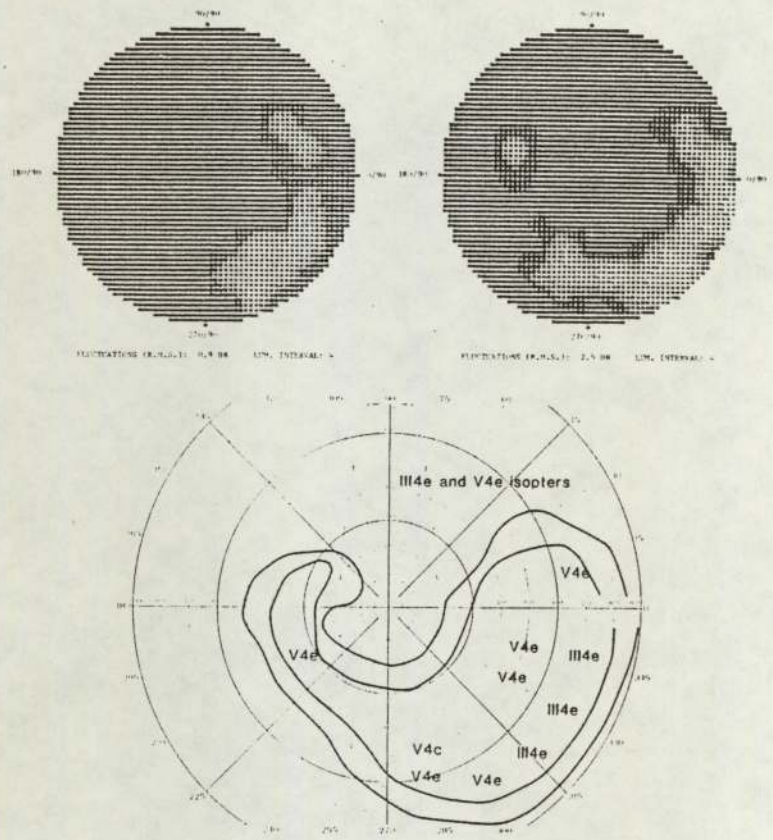
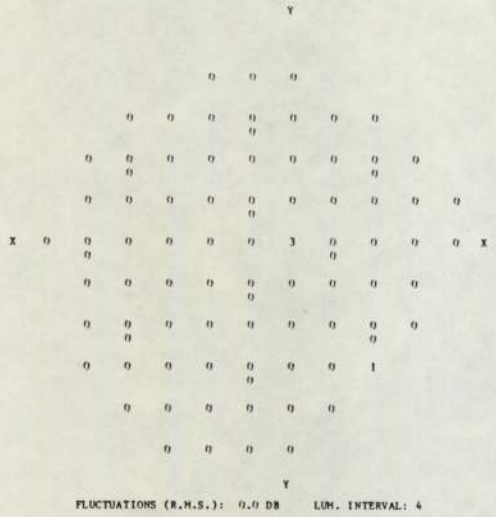


Figure 4. Stato-kinetic dissociation in the right eye of a 47 year old male with retinitis pigmentosa: (top left) Octopus target size 3 plot; (top right) Octopus target size 5 plot; (bottom) Goldmann III4e and V4c isopters and corresponding static thresholds.

less sensitivity than a moving one (infinitely short presentation time at any given stimulus location). The findings suggest that the kinetic nature of the stimulus is more effective in detecting small degrees of residual field in retinitis pigmentosa than either stimulus intensity or background luminance.

It is possible that SKD may be related to the existence of separate channels for sustained and transient responses. These channels have been suggested on the basis of both electrophysiological studies (Enroth-Cugell and Robson, 1966) and psychophysical studies (Kulikowski and Tolhurst, 1973). Movement channels are very sensitive to low spatial frequencies and are analogous to the Y cells, whilst the pattern channels are most sensitive to high spatial frequencies and are analagous to X cells (Tolhurst, 1973; Kulikowski and



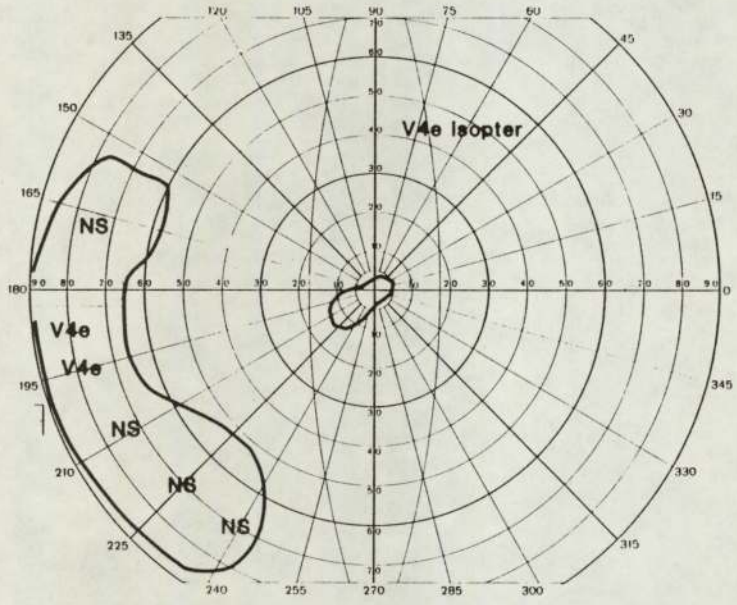


Figure 5. Stato-kinetic dissociation in the left eye of a 52 year old female with retinitis pigmentosa: (top) Octopus numeric printout of sensitivity to target size 5; (bottom) Goldmann V4e isopter and corresponding static threshold (NS indicates static target not seen). In this patient, Octopus target size 3 was not visible at any eccentricity examined with program 21.

Tolhurst, 1973). The receptive fields of Y transient cells have large centres and sloping sensitivity gradients; anatomically their correlate cells have large somas and wide dendritic fields. Conversely, X cells have small centres, sharp sensitivity gradients and their anatomical correlate cells have medium somas and narrow dendritic fields (Ikeda and Wright, 1972; Cleland and Levick, 1974). It can be speculated that the disease process in retinitis pigmentosa either affects the channels subserving sustained vision (X channels) to a greater extent than the transient channels (Y channels) or alternatively that the Y ganglion cells with their wider dendritic fields may be more resistant to damage than the X ganglion cells. The distinction between X and Y cells made on the basis of sustained and transient responses is not, however, felt to be completely satisfactory (Lennie, 1980), and there is also overlap in the temporal characteristics between the two groups (de Monasterio, 1978).

A quantitative analysis was undertaken whereby spatial summation coefficients (Gougnard, 1961) for each patient were derived from the Octopus and Tubinger fields. The results suggest enhanced spatial summation across the islands of residual vision. Caution must be exercised, however, owing to the short and long term fluctuations (Bebie et al., 1976; Flammer et al., 1984) which are inherent in any perimetric examination and which particularly confound any quantitative analysis. Sloan and Brown (1962) found normal spatial summation in 4 cases of retinitis pigmentosa, but an abnormal effect in 2 subjects with progressive cone degeneration. They concluded that anomalies of spatial summation could be associated with impairment of the inhibitory mechanisms of the cone receptor system. Such a conclusion assumed that rods and cones do not interact. Mediation through gap junctions, however, has been reported between vertebrate photoreceptors (Cohen, 1969; Raviola and Gilula, 1975) and via horizontal cells (Alexander and Fishman, 1985).

A sample of 5 patients from the second group were examined on a separate occasion at 3 background luminances (10 asb., 31.5 asb., 45 asb.) with the Dicon Autoperimeter 3000 in order to investigate whether adaptation level was significant to apparent field retention and thus the validity of Webers law in retinitis pigmentosa ($\Delta L/L = k$; where ΔL defines the stimulus luminance, L is the background luminance and k is a constant). It could be hypothesized that greater field retention would have resulted at higher bowl luminances since in retinitis pigmentosa the rods are traditionally believed to degenerate before the cones. Ultrastructural studies from a young X-chromosome linked patient (Szamier et al., 1979) and an elderly X-chromosome linked carrier (Szamier, 1981), however, have demonstrated a reduction in the number, and a distortion, of both the rods and cones. Indeed, in 4 of the 5 cases investigated, the results appeared to follow the normal laws of perimetry such that enhanced sensitivity was demonstrated at the lower adaptation level.

The sensitivity values displayed by the Dicon, are not calibrated in terms

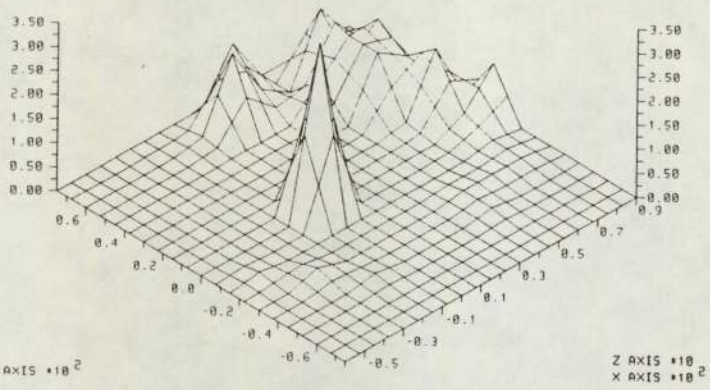


Figure 6. Three dimensional display, rotated clockwise through 90°, of the Octopus Target size 3 field from the left eye of a 49 year old male with retinitis pigmentosa illustrating the residual peripheral island of vision in the infero-temporal quadrant. The X and Y axes denote eccentricity in degrees $\times 10^{-1}$, the Z axis sensitivity in decibels $\times 10^{-1}$.

of ΔL but are the absolute value of the light emitting diode (LED) stimuli and thus the validity of Webers law ($\Delta L/L$) cannot be verified using this perimeter. Indeed, the use of LED stimuli without reflecting covers merely measures the sensitivity of the visual system to a light flash in a black hole with the ambient background luminance acting as a secondary stimulus. A further restriction in the use of the Dicon is the lack of stimuli beyond 60° available in the majority of the standard test programs.

Many patients in the study demonstrated greater areal field retention inferiorly than superiorly. This finding is in agreement with that of Lyness, et al., (1985). Indeed, in the more advanced cases of field loss, the peripheral field was usually retained in the inferior temporal quadrant (Figure 6). It can be speculated that this retention arises either because the superior nasal quadrant of the retina is more resistant to damage due to the underlying retinal architecture or because less light falls upon the superior retina by virtue of the eyelids. This latter hypothesis is commensurate with the theory from animal studies that light acts as a catalyst to the pigmentary changes in retinitis pigmentosa. Various studies on animals with retinal degeneration, RCS albino rats (Dowling and Sidman, 1962), vitamin A depleted rod dominated rats (Noell et al., 1971) and vitamin A depleted 13-lined ground squirrel (Berson, 1973) have suggested that light exposure results in further photoreceptor destructure once the photoreceptor-pigment epithelial cell complex has become abnormal. Such findings led to the proposal by Berson (1971) that light deprivation may act as a therapeutic measure for patients with early retinitis pigmentosa. Whatever the fundamental reason for the pattern of field loss, the end product is advantageous to the

patient in that the inferior temporal vision provides some aid towards mobility.

Conclusions

The majority of patients demonstrated stato-kinetic dissociation across the peripheral islands of residual vision. Furthermore 4 of 9 patients examined with the Tubinger exhibited an enhanced sensitivity to the shorter presentation time. In the spatial dimension, retinitis pigmentosa patients would seem to demonstrate enhanced spatial summation across the islands of residual field; the presence of fluctuations in the perimetric response, however, make quantitative analysis tenuous.

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Isolation of the Mechanisms Determining the Normal Perimetric Differential Light Threshold

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1. Introduction

The introduction of computer assisted perimetry over the last decade has revolutionized the role of the visual field examination in the diagnosis of abnormality. Although several authors have remarked upon the similarity between the perimetric response obtained with manual instrumentation and the distribution of retinal elements /1,2,3/ the mechanisms generating the perimetric response remain obscure. Computer assisted perimetry, in particular, facilitates the rapid and comprehensive assessment of the differential light sensitivity and this facet, together with the range of possible stimulus parameters provided by the instrument software, permits investigation of spatial and temporal characteristics supplementary to the conventional clinical requirements. The purpose of the study was to relate the size dependence in the normal eye of sensitivity and peripheral angle to the underlying retinal architecture. A knowledge of such a relationship would further enhance the diagnostic efficiency of perimetry.

2. Method

The sample comprised 10 clinically normal, age-matched emmetropes (mean age 21.4 years S.D. 1.35 years), experienced in psychophysical tests, and with distance visual acuity of 6/6 (20/20) or better. The differential light threshold for the visual field of the right eye was determined with the Octopus Automated Perimeter, a computer driven projection perimeter, which uses a staircase double threshold strategy. The sensitivity is recorded in dBs referenced to a 1000 asb maximum stimulus intensity. The Octopus was chosen as it is currently used as a standard for other computer-assisted perimeters. Threshold was determined for each of the six standard Goldmann equivalent stimulus sizes (0.054 degrees, 0.108 degrees, 0.216 degrees, 0.431 degrees, 0.862 degrees, and 1.724 degrees projected diameter). Stimuli were presented over a 15-degree square stimulus grid across the full field (Octopus program 21) and over a 6-degree square stimulus grid out to an eccentricity of 30 degrees (Octopus program 31). Stimulus presentation time was 100 msec. The head was steadied with the head clamps and chin bar of the instrument; fixation was constantly monitored with the instrument video camera. Natural pupils were used throughout; the mean pupil size was 7.03 (S.D. 0.71 mm). The subjects attended at approximately the same time of day for seven sessions within a maximum period of four weeks. Each session consisted of a 10-minute adaptation period to the perimeter bowl luminance (4 asb) followed by two test programs separated by a short rest period. The order and combination of program and stimulus size were randomized for each subject. The first session was used as a familiarization period, the results of which were discarded prior to data analysis. The equations proposed by ROVAMO and VIRSU /4/ were used to derive the cortical representation (Me) and ganglion cell receptive field density at each eccentricity examined along the 4 principal meridians. The diameter of the retinal target (Le) stimulating an equivalent cortical area to stimulus size 0.054 degrees at the fovea (Lo) was then calculated by the ratio $Le = (Mo/M_e)Lo$ where $Mo = 7.99$ mm/deg. The values of differential sensitivity for each eccentricity were then obtained by graphical interpolation from the experimental data using the calculated values of Lo and plotted against peripheral angle.

The equations of ROVAMO and VIRSU /4/ were selected on the premise that they have previously been used in relation to the interaction of spatial summation and cortical magnification. The value of 0.054 degrees for Le was arbitrarily chosen to ensure that the M-scaled targets remained within the stimulus range provided by the instrument.

3. Results and Analysis

The group mean differential sensitivity profile for the six stimulus sizes along the cardinal and the oblique meridia of the visual field for the right eye are represented in Fig. 1. The standard error of the mean increased with increase in peripheral angle and was greatest for the small stimuli. A three-way analysis of variance of the data showed that stimulus size, eccentricity and meridian all statistically significantly influenced sensitivity. Having confirmed an overall significant difference, two-tailed paired t-tests using Scheffe's correction with a rejection level set at $p < 0.05$, were applied to the sensitivity values between meridians for each stimulus size at a given eccentricity.

4. Discussion

The attenuation of sensitivity with increase in peripheral angle is less marked with increasing stimulus diameter and is in agreement with classical manual perimetry investigations /5,6,7/. A good correlation is found between log ganglion cell receptive field density and differential light sensitivity for all meridians. This relationship is linear for stimuli of 0.054 degrees and 0.108 degrees projected diameters and becomes increasingly nonlinear with increases in stimulus size. This finding indicates that factors other than ganglion cell density are implicated with larger stimulus sizes and is likely to result from the increase in spatial summation

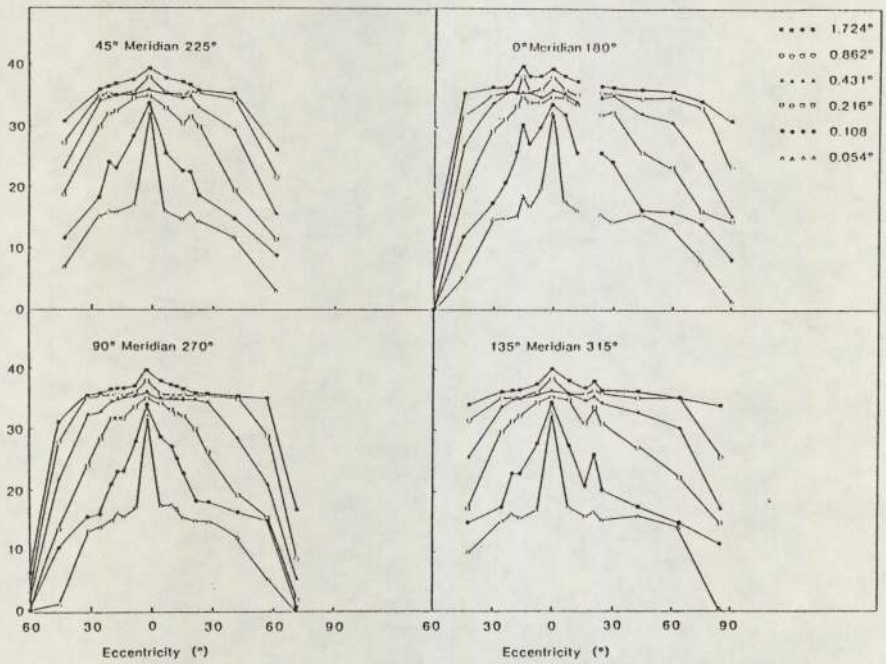

Fig. 1 Differential sensitivity with eccentricity for the 6 Goldmann stimuli along the cardinal and oblique meridians

exhibited by the peripheral retina. In addition, log rod density against differential sensitivity demonstrates a similar profile to that of ganglion cell density against sensitivity.

Mean and individual differential sensitivity profiles out to an eccentricity of 30 degrees along the horizontal meridian of the field are clinically isosensitive with a stimulus of projected diameter 0.431 degrees. An isosensitive profile can be obtained from the profiles in Fig. 1 by determining the eccentricities at which increasing Goldmann stimulus sizes would produce an equivalent sensitivity relative to the smallest foveal stimulus (0.054 degrees projected diameter). Such a profile, based upon the minimum stimulus diameter necessary to produce an equal response at each eccentricity, would avoid saturating the spatial summation properties of the neural elements. Interestingly, the coverage factor of the pß ganglion cells has been demonstrated to be remarkably constant across the retina /8/ which seems to imply that, at larger stimulus sizes, sensitivity depends upon coverage factor rather than on ganglion cell density or spatial summation alone.

An increase in the group mean sensitivity was found between 15 degrees and 18 degrees along the nasal meridian, for all target sizes with the exception of 0.431 degrees projected diameter. In addition, a similar region of enhanced sensitivity was found along the 315 degree meridian at 21.21 degrees eccentricity; the magnitude of which was also stimulus size dependent. A further sample of similarly age-matched clinically normal emmetropes have been examined with Octopus program 61 in order to confirm the two areas of enhanced sensitivity. The program undertakes three separate threshold determinations for each of 25 stimuli arranged in a 5 x 5 stimulus grid which possesses an inter-stimulus resolution of 3 degrees, the center of which is user-defined. The program was centered in separate investigations using both the left and right eyes on the 15-degree point nasally and on the 21.2-degree point along 315 degree inferio-temporally.

The area of enhanced sensitivity in the region of 15 degrees has been previously reported at scotopic luminances for stimuli of 0.3 degrees and 1 degree angular subtents /9,10/. OSTERBERG /11/ reported that rod densities were highest between 15 and 18 degrees nasally extending in an arc around the horizontal meridian at this eccentricity. These areas of enhanced sensitivity also coincide with regions of increased ganglion cell density /12/. This increase in sensitivity may thus arise as a consequence of underlying retinal anatomy and, being operative at low luminances and with a short stimulus duration, may be derived from ganglion cells with large summation areas and rod connections. Interestingly the resting position of accommodation and convergence in darkness is between 60-100 cm /13/, the area of enhanced sensitivity at 15 degrees nasally when projected into space will thus fall at a point approximately 10 cm from in front of the face permitting inspection of near objects in darkness. This is further supported by the fact that binocular summation is enhanced in scotopic vision. Alternatively, it has been hypothesized that the enhanced sensitivity may act as a compensatory measure in binocular summation for the blindspot of the contralateral eye /10/.

Statistical comparison of the data between meridians at a given eccentricity for the various stimulus sizes reveals trends which relate to the regional variations in ganglion cell density. In particular, sensitivity at 12 degrees eccentricity in the 90-degree (superior) meridian of the field for stimuli of 0.054 degrees, 0.108 degrees, and 0.216 degrees projected diameters was significantly lower ($p < 0.05$) than that at 12 degrees in the inferior meridian. It is interesting in this context to note that ABRAHAMS et al. /14/ demonstrated that the absolute threshold for a 1-degree stimulus at 15 degrees eccentricity along the 90-degree meridian of the superior visual field exhibited a reduced sensitivity relative to the inferior field at the same eccentricity. Furthermore, VILTER /15/ found increased neuronal contiguity and greater ganglion cell numbers in the superior retina than inferiorly in the region of the fovea. The superior field at 6 degrees eccentricity (stimuli 0.054 degrees, 0.108 degrees, and 1.724 degrees) at 12 degrees eccentricity (stimuli 0.054 degrees, 0.216 degrees, and 1.724 degrees) and at 15 degrees eccentricity (stimuli 0.054 degrees, 0.216 degrees, 0.431 degrees, and 1.724 degrees) exhibited statis-

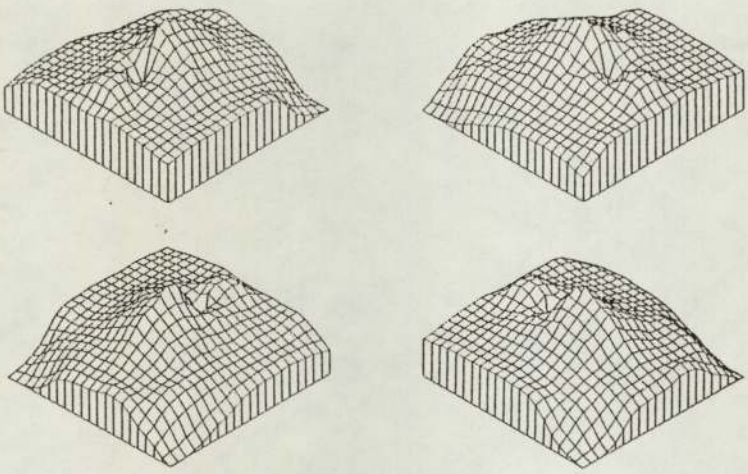

Fig. 2 Three-dimensional representation of differential sensitivity with eccentricity for stimulus size 0.108 degrees rotated through 360 degrees (the x and y axes denote eccentricity in degrees; the z axis sensitivity in decibels)

tically significant reductions in sensitivity compared with the corresponding nasal points ($p < 0.01 - p < 0.05$).

The presence of the two areas of enhanced sensitivity at 15 degrees nasally and 21.2 degrees inferio-temporally together with the reduction in sensitivity for the superior field at 12 degrees produce a remarkably similar correlation with the ganglion cell isodensity lines reported in human by STONE and JOHNSTON /16/ and support the concept of a visual streak in humans. Indeed, the elliptical nature of the enhanced sensitivity in the central region of the field for stimulus size 0.108 is illustrated in Fig. 2.

The M-scaled data for sensitivity along all 4 meridians exhibit an increase in sensitivity with eccentricity relative to the theoretical flat profile through the foveal point. The discrepancy rises to approximately 3 dB at 30 degrees. The failure to produce the predicted isosensitive profile indicates that M-scaling stimulus area alone does not result in sensitivities which are independent of retinal location. A similar discrepancy is also found for the isosensitivity profile derived from the data when compared with the corresponding M-scaled values. Currently, doubt has been expressed as to the degree of foveal enhancement of the cortical magnification factor /17,18/. The use of DRASDO's /19/ equations or any estimations predicting greater foveal enhancement would produce similar trends but the overcompensation, which is most probably due to spatial summation, would result in greater differences between the two profiles thereby further increasing the incompatibility of M-scaled stimuli with an isosensitive profile.

5. Conclusions

Variations in the topography of the normal visual field demonstrate a good correlation with retinal anatomy and physiology. Failure to produce an isosensitivity profile by manipulation of sensitivity data using the current M-scaling equations demonstrates that stimulation of equivalent cortical areas across the visual field does not occur. The findings suggest that the topography of the normal perimetric differential light threshold appears to be significantly influenced by retinal configuration and processing and in particular the combination of ganglion cell density and their spatial summation characteristics.

6. Acknowledgments

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Serial examination of the normal visual field using Octopus automated projection perimetry Evidence for a learning effect

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Abstract. The influence of prior perimetric experience on the magnitude of both differential sensitivity and the short and long term fluctuations remains unclear, and confounds accurate interpretation of visual field data obtained by computer-assisted perimetry. The purpose of the experiment was to identify and quantify any influence of training on the automated perimetric response. The full field of the right eye of 10 clinically normal, naive subjects was examined on 8 occasions with Octopus Program 21 (target size 3) on days 1–5 inclusive, 15, 16 and 44. Sensitivity increased with serial examination in 8 subjects. By dividing the field into zones, it was demonstrated that the learning effect was greatest in the superior field and for eccentricities beyond 30°.

Key words: differential light sensitivity – computer-assisted perimetry – learning effect.

The development of computer-assisted perimetry over the last decade has revolutionised the role of the visual field examination in the clinical diagnosis. The technique has minimised the influence of the perimetrist on the outcome of the examination, but the subjective components associated with the determination of any psychometric function still remain. These latter factors have been discussed with reference to manual perimetry (Aulhorn & Harms 1972; Tate & Lynn 1977), whilst the statistical nature of the response has been studied in relation to automated perimetry (Spahr 1975; Bebie et al. 1976; Flammer et al. 1984a). Indeed, it is now accepted that both short and long term fluctuations are inherent in the perimetric measurement of differential light sensitivity (Fankhauser & Bebie 1979). The spread of values associated with the measurement of sensitivity at any one particular location during a single field examination is termed the short term fluctuation (Bebie et al. 1976; Flammer et al. 1984a). The variation in threshold observed from one examination to another is termed the long term fluctuation (Bebie et al. 1976; Flammer, et al. 1984b) and consists of two components: the homogenous component which affects all parts of the field equally, and the heterogenous component which affects different areas of the field by different amounts. The evaluation and interpretation of abnormality is confounded by the short term fluctuations whilst the use of serial visual field investigation to monitor changes in visual function with time is undermined by the long term fluctuations.

The effect of prior perimetric experience on both the magnitude of the differential threshold and on the short and the long term fluctuations has not been quantified in computer assisted perimetry. In particular, the effect of sequential examination from the first to the second eye of a patient at a given session is unknown as is that from one session to another for a given eye.

Evidence from the literature on manual perimetry would suggest the possibility of a learning effect in automated perimetry. Indeed, Aulhorn & Harms (1967) reported approximately one log unit increase in sensitivity in normal subjects following 20 consecutive manual perimetric threshold determinations within one day. The increase in sensitivity was greatest in the early trials, plateaued in subsequent sessions and was independent of eccentricity. In addition, Low (1946) demonstrated that trained subjects responded to peripheral visual acuity stimuli up to 11 times more efficiently than untrained subjects. Several studies utilising computer-assisted perimetry have acknowledged the presence of a learning effect, but believe it to be eliminated by excluding either the first (Flammer, et al. 1984c) or the first two sessions (Wilensky & Joondeph 1984) or have considered any improvement in sensitivity to be counterbalanced by a decrease in sensitivity associated with a fatigue effect arising from the examination itself (Katz & Sommer 1986; Brenton et al. 1986).

A lack of understanding of the learning effect in the automated measurement of perimetric sensitivity is clearly unsatisfactory. The purpose of the experiment, therefore, was to quantify the improvement in differential sensitivity arising from repeated examinations of the visual field by computer-assisted perimetry.

Material and Methods

A homogenous sample of young subjects was selected in order to provide a sample with the greatest potential for learning compatible with the constraints of a logistically viable experimental design. It consisted of 10 clinically normal emmetropic males mean age 23.8 years (SD 2.8 years) free of ocular and systemic medication and naive to the purpose of the study, to perimetry and to visual psychophysical measurements in general. Vision was 6/5 or better in each eye.

Differential light sensitivity for the visual field of the right eye was measured using the Octopus 201 automated perimeter, a computer-assisted projection perimeter, as this has become the standard by which others are judged. The full visual field was examined with stimulus size 3 (projected diameter 0.431°) for a presentation time of 100 msec using Program 21. This program thresholds 76 points across the field with an inter-stimulus separation of 15°. Each subject attended a total of 8 sessions comprising days 1 to 5 inclusive, and days 15, 16 and 44. Each examination was conducted at approximately the same time of day and consisted of a 10 min adaptation period to the bowl luminance of 4 asb followed by the test program. The head was steadied with the head clamps and chin rest of the instrument and fixation was constantly monitored with the video

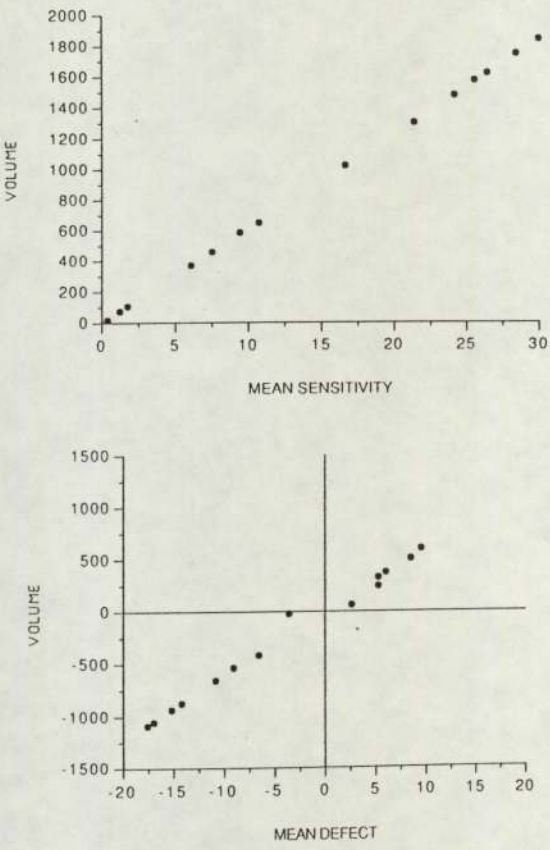


Fig. 1.
Graph illustrating the linear relationship between volume sensitivity (dB radians²) and mean sensitivity (Top) and between volume sensitivity (dB radians²) corrected with respect to normative age values, and mean defect expressed as a negative value for reduced sensitivity and as a positive value for increased sensitivity relative to the normal value (Bottom) for 14 individuals.

camera. Subjects were encouraged to rest at intervals throughout the examination and advised if fixation was incorrect. Natural pupils were used throughout; the mean pupil diameter was 6.70 mm (SD 0.69).

The results for each field plot were analysed in terms of the volume of the three-dimensional representation of sensitivity. This was determined using the Monte Carlo technique, a statistical sampling procedure based upon the binomial principle, for the evaluation of multiple integrals which are unsuited to classical mathematical methods. The application of this technique to visual field analysis has been discussed elsewhere (Wild et al. 1987). Volumetric analysis is an established method for analysing perimetric data (Suzumura et al. 1985; Jaffe et al. 1986) and was used since the derived index is dependent upon the areal dimensions of the field and can also be divided into aggregate parts. The relationship of the volume to the recently described Mean Sensitivity and Mean Defect statistics of Flammer et al. (1985) is linear and is illustrated in Fig. 1.

Results

Eight of the 10 subjects exhibited an increase in volume sensitivity over the 5 consecutive examinations (days 1 to 5). The sample could be divided into three distinct types (Fig. 2): those who exhibited a large increase in sensitivity at the second examination (day 2) which then plateaued over the subsequent sessions (Type 1); those showing a gradual increase in sensitivity over each of the 5

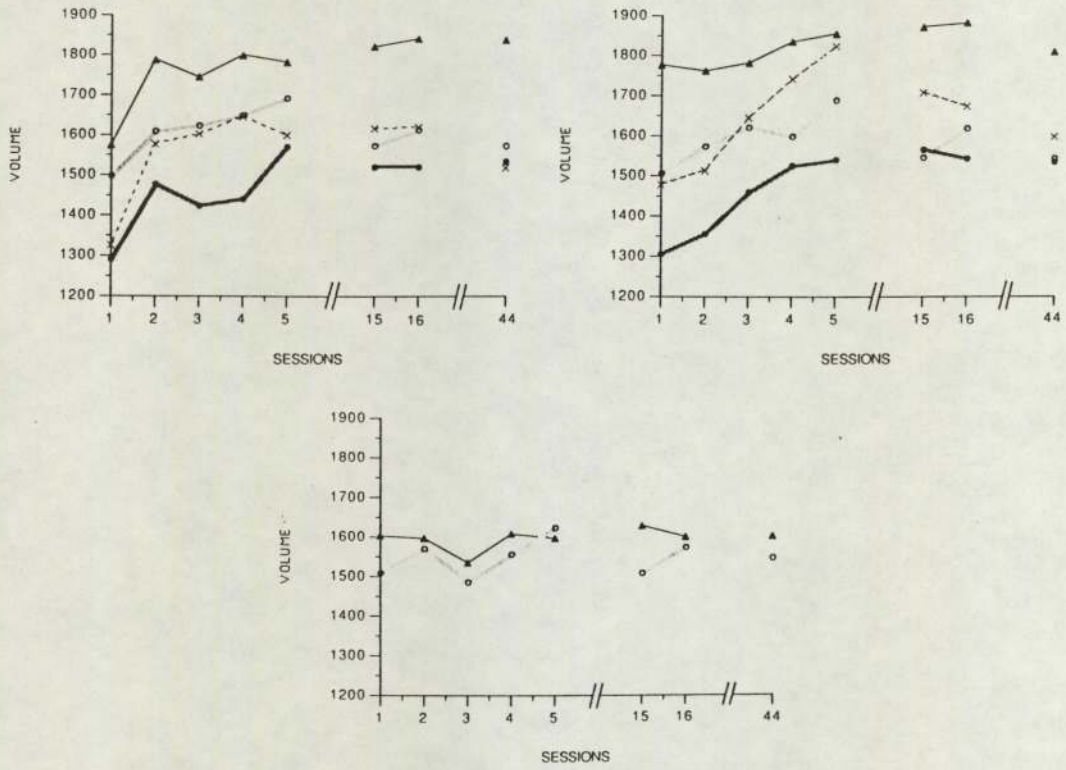


Fig. 2.

Volume sensitivity (dB radians²) with serial examination (days). Top left: 4 subjects who exhibit a large increase in sensitivity at the second examination which plateaus over the subsequent sessions (Type 1). Top right: 4 subjects who exhibit a gradual increase in sensitivity over the five sessions (Type 2). Bottom: 2 subjects in whom no obvious increase in sensitivity is demonstrated (Type 3).

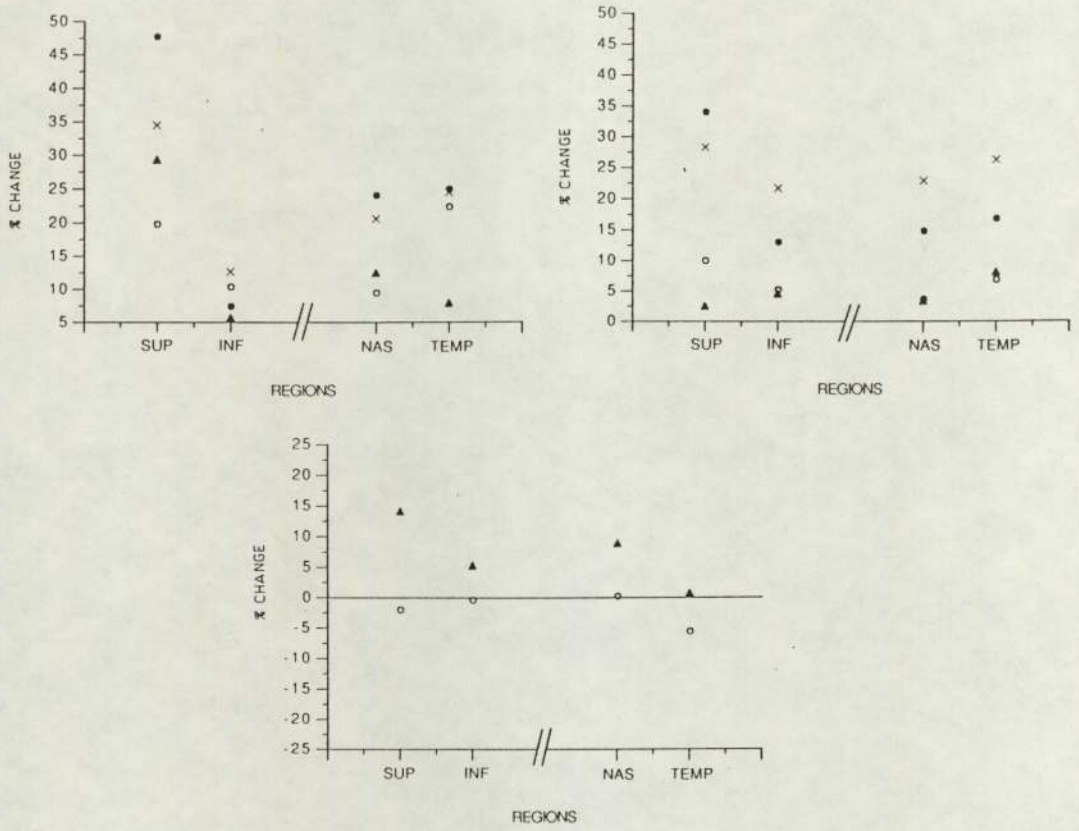


Fig. 3.

The percentage change in volume sensitivity between the first and fifth examinations for the superior, inferior, nasal and temporal hemifields. Top left: Type 1 subjects. Top right: Type 2 subjects. Bottom: Type 3 subjects.

sessions (Type 2); and those in whom no obvious improvement in sensitivity was shown (Type 3). Considerable inter subject variation was present at both the initial and the final volume for the 8 subjects who exhibited a learning effect. The increase in sensitivity persisted in the 8 subjects at the follow-up examinations on days 15, 16 and 44 and in five the magnitude on each of these occasions was at a similar level to that recorded at day 5.

The percentage change in volume sensitivity between examinations 1 and 5 for each subject was determined for the superior and inferior hemifields and for the nasal and temporal hemifields excluding points lying on the vertical and horizontal midlines, respectively (Fig. 3). Interestingly, in 8 subjects the sensitivity of the superior field increased to a greater extent than that of the inferior field. The ratio of volume sensitivity between the superior and inferior fields for these 8 subjects increased from a mean of 0.65 (SD 0.07) on day 1 to a mean of 0.74 (SD 0.03) on day 5. The low SDs indicate the relative constancy of this relationship between subjects in both the naive and the experienced states. The increase in sensitivity, expressed in dBs, along the superior meridian further illustrates the trends revealed by the volumetric analysis (Fig. 4). The corresponding ratio for the nasal and temporal hemifields yielded an identical value of 0.45 on both occasions (SD 0.31 and 0.28).

The percentage change in volume sensitivity for each subject with increase in eccentricity over a series of five 15° annular zones is shown in Fig. 5.

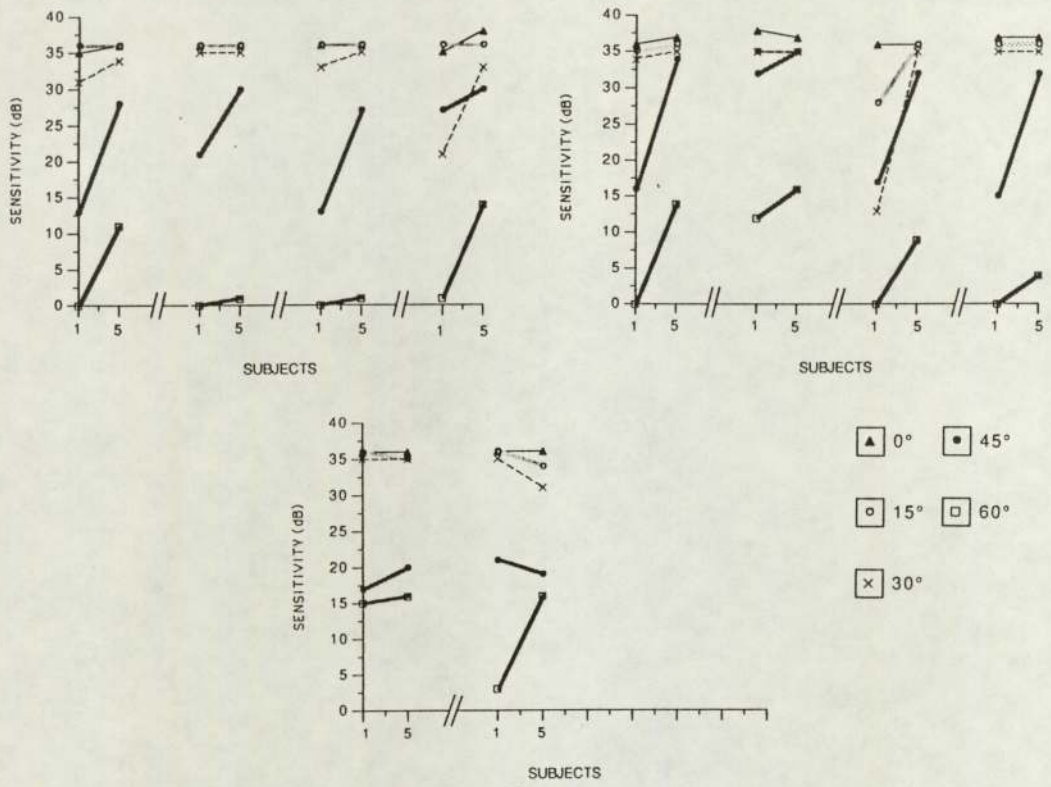


Fig. 4.
The increase in sensitivity (dB) between examinations 1 and 5 for the superior meridian as a function of eccentricity (°). Top left: Type 1 subjects. Top right: Type 2 subjects. Bottom: Type 3 subjects.

The greatest increase in sensitivity occurred beyond the 30° annulus although the magnitude was less beyond 60° primarily due to a lack of points in the superior field at this eccentricity. The interaction effect of hemifield and annuli was not analysed owing to the limited number of common data points out to an eccentricity of 30°.

Considerable inter subject variation occurred in the depth of the blind spot measured at the 15° nasal point. In 2 subjects the blind spot increased in depth with successive examinations over the five days; the majority of subjects, however, exhibited little change over this period (Fig. 6).

The variability in the visual field response for each examination, expressed as the root mean square fluctuation derived from the double threshold determination at each of 10 individual test locations, decreased in 9 subjects (Fig. 7) over days 1 to 5. This improvement was sustained over the respective follow-up examinations.

Discussion

The increase in sensitivity with serial examination and the retention of this effect is in agreement with the findings of Aulhorn & Harms (1967) for manual perimetry. The greater increase in sensitivity of the superior field may arise from the patient learning to consciously raise the upper lid; an increase in vertical visible iris diameter was not evident, however, from observations of the video monitor during the examination. Interestingly, the superior region of the central field exhibits the highest fluctuations (Flammer et al. 1984a; Jaffe et al. 1986) and is influenced by age to a greater extent than the inferior field (Haas et al. 1986; Jaffe et al. 1986). The improvement in the superior field may alternatively be accentuated by the relatively small improvement in the inferior field which may be functioning at its optimum level. This latter hypothesis is consistant with the fact that in the primary position of gaze, the

horizontal plane of the horopter passes through the feet. The greater increase in sensitivity with increasing eccentricity is in accord with Low's (1946) concept of the periphery as an unpractised sensory area. Indeed, a learning effect has not been found for the central field in the retrospective study of Gramer et al. (1986) with the Octopus and by Kosoko et al. (1986) with the Humphrey Field Analyser. The decreased spread of results associated with the threshold response indicates a greater consistency in response and is in agreement with the manual perimetric results of Aulhorn & Harms (1967) and of Greve (1973) on the frequency of seeing curves of trained and untrained observers and also with the automated perimetry findings of Parrish et al. (1984), Rabineau et al. (1985) and Gramer et al. (1986).

The results have shown that with the Octopus automated perimeter, sensitivity beyond an eccentricity of 30° particularly in the superior field exhibits a potential to improve with serial examination. The extent of this effect can be expected to vary in the population as a function of the alteration in the general learning curve with age, but should always be considered when monitoring changes outside 30°.

The exclusion of the results from the first examination in serial field investigation would seem to be acceptable in the case of those who exhibit Type 1 learning, but not for those with Type 2 where the potential to learn beyond an eccentricity of 30° remains until at least the fifth examination. The retention of the increased sensitivity beyond the fifth examination indicates that such an effect must also be considered in serial field analysis.

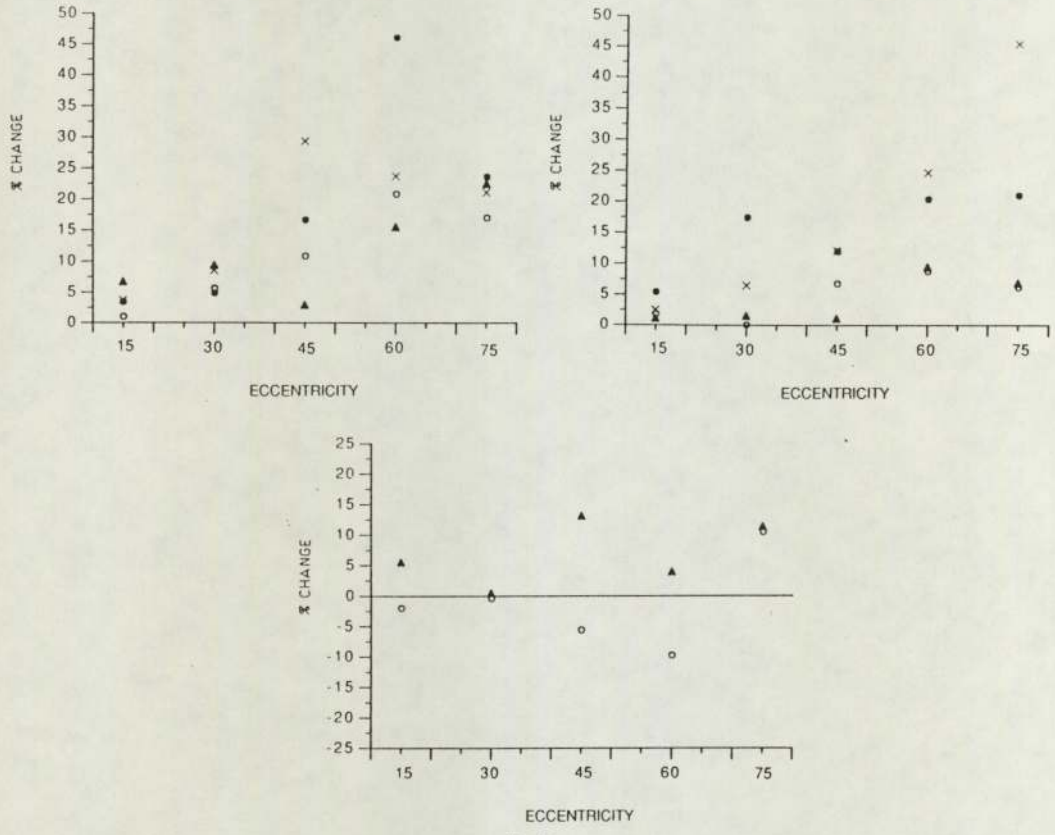
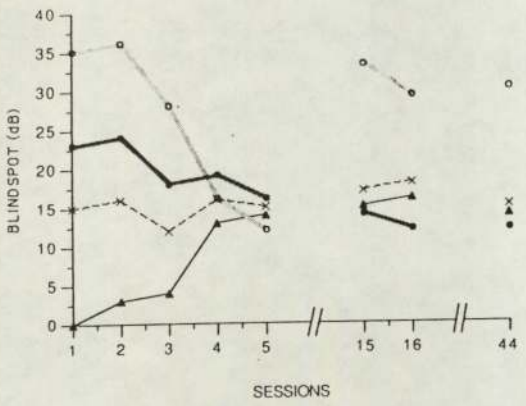
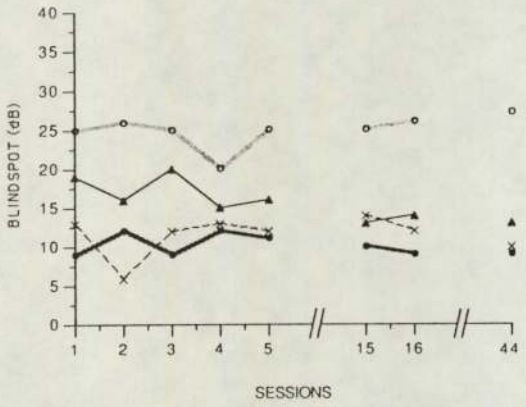


Fig. 5.
The percentage change in volume sensitivity between examinations 1 and 5 for the five 15° annular zones. Top left: Type 1 subjects. Top right: Type 2 subjects. Bottom: Type 3 subjects.





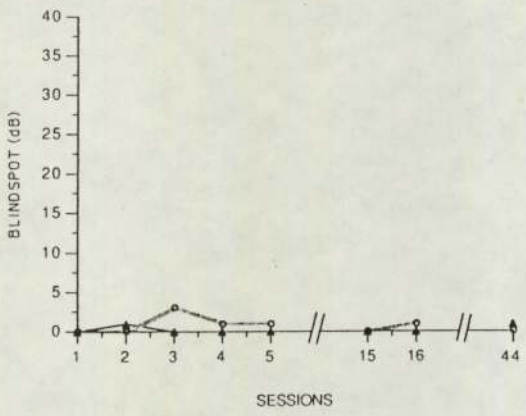
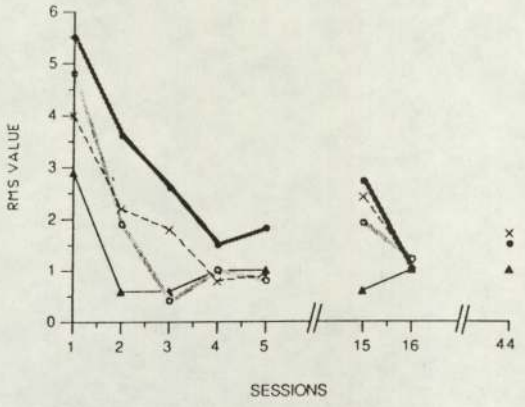
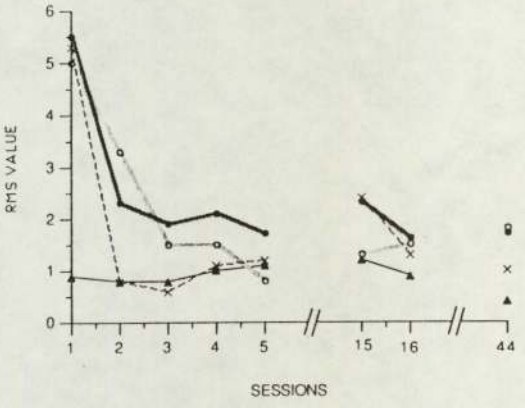


Fig. 6.
The variation in sensitivity (dB) of the blindspot at the 15° temporal stimulus point with serial examination (days). Top: Type 1 subjects. Middle: Type 2 subjects. Bottom: Type 3 subjects.





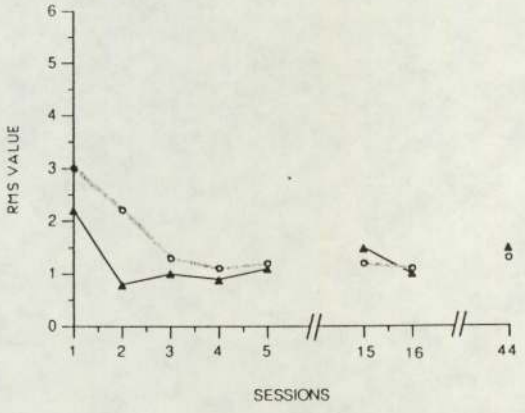


Fig. 7.
The variation in magnitude of the root mean square value with serial examination (days). Top: Type 1 subjects. Middle: Type 2 subjects. Bottom: Type 3 subjects.

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I.8 The role of intraocular light scatter in the attenuation of the perimetric response

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Abstract

The relationship between perimetric attenuation and intraocular light scatter was investigated in normal subjects using latex bead cells and in patients with unioc-ular media opacities. The Octopus and Dicon 3000 automated perimeters were used to measure perimetric sensitivity and the Nicolet CS2000 system employed to measure contrast sensitivity with and without glare light in order to calculate intraocular light scatter. A high correlation for both samples was found between intraocular light scatter and perimetric attenuation as measured by both instruments. Attenuation was greatest at the 10 asb bowl luminance for the Dicon, and was greater at fixation than at 27.5°. For the Octopus attenuation was lowest at fixation.

Introduction

Perimetric assessment of patients with media opacities is currently confounded by the problem of separating the reduction in sensitivity arising from optical degradation from that due to neural attenuation.

Several studies have qualitatively investigated the effect of cataract on the visual field profile. In manual kinetic perimetry cataracts have been shown to produce contraction of the isopters, pseudo-defects or exaggeration of existing field loss [4, 9, 15, 17, 19] while in manual static perimetry a general decrease in sensitivity is found with the central field being more depressed than the periphery [8, 9]. Clearly, it is necessary to derive a quantitative relationship between sensitivity determined by computer assisted perimetry and the degree of media opacity.

In recent years, contrast sensitivity has been shown to be a more representative measurement of visual function in the presence of cataract than Snellen acuity [11]. Furthermore, the foward intraocular light scatter arising from lenticular

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opacities which produces retinal image degradation has been investigated by Paulsson and Sjostrand [18] using contrast sensitivity in the presence and in the absence of glare light. Indeed, it has been recently reported that an increased glare score is related to an increase in the turbidity of the media while visual acuity correlates poorly with glare score [1].

The neuro-visual integrity of patients with cataract cannot be established with certainty. Several studies have therefore employed cataract simulations in order to investigate various psychophysical functions. These simulations include, for example, petroleum jelly spots distributed over the surface of a lens system [22] suspensions of particles 5 μm in diameter [11] varying concentrations of latex beads 10 μm in diameter [16] and ground glass [7]. In addition, a recent study has investigated the influence of 'simulated glare' produced by diffusing lenses on the differential threshold obtained with the Octopus and Humphrey perimeters [12].

We report an ongoing study the aim of which is threefold: to produce a source of intraocular light scatter; to devise a method whereby the relationship between intraocular light scatter and the perimetric attenuation of both projected stimuli and light emitting diode stimuli could be determined; and to further investigate this relationship utilizing a sample of patients with media disturbances.

Methods

The study has been divided into two sections. The sample for the first part comprised 12 clinically normal age matched subjects (mean age 24.1 years; SD 2.9 years) familiar with psychophysical techniques. Intraocular light scatter was simulated by suspending 0.01%, 0.02% and 0.025% solutions of latex beads in cells consisting of plano powered CR39 optical lenses. A bead diameter of 500 nm was selected since it has been demonstrated that the diameter of the protein aggregates producing intraocular light scatter is between 300–500 nm [2, 6] in human and calf cataractous lenses respectively. Different concentrations of beads were employed since it has also been demonstrated that interparticle separation is an important parameter in intraocular light scatter [2].

The second sample comprises patients displaying a marked asymmetry in the degree of cataract. Criteria for selection of the better eye is a distance acuity of better than or equal to 6/9 and minimal disturbance of the media. As far as can be ascertained the patients are free of other ocular or neurological pathology and of systemic disease with known serious ophthalmic complications; those in whom a fundal view cannot be obtained undergo flash E.R.G.s and V.E.R.s. Patients with marked nuclear cataracts are excluded.

Contrast sensitivity for both samples is measured using the apparatus devised by Griffiths, Barnes and Drasdo [10] which utilises the Nicolet CS 2000 contrast sensitivity system in the presence and absence of narrow angle (3.5°) and wide angle (30°) glare light (Fig. 1). A sine wave grating is used with a spatial frequency

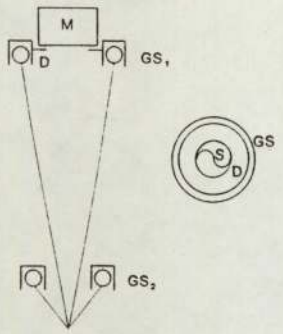

Figure 1. Diagrammatic representation of the apparatus used to derive the light scattering factor in the two experimental samples. GS_1 and GS_2 denote the narrow and wide angle glare sources respectively. M is the monitor. D is the diffusing screen and S is the sine wave grating.

of 1 c/deg, counter phased at a rate of 2 Hz, as this frequency is not considered to be attenuated by optical blur [5]. The viewing distance is 3 m and the screen luminance 94 cdm^{-2}. Differential light sensitivity for both samples is measured with the Dicon AP3000 (target projected diameter 0.28°; peak wavelength 580 nm) at bowl luminances of 10 asb and 45 asb and with the Octopus 201 automated perimeter. The meridional threshold and macula threshold programs of the Dicon are used along the 85° and 265° meridians at eccentricities of 0°, 1°, 3°, 5°, 7.5°, 20°, 27.5° with a stimulus presentation time of 400 ms and interstimulus duration of 1s. Octopus program 31 is used in conjunction with stimulus size 3 (projected diameter 0.431°) the standard bowl luminance of 4 asb and the stimulus presentation time of 100 ms.

Using these procedures, contrast sensitivity and the visual fields were measured in the right eye of the first sample with and without the simulated light scatter. The examinations for the second sample are undertaken on each eye of the patient. The contrast sensitivity and the Dicon examinations are determined at one session; the sequence of examination within this session is randomized. The Octopus examination is conducted at another session on a separate occasion. The order of the two sessions, the experimental condition in the case of the first sample and the order of eye examined in the case of the second sample are all randomized. Patients with no experience of automated perimetry and/or contrast sensitivity receive suitable training. Distance correction is used with the appropriate near correction for the particular viewing distance. Natural pupils are used throughout since the procedure is intended for clinical application; the changes in pupil size, however, compensate to some extent for the changes in illumination associated with the glare light.

The intraocular light scatter with and without the various concentrations of latex beads was calculated from the equation of Paulsson and Sjostrand [18]:

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$$\mu = L/E\ (M_2/M_1 - 1)$$

where L = the screen luminance, E = the illuminance of the glare source and M_2 and M_1 are the contrast thresholds with and without glare light respectively. In the first sample results for a given subject are presented in terms of the differences in scatter factor and in perimetric sensitivity between the eye in the normal state and in the particular experimental condition. In the second sample, a similar calculation is carried out for both eyes of a given patient and the results are presented in terms of the differences between the two eyes.

Results and discussion

The attenuation in perimetric sensitivity for the Octopus, expressed as a volumetric index derived by the Monte Carlo technique [21] due to the increasing intraocular light scatter arising from the latex bead simulations shows a linear relationship for both the narrow and wide angle glare sources (Fig. 2). The degree of scatter is less for the wide angle light source than for the narrow angle due to the line spread function of the eye.

The depression in Octopus sensitivity expressed as the mean of the 4 measure-

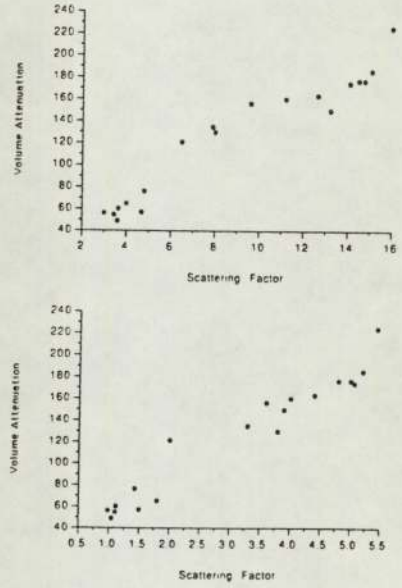

Figure 2. Scattergram illustrating the increase in volumetric attenuation (dB_r radian^2) for Octopus Program 31 with increase in the narrow (top) and the wide angle angle (bottom) scattering factor for the normal subjects in combination with the varying concentrations of latex beads.

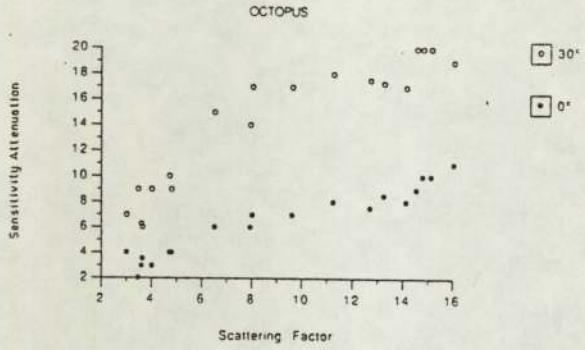

Figure 3. Scattergram illustrating attenuation of sensitivity (dB) for Octopus program 31 against narrow angle scattering factor as a function of eccentricity for the normal subjects in combination with the varying concentrations of latex beads.

ments at a given eccentricity, as a function of peripheral angle, shows a greater attenuation with increasing intraocular light scatter for the peripheral eccentricities than for fixation (Fig. 3). This arises because the foveal region is saturated and therefore relatively insensitive to small changes in light intensity, for the larger targets such as Goldmann 3 at the low photopic bowl luminance of 4 asb [20]. This has the effect of steepening the normal sensitivity gradient within the central field (Fig. 4) and has also been reported to occur with age [13]. The depression in sensitivity, expressed as the mean of 2 measurements at each eccentricity, with increasing intraocular light scatter for the Dicon also demonstrates a linear relationship for both glare sources. The attenuation is greater at the lower bowl luminance of 10 asb than at 45 asb bowl luminance and is due to the greater increase in Weber's Fraction at lower luminances (Fig. 5). This is in accord with Greve [8] and is compatible with the conclusions of a recent study [14]. In contrast to the results from the Octopus, the attenuation for the Dicon is greater centrally than peripherally at both bowl luminances (Fig. 6) and arises for

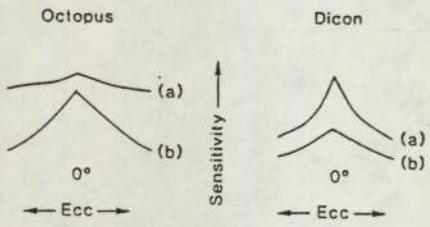

Figure 4. Schematic representation of the influence of intraocular light scatter on the flat sensitivity profile of Octopus program 31 for target size 3 (left) and on the relatively steep profile of the Dicon at 10 asb bowl luminance (right).

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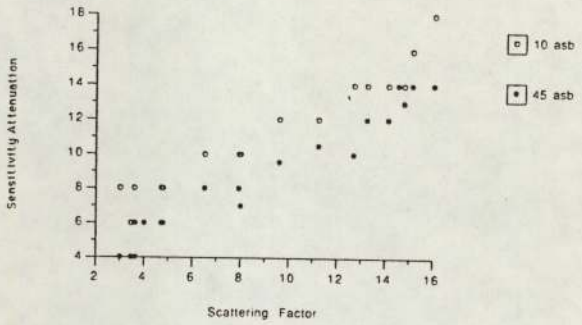

Figure 5. Scattergram illustration attenuation of sensitivity (dB) at fixation for the Dicon against narrow angle light scattering factor as a function of background luminance for the normal subjects in combination with the varying concentrations of latex beads.

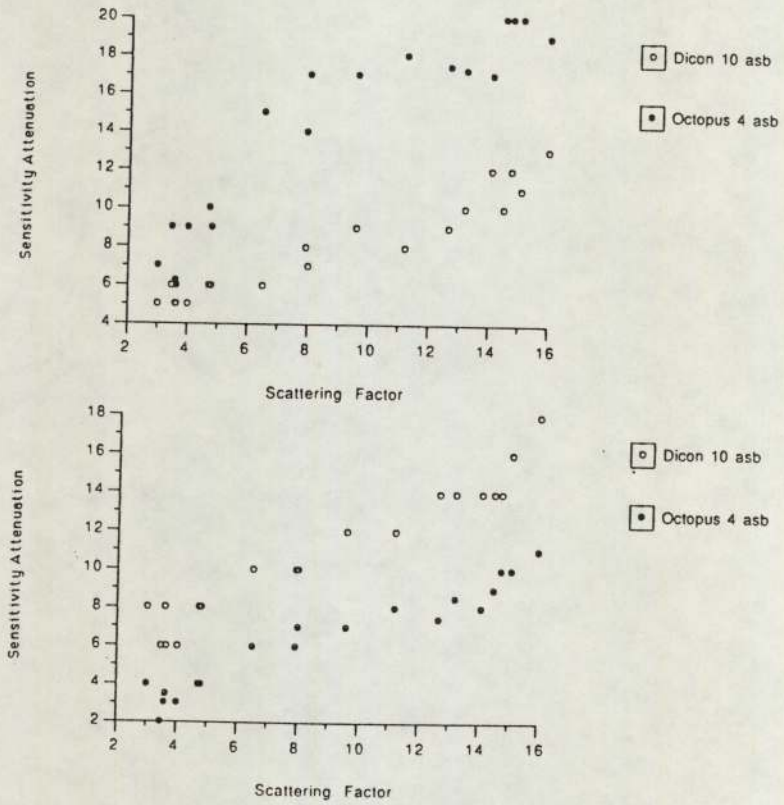

Figure 6. Scattergram illustrating attenuation of sensitivity for the Dicon (10 asb) and Octopus as a function of eccentricity (top) 27.5° (Dicon) and 30° (Octopus) and fixation (bottom).

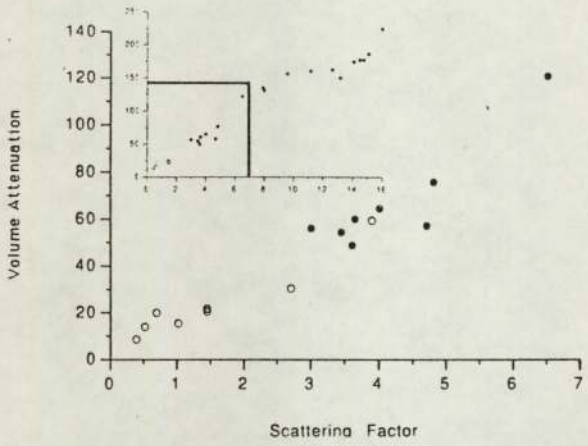

Figure 7. Scattergram illustrating increase in volumetric attenuation (dB · rad²) against light scattering factor for cataractous patients with low scattering factors (open circles) and for the normal subjects in combination with the varying concentrations of latex beads (filled circles). The inset shows the relationship of the cataractous data to the corresponding scattergram shown in Fig. 2.

the small LED target configeration because of the relative sensitivity of the central areas to small changes in light intensity (Fig. 4). This has the effect of flattening the Dicon sensitivity gradient and is in agreement with the classical belief that cataract reduces central sensitivity more than peripheral sensitivity thus resulting in a flattening of the sensitivity gradient. The use of visual field data in this manner, however, is always subject to the short and the long term

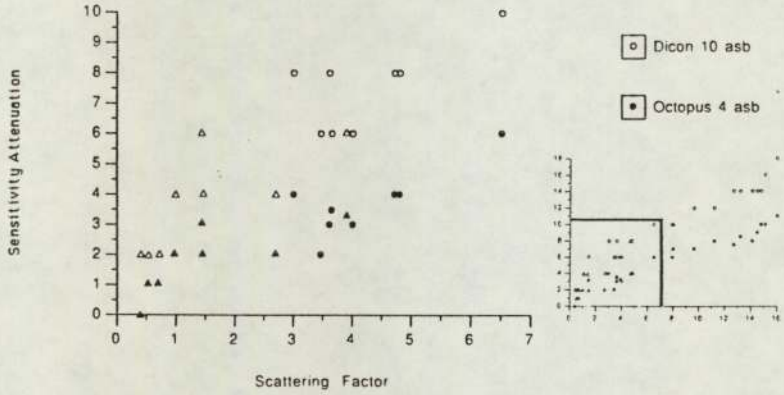

Figure 8. Scattergram illustrating the attenuation of sensitivity at fixation for the cataractous patients with low light scattering factors (open triangles Dicon (10 asb); closed triangles Octopus). The inset shows the relationship of the data to the corresponding scattergram in Fig. 6.

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fluctuations inherent in this type of threshold psychophysical investigation.

The results for the unilateral cataractous patients with low scattering factors (Figs 7 and 8) follow the general relationship between intraocular light scatter and perimetric attenuation described in the first part of the study. The effects of intermediate scattering factors are currently under investigation. Patients with hand movements or less were unable to resolve the grating at the maximum contrast or appreciate the visual field targets. The use of the contralateral eye as a control to determine the perimetric attenuation of the cataractous eye depends upon the assumption that the visual fields of the two eyes are symmetrical. This would seem to be valid since it has been reported for the Humphrey Field Analyser that asymmetry exceeding 6 dB between the two eyes of a given patient at corresponding locations will occur at less than 1% of the test locations [3].

Conclusions

A high correlation is found between perimetric attenuation and the intraocular light scattering function in both normal subjects with the simulated intraocular light scatter and in patients with uniocular media opacities exhibiting low scattering factors. It is proposed that the degree of perimetric attenuation of a patient with media opacities can be predicted from a measure of the light scattering function. Further work will, however, be necessary to investigate the format of such a relationship in subjects with field loss.

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III.5 The quantification of the visual field in computer-assisted threshold perimetry

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Abstract

Computer simulations were carried out to investigate the suitability of the Monte Carlo technique as a means for deriving the integral of sensitivity as measured over the three-dimensional surface area and thus providing a quantitative expression of the visual field. The simulations were based upon the standard normal data of Octopus programs 21 and 31 and upon age matched data for the central 30° threshold program of the Dicon AP3000. In addition, the sensitivity values at each eccentricity derived by the Octopus were also weighted for the product of retinal ganglion cell receptive field density and spatial summation and a further integration carried out. The indices for various types of field loss are illustrated.

Introduction

A single index to express the extent and depth of the visual field has been sought for many years. The demand for such an index arises in particular from the need to enhance diagnostic capability, to simplify analysis of serial visual field examinations and to describe the functional visual field in disability assessment.

Previous studies have generally derived a quantitative expression by applying various arbitrary transformations of the data which in some cases have also emphasized the different regions of the field. Some authors have adopted this approach merely for statistical handling of the data [2, 8, 14] whilst others have utilized the process to formulate a measure of the field based upon functional performance [18, 1, 7]. The relative crudity of many of these previous attempts stems largely from the complexity of the necessary mathematical computations and from the lack of electronic data processing techniques. Indeed, the representation of kinetic information has been particularly retarded by these limitations although more recently techniques to handle this type of data have been reported [11, 15]. In addition, the various functional assessments have adopted criteria

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which have been based in general upon empirical clinical judgement rather than the underlying visual anatomy and physiology. Nevertheless, an assessment of the field based upon neural representation has been proposed [6]. Furthermore, the use of a volume calculation for the three-dimensional representation of kinetic sensitivity has been reported [19] and a similar analysis weighted for retinal ganglion cell receptive field density has been described [12].

The aim of the present study was threefold: to investigate the suitability of a procedure by which the volume of the three-dimensional representation of sensitivity could be determined: to develop and apply a weighting factor for each examined eccentricity based upon the underlying visual physiology and to derive indices for varying types of field loss.

Method

Sensitivity plots were utilised from two computer assisted perimeters the Octopus 201 and the Dicon AP3000. These perimeters were chosen as they provide widely different approaches to visual field investigation e.g. the type and size of the target: and the thresholding strategy.

Computer simulations and analysis using a VAX series 11/750 computer were undertaken on the normative data corresponding to the under 25 age group catagory of Octopus programs 21 and 31 (target size 3) and on normal age matched values obtained for the Dicon 70 point threshold central 30° field (10 asb background luminance: presentation time 400 msec: inter stimulus duration 1 sec).

The Monte Carlo technique was applied to derive an integration of the sensitivity measure over the three dimensional surface area. This technique is discussed in detail [17] and estimates the integral by a statistical sampling process which has proved very useful in areas such as the evaluation of multiple integrals which do not lend themselves to classical mathematical methods. It has, for example, been recently applied to problems in visibility [3].

Two Monte Carlo methods were utilised, the expected value method and the hit and miss method, to evaluate the integral V where

$$V = r^2 \int_A F(\varnothing, \Omega)\, d\varnothing\, d\Omega$$

over the irregular surface area A on the perimeter bowl, for the bowl radius r and the polar angles $\varnothing$ and Ω defining the respective stimulus points.

The volume V_1 corresponding to the weighted data was determined similarly where

$$V_1 = r^2 \int_A F(\varnothing, \Omega)\, W(\varnothing, \Omega)\, d\varnothing\, d\Omega$$

and $W(\varnothing, \Omega)$ is the appropriate weighting function.

Because of the irregular shape of the surface area of the field on the bowl a pseudo area A_1, which was regular, was defined and points were selected at random within the pseudo area. The required random distribution of points was obtained by defining $F(\varnothing, \Omega)$ as zero within the region R, where $A_1 = A + R$. In the case of the Octopus programs the technique assumed orthogonal axes for the integration as opposed to the actual curvilinear lines. Since the integral is used or comparative purposes, the error arising from this assumption can be discounted. One hundred thousand replications were used for each integral. This sample size was selected to provide an optimum compromise between minimum error and the length of the pseudo random number cycle generated by the computer.

The point at 15° eccentricity temporally corresponding to the blind spot was assigned a value of zero in the integration of the sensitivity data derived by program 21. In the case of program 31, however, the measured values of the 12° and 18° points temporally lying within the blind spot region were included in the calculation. The index for the Dicon, however, was derived without reference to the blind spot region as the Dicon system does not permit thresholding of the points in this area.

The Octopus sensitivity values at each eccentricity were weighted for the physiological coverage factor defined as the product of retinal ganglion cell receptive field density and ganglion cell receptive field size. Ths was selected as it is thought to represent the number of ganglion cells which sample a given point on the retina and may be a more appropriate index of cortical representation than ganglion cell receptive field density alone [16]. An estimate of receptive field density was obtained using the equations of Drasdo [5] which are corrected for the effects of optical magnification with increasing eccentricity. The receptive field size was estimated from spatial summation data which is considered to be an index of receptive field size [9, 20]. The summation values at each eccentricity for programs 21 and 31 of the Octopus were calculated using Gougnard's equation [10] from the sensitivity data obtained for an age-matched sample of 10 emmetropic obsevers using the six standard Goldmann stimuli [21].

Results and discussion

The volume of the unweighted normal sensitivity values of the under 25 age group for the full-field Octopus program 21 and for the central 30° program 31 are shown in Fig. 1 together with the corresponding values for the Dicon 70 point central 30° program. The units of these integrals are linearly related to the true units which are $dB.Rads^2$. The Monte Carlo technique is based upon the principals of random sampling and the evaluation of each integral therefore has an associated precision error. It can usually be assumed that the exact value of the integral will lie within plus or minus three standard deviations of the estimate. The index is not comparable mathematically between instruments possessing different bowl radii and, in

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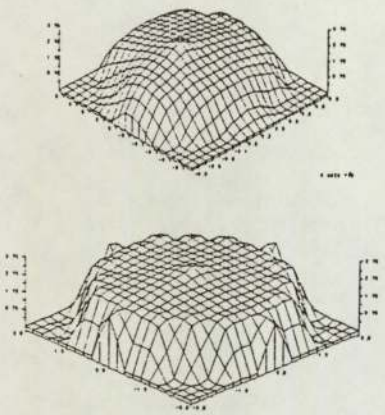

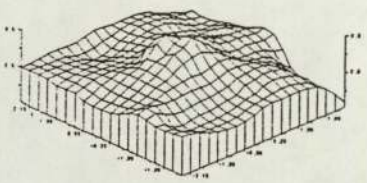

	EXPECTED VALUE METHOD	HIT AND MISS METHOD
Octopus program 21		
unweighted	1248.1 ± 3.23	1236.28 ± 5.4
weighted	106171.0 ± 1930.01	-
Octopus program 31		
unweighted	278.79 ± 0.76	279.04 ± 1.02
weighted	83796.5 ± 674.22	-
Dicon (10asb) central 30°		
unweighted	446.48 ± 0.19	447.07 ± 0.93

Figure 1. The unweighted and weighted volumes for the right eye under 25 age group normal values of Octopus programs 21 and 31 and the age matched normal unweighted volume for the Dicon (10 asb) central 30° threshold program derived by the Expected Value and Hit and Miss Monte Carlo methods (table). The three dimensional representations of snsitivity are shown for comparison (x and y axes eccentricity [° × 10^{-1}]: z axis sensitivity [dBs × 10^{-1}]: program 21 (top left) program 31 (bottom left) and central 30° program (top right). It should be noted that the volumetric indices are not derived from these graphical representations. The blind spot has been omitted from the program 21 plot to avoid artificial enlargement arising from the computer interpolation.

addition, is not comparable clinically between instruments with different stimulus and dynamic ranges.

The normalised volumetric indices for programs 21 and 31 respectively for five different forms of simulated field loss as a function of perimetric attenuation are shown in Figs 2 and 3. The volumes corresponding to the simulated fields with the Dicon are shown in Fig. 4. The effect on the volume of reduction in sensitivity at a single point is insignificant and is independent of eccentricity; an attenuation of 35 dB at fixation with the Octopus, for example, accounts for approximately 2% of the unweighted volume. The technique could, however, be applied on a more local basis with an increased resolution to provide a measure of the reduced sensitivity less identifiable on the global integral. Similarly, the influence of the short term fluctuation inherent in the visual field examination has little effect on the magnitude of the index. The volumetric indices for programs 21 and 31 normalised with respect to the corresponding age-matched values for six patients exhibiting various types of field loss are illustrated in Fig. 5.

The effect of the weighting function (Figs 1, 2, 3 and 5) is to enhance the contribution arising from the central field and reduce that from the peripheral

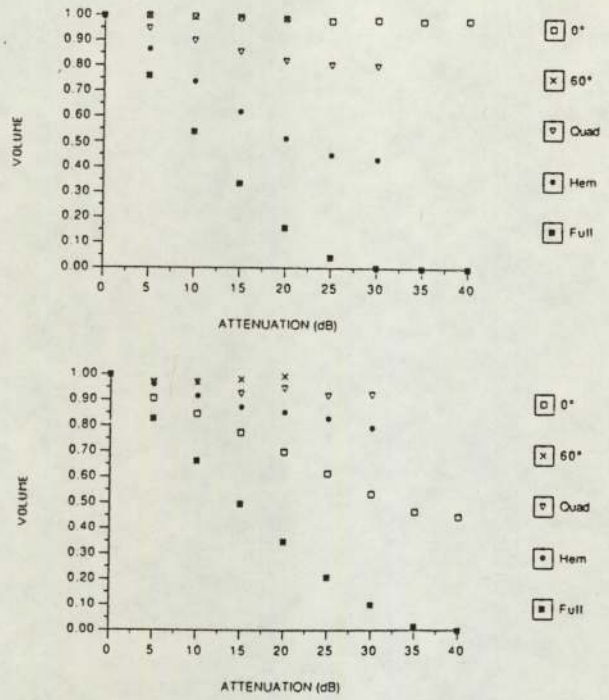

Figure 2. Normalised unweighted (top) and weighted (bottom) volumes against attenuation for Octopus program 21 for various types of simulated field loss. The quadrantic defect is arbitrarily defined as an upper temporal loss bounded by, but not including, points on the horizontal and vertical midlines. The temporal hemianopia is defined similarly whilst the full field indicates attenuation at all points.

field and is in accord with those advocating a parabolic projection of the visual field chart [2, 4]. The units corresponding to the weighted integral are directly related to the true units which are dB · radians^2 · receptive fields per solid degree · coefficient of spatial summation. The error term of the weighted integral is larger than that for the unweighted volume and arises from the inclusion of the extra dimension in the calculation. Intuitive clinical assessment of functional performance would suggest that the weighting underestimates the importance of peripheral vision. The spatial summation values in the weighting function currently represents the best correlate of receptive field size available in human while the cell counts are also the most accurate available. In addition, the weighting function does not allow, by any further weighting, for the increased diagnostic significance of clusters of adjacent points of reduced sensitivity [13]. The derived index could however, be further transformed to reflect the relative topographical functional importance of the visual field while, clearly, the Monte Carlo technique could accommodate any more suitable weighting function which may arise.

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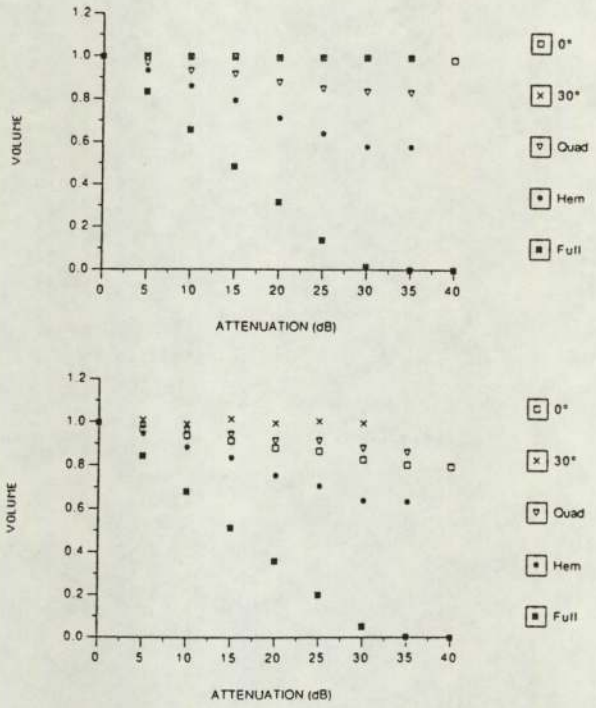

Figure 3. Normalised unweighted (top) and weighted (bottom) volumes against attenuation for Octopus program 31 for various types of simulated field loss. The criteria for field loss is that described for program 21 in Fig. 2.

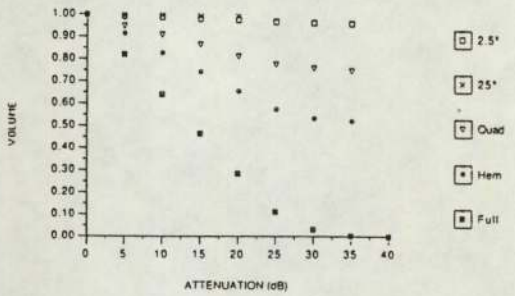

Figure 4. Normalised unweighted volume against attenuation for the Dicon (10 asb) 70 point central 30° threshold program for various types of simulated field loss. The criteria for field loss is that described in Fig. 2.

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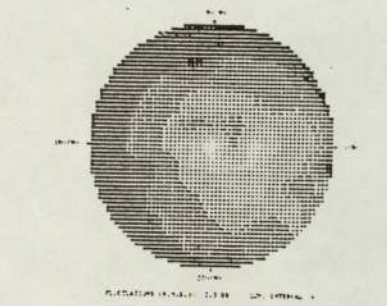
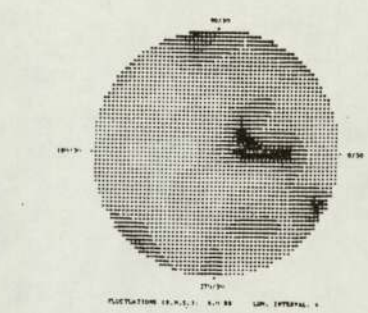
Figure 5. Unweighted and weighted volumes normalised with respect to the corresponding normal age matched values for six patient exhibiting various types of field loss with either Octopus program 21 (left) or program 31 (right).



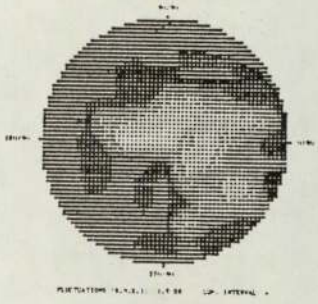
VOLUME 0.789

WEIGHTED VOLUME 0.878



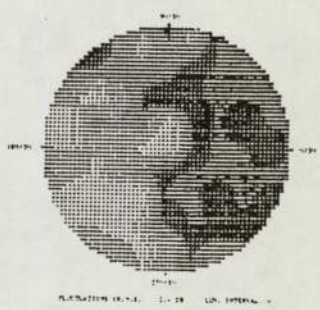
VOLUME 0.712

WEIGHTED VOLUME 0.622



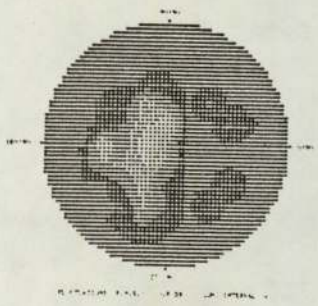
VOLUME 0.460

WEIGHTED VOLUME 0.765



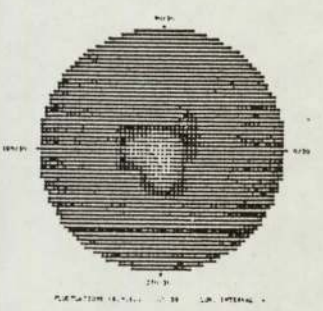
VOLUME 0.304

WEIGHTED VOLUME 0.330



VOLUME 0.193

WEIGHTED VOLUME 0.362



VOLUME 0.006

WEIGHTED VOLUME 0.138

Symb									
dB	51–36	35–31	30–26	25–21	20–16	15–11	10–6	5–1	0
asb	0.008–0.25	0.31–0.8	1–2.5	3.1–8	10–25	31–80	100–250	315–800	1000

1 asb = 0.318 cd/m²

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Conclusions

The Monte Carlo technique has been found to be theoretically suitable for the multi dimensional analysis of threshold static visual field data. Indeed, the technique would appear to be equally suitable for the analysis of any form of suprathreshold static data e.g., gradient adapted; two or three zone methods and for kinetic information and could be utilized to provide a measure of function based upon the binocular field. The method in this context requires the use of a mainframe computer in order to generate a sufficiently large random number cycle. Nevertheless, this could easily be facilitated by interfacing the computer assisted perimeter with the clinic or hospital mainframe.

Acknowledgements

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Some concepts on the use of three-dimensional isometric plots for the representation of differential sensitivity

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Key words: differential light sensitivity, octopus automated perimeter, three-dimensional isometric representation

Abstract. An increasing use is being made of three-dimensional isometric plotting to represent the topography of the visual field. The format of such plots, however, can be manipulated depending upon the parameters of the plotting routine. Problems associated with generating these plots such as resolution of the plotting grid, scaling of sensitivity and orientation of the plot are discussed with reference to both normal and abnormal fields derived by the Octopus 201 automated perimeter (stimulus size III). Recommendations for this type of perimetric representation are suggested.

Introduction

The development of computer assisted perimetry has enhanced the role of the visual field examination in the diagnostic procedure. The technique, in particular, provides the facility for rapid and reliable data collection whilst the additional computer capacity permits the analysis and representation of differential sensitivity in a wide variety of numerical and pictorial displays.

The technology of three-dimensional isometric plotting has been available via the software packages of both mainframe and microcomputers for a number of years. More recently the technique has been applied to illustrate the three-dimensional representation of differential sensitivity derived by both manual and computer-assisted perimetry (Flammer et al., 1981; Hart and Hartz, 1982; Hart and Burde, 1983; Accornero et al., 1984; Jaffe et al., 1986; Haas et al., 1986; Swann and Bloesch, 1986). These plots are analagous to the two dimensional gray scales of automated perimetry but possess the added advantage of an instantaneous visualization of the topography of the visual field particularly in the vertical dimension. Nevertheless, comparison of these plots from one publication to another reveals considerable differences in terms of such features as the degree of vertical scaling, the resolution of the plot and the techniques used to remove the hidden surfaces. Indeed, the format of the generated isometric plot depends upon the parameters available for generating the plot which can be altered within a software package and which can vary from one particular package to another. The purpose of this paper is to discuss some of the problems

arising in the generation of a visual field surface plot and to suggest certain standard forms of notation for representation of differential sensitivity.

Methods

The Ginosurf package, a typical surface plotting routine, written in Fortran and suitable for most mainframe and mini computers, was used in conjunction with a Vax 11/750 Series minicomputer to generate isometric plots of differential sensitivity in the normal and abnormal eye recorded with the Octopus 201 automated perimeter using stimulus size III. The procedure, however, is applicable to data from any program of any computer-assisted perimeter.

Plotting routine

In order to prepare the perimetric results for data storage by computer and in order to read the data into the plotting software, the perimetric stimulus locations are formulated in terms of an R rows × C column grid. In the case of the Octopus Program 21, for example, which has 76 test locations on a 15° square stimulus grid over the full field, this necessitates the inclusion of 34 supplementary points around the edges of the field in order to generate the complete 10 × 11 matrix. The non-tested points are designated an arbitrary sensitivity value beyond the measurement range of the perimeter in order to permit identification from the actual measured points. The data comprising the x and y eccentricities together with the corresponding sensitivity value is then read by the software in the form of an array. The data can be plotted at this stage as a 10 × 11 isometric plot or the resolution of the plot can be artificially increased by using a software routine which generates extra intermediate points based upon interpolated values derived from the original measured data. The apparent increase in resolution is achieved by specifying a finer plotting grid within the boundaries of the matrix for the original measured data. A supplementary value of sensitivity is derived at every intersecting point on the new grid by an interpolation process which calculates the sensitivity at each point from the nearest 24 measured points weighting the contribution of each for the linear distance from the particular interpolated position. In the extreme eccentricities the default value of 24 points is reduced by three quarters to 6 points due to the involvement of the corners of the data matrix. The number of points for the interpolation process can be infinite; the lower limit is governed by a loss of accuracy when using less than 6 points whilst 24 is the optimum number for accuracy and computational time. If a point on the finer grid coincides with a measured data point, the interpolation process is still operative but the extreme proximity of the two locations overrides the contribution of the surrounding points and the interpolated and measured values are identical.

Results and discussion

The appearance of the three-dimensional isometric surface plot can be altered by the resolution of the specified plotting grid (Fig. 1). A theoretically convenient separation is a doubling of the underlying data matrix e.g., a 19

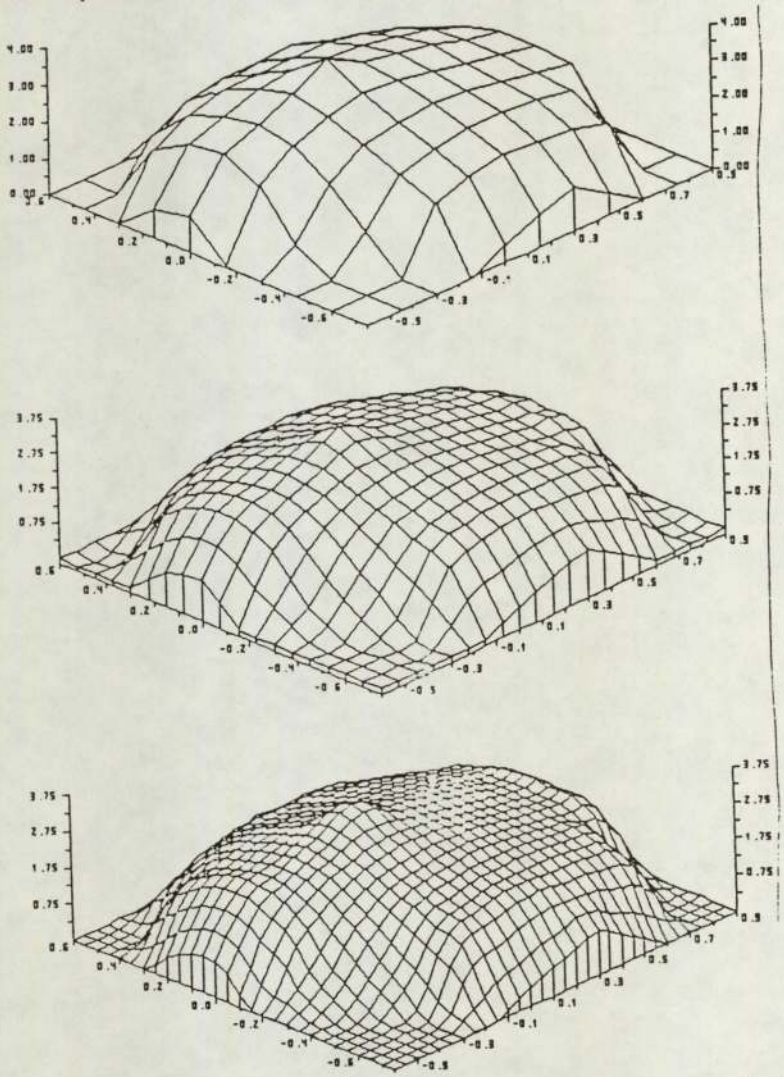

Fig. 1. The effect of differing resolutions of the specified plotting grid on the appearance of the full field Octopus Program 21 (15° interstimulus separation) illustrated for the right eye (stimulus size III) under 25 age group normative data (x and y axes eccentricity (°) × 10^{-2}; z axis sensitivity (dB) × 10^{-1}). The blind spot has been omitted. Top: 10 × 11 resolution. Middle: 19 × 21 resolution. Bottom: 28 × 31 resolution.

rows × 21 columns array in the case of the full field Program 21. This separation has the advantage of presenting a plotting grid in which every other point comprises a measured point. With increase in resolution, the plot assumes a better representation of a surface but excessive smoothing of the plot can occur when too fine a resolution is used. Interestingly, a 41 × 41 plotting grid has recently been adopted by Swann and Bloesch (1986) to illustrate the 275 data points within the central 15 °C measured with the Friedmann VFA II.

The appearance of the surface plots for those programs which do not examine the peripheral field out to the limits of visual resolution can also be radically altered by omitting the arbitrary sensitivity value used to complete the initial data array. In the case, for example, of the central field Program 31, which thresholds 73 points with a resolution of 6° out to an eccentricity of 30°, the inclusion of such values results in a grounding of sensitivity beyond the tested eccentricities with a steep cliff-like appearance enhancing the island of vision concept (Fig 2). At the same time, however, the sensitivity range of the measured points is collapsed over a narrow band. With omission of the arbitrary values, only measured points and their interpolated derivatives are used to generate the plot. This results in a smaller range of values over a larger vertical scale. The interpolation, however, produces a misrepresentation of sensitivity particularly towards the corners due to the absence of measured points in these regions. This latter difficulty can be overcome by excluding those measured points lying beyond the maximum square matrix compatible with the particular program e.g., a reduction of the central Program 31 to an 18° × 18° grid. By these means the interpolation process is then able to utilize those measured values beyond 18° in the corner regions of the reduced plot.

The representation of the blind spot, and indeed any localised reduction in sensivity, in terms of both depth and area, is influenced by the interpolation procedure since an intepolated point lies midway between the most proximal measured point and the measured point situated within the blind spot or scotoma. The interpolated point consequently has a lower sensitivity than it would normally have due to the proximity of the measured point emanating from the scotoma and exhibiting, by definition, a reduced sensitivity. This has the effect of artificially increasing the area and depth of the field loss. The blind spot, for example, influences an area of up to 30° by 30° with Octopus Program 21 and a potential area approaching 18° by 18° with Program 31 (Fig. 3). This particular problem is also present in the gray scale method of representation, which also uses interpolation procedures, and further emphasises the need to consider the original numerical data in addition to such computer-aided presentations.

The scaling of both the horizontal, and more particularly the vertical axes, can be expanded to any limits in terms of both the height of the sensitivity axis and the range over which sensitivity is plotted in order to emphasise or minimise any feature (Fig. 4). Most software packages permit the inclusion of axes with specified labelling of eccentricity and sensitivity together with other details of the test such as the patient name, perimetric program etc. The generated plot can

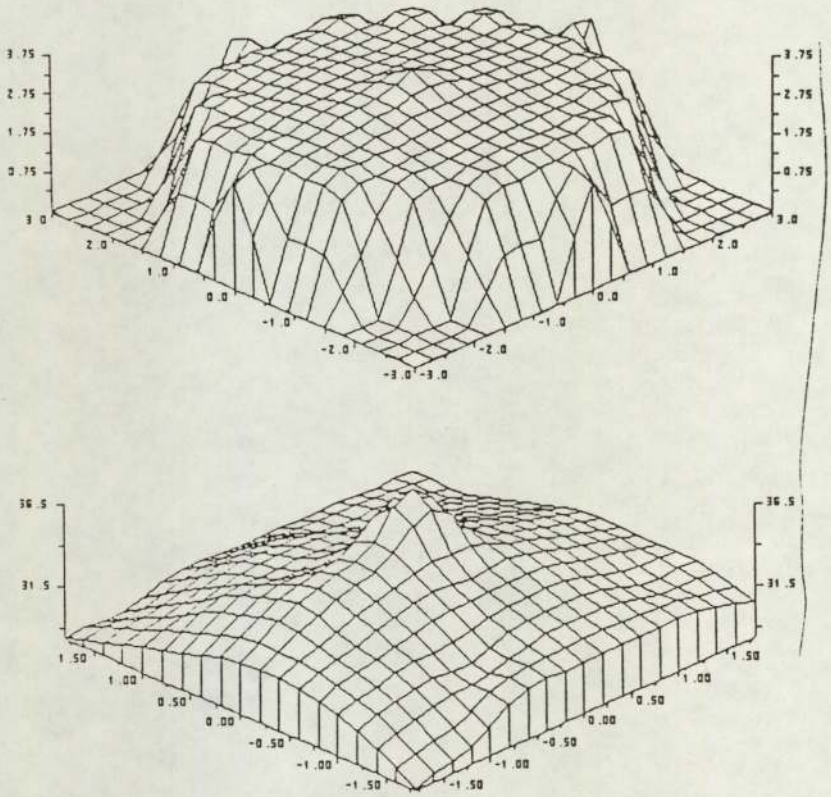

Fig. 2. Top: the effect of grounding sensitivity beyond the tested eccentricities for the central 30° field Octopus Program 31 (6° interstimulus resolution) illustrated for the right eye (stimulus size III) under 25 age group normative data, resulting in a steep cliff-like appearance enhancing the island of vision concept (x and y axes eccentricity (°) × 10^{-1}; z axis sensitivity (dB) × 10^{-1}). The blind spot has been omitted. Bottom: the same data illustrated for the central 18° × 18° of Program 31 (x and y axes eccentricity (°) × 10^{-1}; z axis sensitivity (dB)). The blind spot has been omitted.

be printed out in any orientation, but is usually represented with both negative quadrants facing the viewer i.e. the intersection of the inferior and nasal quadrants for the right eye and the intersection of the inferior and temporal quadrants of the left eye in accordance with traditional clinical practice although the cartesian coordinates are identical. The orientation of the plot can be rotated about the vertical axis in four increments (Fig. 5) and this procedure may be necessary to illustrate "hidden" areas of field loss. Nevertheless, it may lead to further problems in interpretation unless the respective meridians are specified. The plot can also be represented as a perimetric cut through any eccentricity along the horizontal or vertical meridians by appropriate specification of the dimensions of plotting grid (Fig. 6) and can be further localised to any particular region within the field.

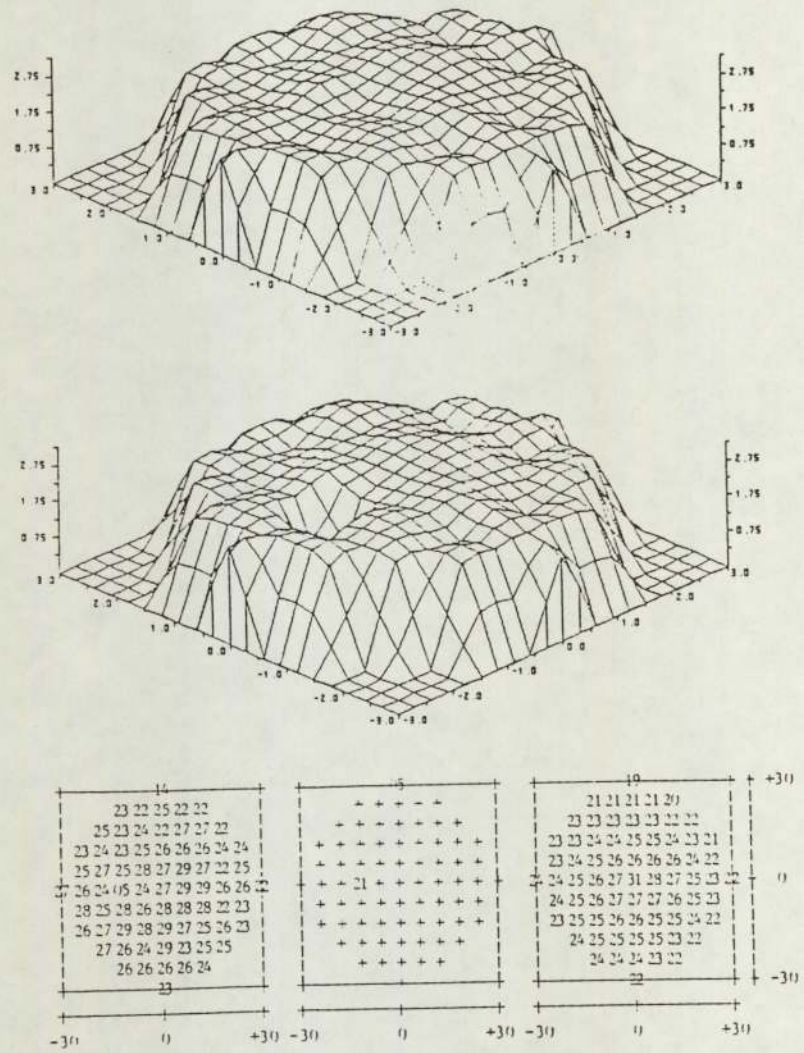

Fig. 3. Top: the central 30° field Octopus Program 31 (stimulus size III) illustrated for the left eye of a normal 66 year old (x and y axes eccentricity (°) × 10^{-1}; z axis sensitivity (dB) × 10^{-1}). The blind spot has been omitted. Middle: The same data with the blind spot included (x and y axes eccentricity (°) × 10^{-1}; z axis sensitivity (dB) × 10^{-1}). The blind spot influences a potential area approaching 18° × 18°. Bottom: the corresponding comparison printouts (dB) left: recorded data; right: age matched normative data; middle: difference.

The surface of the plot can be represented by parallel lines or by crossed lines. Both representations would seem to be equally suitable; the use of parallel lines in conjunction with a low resolution tends to underrepresent the topography

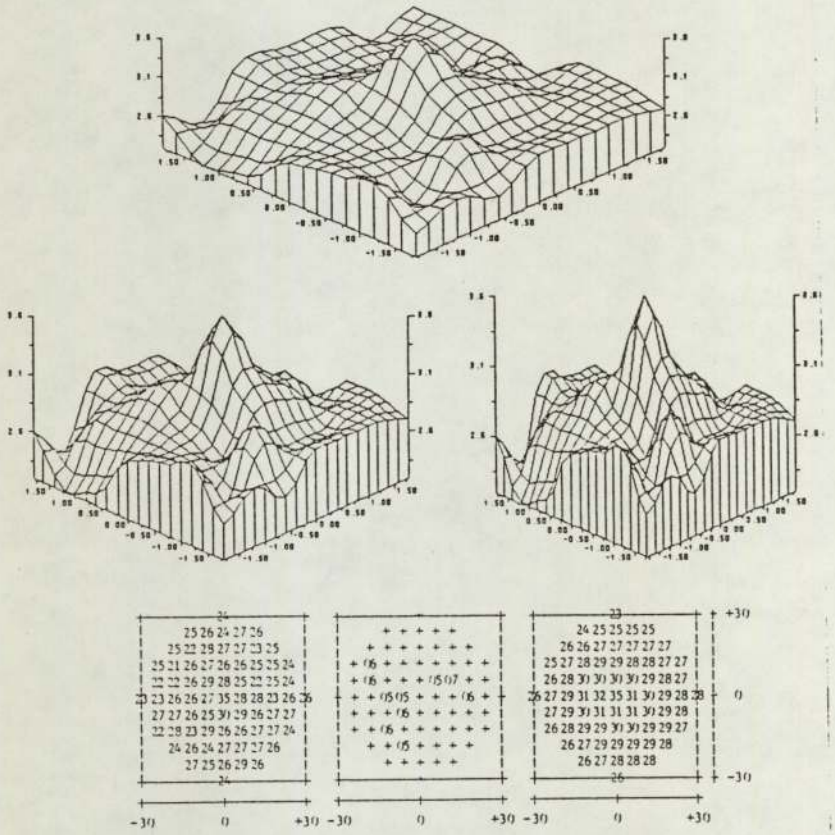

Fig. 4. The effect of manipulating the scale of the sensitivity axis to either minimise or maximise respectively the extent of field loss, illustrated for the central 18° × 18° field of the left eye of a 25 year old with ocular hypertension using Octopus Program 31 (stimulus size III) (x and y axes eccentricity (°) × 10^{-1}; z axis sensitivity (dB) × 10^{-1}). The blind spot has been omitted. Top: vertical scaling 5 dBs per cm. Middle left: vertical scaling 3.3 dBs per cm. Middle right: vertical scaling 2.7 dBs per cm. Bottom: the corresponding comparison printouts (dB) left: recorded data; right: age matched normative data; middle: difference.

whilst the crossed lines require greater computational effort. Some packages also include the provision for use of colour and this facility can be used to further represent such features, as for example the variation of the short term fluctuations with eccentricity or the attenuation of sensitivity from one examination to another, with the advantage of an instantaneous visualisation of the particular feature at all points on the surface (Lombrou et al., In Press). The use of colour, however, can sometimes obscure the intended appearance of surface texture.

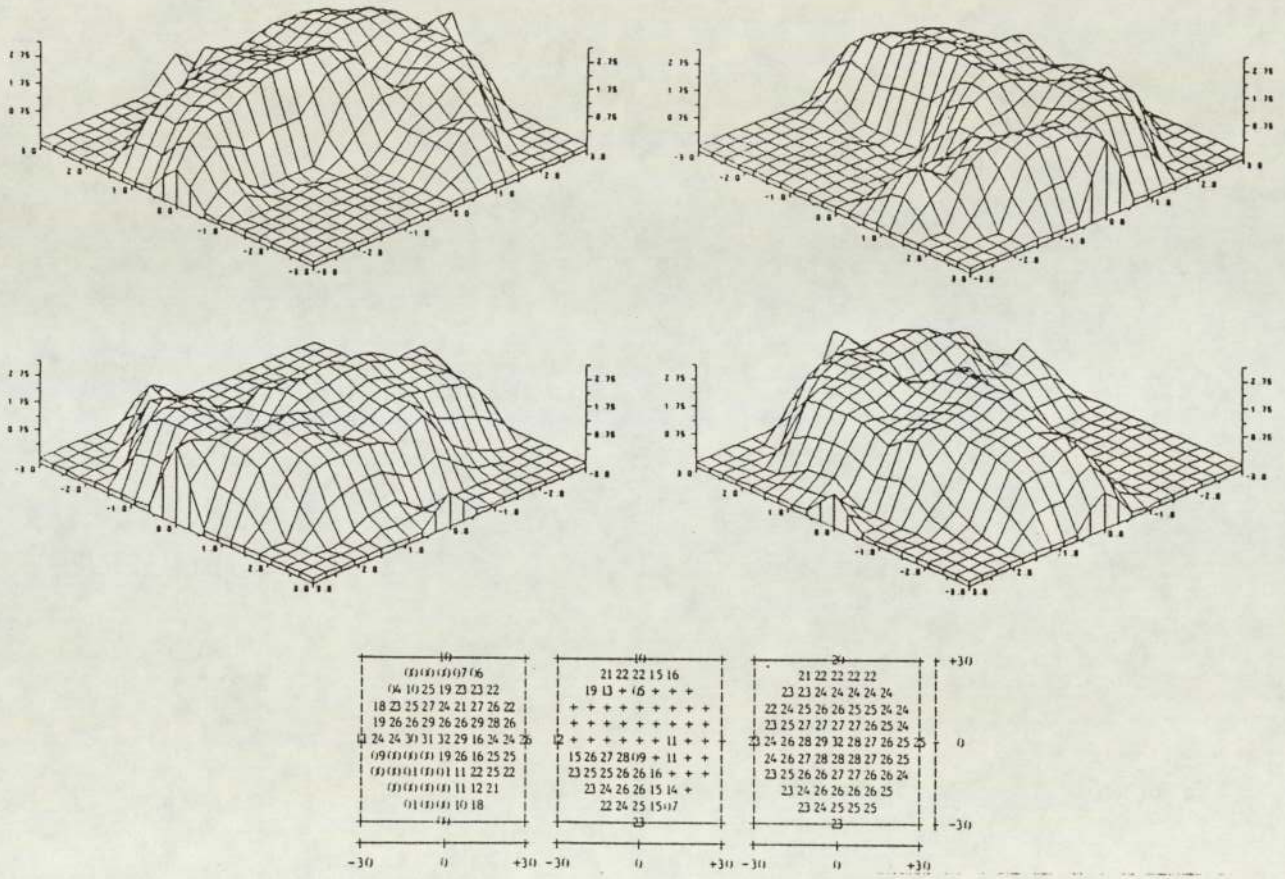

Fig. 5. Top and Middle: the effect of rotating the field in four increments about the vertical axis illustrated for the right eye of a 61 year old patient with an inferior nasal field loss arising from a suspected ischaemic optic neuropathy using Program 31 (stimulus size III) (x and y axes eccentricity (°) × 10^{-1}; z axis sensitivity (dB) × 10^{-1}). The blind spot has been omitted. Bottom: the corresponding comparison printouts (dB) left: recorded data; right: age matched normative data; middle: difference.

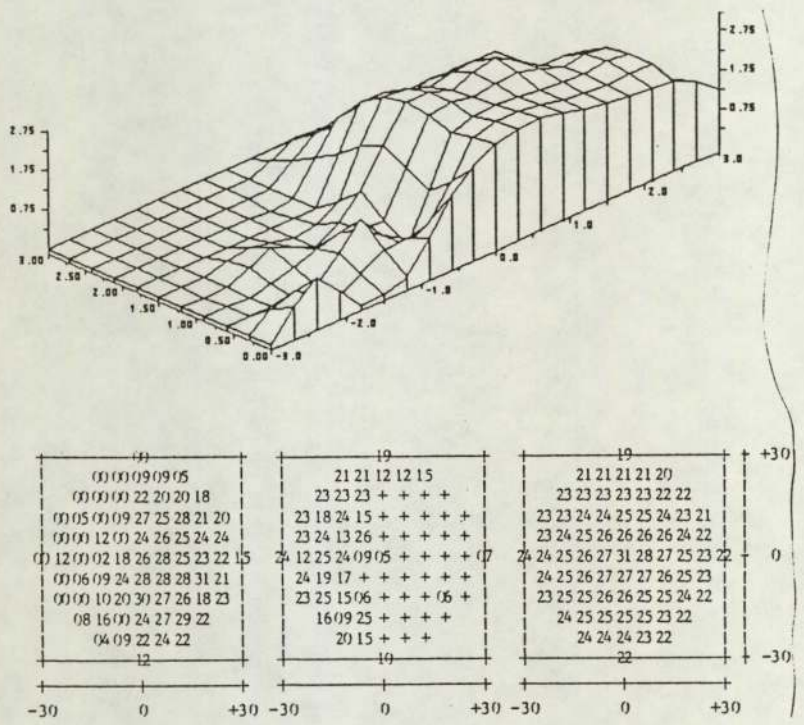

Fig. 6. Top: Representation of sensitivity in terms of a perimetric cut, illustrated for the left eye of a 67 year old patient with a bitemporal hemianopia secondary to acromegaly using Program 31 (stimulus size III) (x and y axes eccentricity (°) × 10^{-1}; z axis sensitivity (dB) × 10^{-1}). The blind spot has been omitted. Bottom: the corresponding comparison printouts (dB) left: recorded data; right: age matched normative data; middle: difference.

Suggestions for standardisation

In order to standardise the three-dimensional representation of differential sensitivity, it is suggested that the vertical scale of the plot should include the zero sensitivity level and ideally be referenced with respect to a value approaching the maximum normal sensitivity for the particular stimulus combination of the perimeter. This maximum value will often vary between instruments, as indeed does the maximum stimulus luminance with which the dB value is referenced and thus the corresponding gray scale notations, but the scale used to represent sensitivity i.e. dBs per unit length should be identical: a suitable scale commensurate with practical requirements is in the region of 15 dBs per cm. Similarly, the scale for representation of the horizontal over the central field should be approximately 10° per 1.25 cm. The ideal resolution would seem to be double that of the data matrix and the plots should represent the entire field

recorded with the particular program of the perimeter and be described with the axes in place indicating sensitivity, eccentricity and meridian respectively. In accord with Fankhauser and Bebie (1979) caution must be exercise when interpreting plots based upon data derived from programs which utilize an interstimulus grid of greater than 6°.

Conclusions

The use of three-dimensional plotting to represent differential sensitivity gives an instantaneous impression of the visual field profile. The format of the plots can be manipulated as a function of the parameters of the plotting routine. It must be emphasised, however, that the technique does not provide the clinician with any additional raw data and does not overcome the inescapable need to refer to the original numeric values of sensitivity, and their accompanying fluctuations, in the diagnostic procedure.

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Spatial Summation and the Cortical Magnification of Perimetric Profiles

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Key Words. Computer-assisted perimetry·Humphrey field analyzer·Visual field·Spatial summation·Cortical magnification

Abstract. M scaling of the conventional spot targets of clinical perimetry at low photopic adaptation levels, such as that of the Octopus automated perimeter, does not result in the expected isosensitive profile using the current equations for humans. This disparity has been attributed to variations in the ganglion cell characteristics across the retina, most notably that of spatial summation. The hypothesis was further investigated by M scaling the perimetric sensitivity recorded under conditions favouring reduced spatial summation, namely an increased adaptation level and a longer stimulus duration afforded by the Humphrey field analyzer. The M-scaled data exhibited a paracentral reduction in sensitivity relative to the theoretical isosensitive profile and an increased sensitivity beyond an eccentricity of 12°. This indicates that for perimetric spot stimuli, the current human M-scaling equations under represent the fovea at the visual cortex. The implications for the design of perimetric routines are discussed.

Introduction

A topographical representation of the visual field is maintained throughout many stages of processing in the mammalian visual pathway. Generally, these topographic representations do not have a uniform emphasis on all parts of the field, but demonstrate a marked amplification of the central region compared with the periphery. In primate, the amplification of the visual field at the striate cortex has been defined by the cortical magnification factor, M, which describes the extent of the striate cortex, in millimetres, corresponding to 1° of arc in visual space. M is believed to be proportional to the square root of ganglion cell receptive field density. Various estimates of M for the fovea have been proposed in human, namely 7.99 mm/degree [Rovamo and Virsu, 1979], 11.5 [Drasdo,

[1] We are grateful to Humphrey Instruments for the loan of the Humphrey field analyzer.

1977] and 15.1 mm/degree [Cowey and Rolls, 1974]. These values are based on the assumptions of a single magnification from retina to cortex and of a one-to-one cone-ganglion cell ratio at the fovea. It has been suggested, however, that the amplification of the central regions of the visual field at the cortex in monkey arises from further magnification provided by subcortical structures [Cynader and Berman, 1972; Malpeli and Baker, 1975; Myerson et al., 1977; Perry and Cowey, 1985] in addition to the increased central retinal ganglion cell density. These findings, however, have not yet been substantiated in human.

The quantification of M in human has made it feasible to investigate how various stimulus parameters should be scaled in order to obtain equal sensitivity across the visual field. It has been proposed that if stimuli are magnified at peripheral visual field locations, in inverse proportion to M, then sensitivity would become independent of eccentricity [Rovamo and Virsu, 1979]. This process has been termed M scaling. The process of M scaling has been sucessfully applied to a number of psychophysical functions, although the scaling factors employed to produce the iso-sensitivity have varied. Findcontrast sensitivity [Virsu and Rovamo, 1979] motion displacement thresholds [Wright and Johnston, 1983] lower thresholds for motion [Johnston and Wright, 1983], and luminance-modulated chromatic gratings [Rovamo, 1983], for example, have been successfully scaled using the equations of Rovamo and Virsu [1979]. Other visual functions have been scaled using either the equations of Drasdo [1977], e.g., colour contrast gratings [Noorlander et al., 1983], or those of Cowey and Rolls [1974], e.g., the fine-grain movement illusion [Foster et al., 1981]. Some functions, however, do not become independent of retinal location when the spatial stimulus parameters are M scaled using the conventional values of human M. These functions include hyperacuity [Westheimer, 1982, 1983], stereoacuity [Fendick and Westheimer, 1983], visual orientation discrimination [Spinelli et al., 1984] and fusional vergence response [Hampton and Kertesz, 1983]. M-scaled critical flicker fusion frequency stimuli have also yielded different sensitivities across the visual field, but these have been equated by additionally adjusting the retinal illuminance, in inverse proportion to Ricco's area – a process termed F scaling [Rovamo and Raninen, 1984].

Recently, M scaling has been applied to automated and semi-automated clinical static perimetry at low photopic luminances, namely the Octopus automated perimeter 201 and the Friedmann visual field analyzer MK II, where the equations of Rovamo and Virsu [1979] have been found to produce enhanced sensitivity at all eccentricities relative to the fovea [Wood et al., 1986; Wild et al., 1986]. The disparity between the theoretical and obtained profiles was attributed to variations in ganglion cell physiological characteristics across the retina, most notably that of spatial summation.

Spatial summation has been shown to increase with increase in peripheral angle (Fankhauser and Schmidt, 1960; Wilson, 1970; Scholtes and Bouman, 1977], with decrease in adaptation level [Barlow, 1958; Fankhauser and Schmidt, 1960; Meur, 1965], and with decrease in stimulus duration [Barlow, 1958]. It was hypothesized that if the enhanced sensitivity found at the peripheral locations of the previously M-scaled Octopus and Friedmann profiles is dependent upon spatial summation, the discrepancy between the theoretical and obtained profiles would

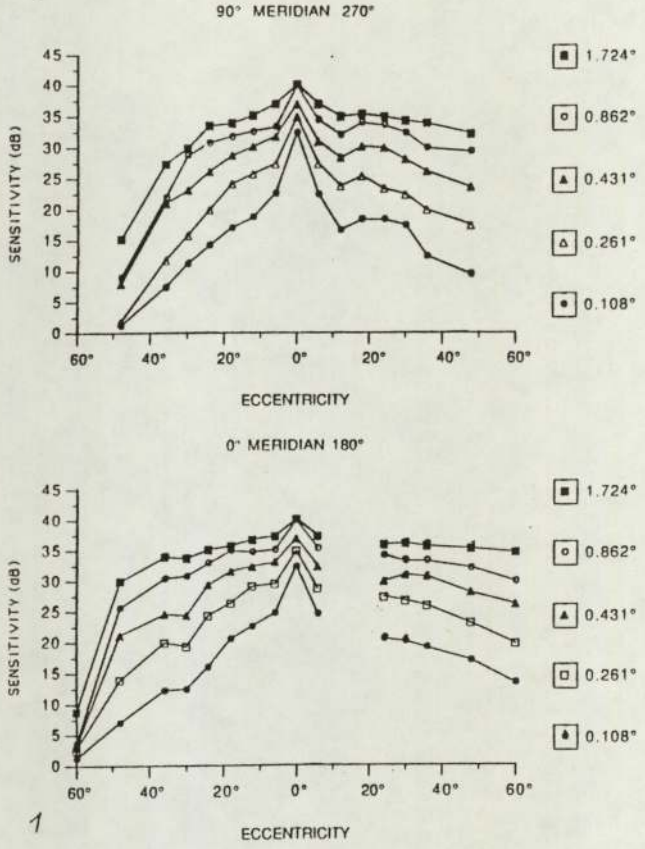

Fig. 1. Group mean differential sensitivity along the vertical (top) and horizontal (bottom) meridian of the visual field of the right eye as a function of target size.

be reduced by the utilization of a higher perimetric bowl luminance and a longer stimulus duration.

Materials and Methods

The sample comprised 10 age-matched emmetropic clinically normal subjects (mean age 22.92 years, SD 1.38 years; 6 males, 4 females) free of ocular and systemic medication and experienced in clinical perimetry and in psychophysical techniques in general.

The differential light threshold for the visual field of the right eye was determined using the Humphrey field analyzer 620. This is a computer-assisted projection perimeter which employs a bowl luminance of 31.5 asb at a viewing distance of 33 cm and a stimulus duration of 200 ms. The threshold is determined for 1 of 5 stimuli sizes (Goldmann I–V equivalents: 0.108, 0.216, 0.431, 0.862 and 1.724° projected diameters) using a 4-2 ~~2 treble~~ staircase strategy based upon a starting value, for a specific test location, developed from 4 primary points ~~at 15~~ in each quadrant and derived from the immediately surrounding test locations. The sensitivity scale measured in decibels is referenced to a maximum stimulus luminance of 10,000 asb.

It was estimated from the data of Barlow [1958] that the increased bowl luminance of the Humphrey perimeter (31.5 asb) produces an approximate twofold reduction in spatial summation compared with that of

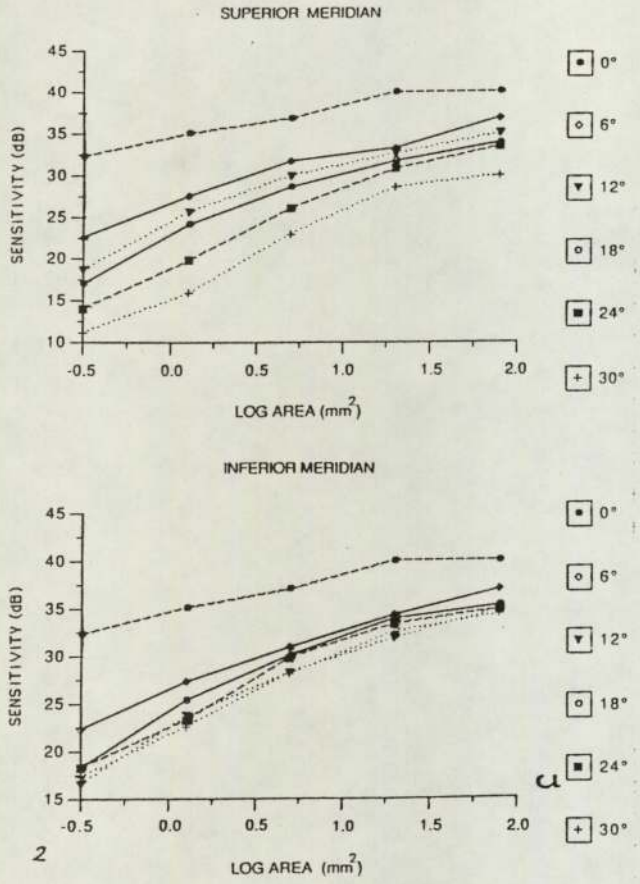

Fig. 2. Differential sensitivity against log target area as a function of eccentricity for the superior (top) and inferior (bottom) meridians of the visual field of the right eye.

the Octopus (4 asb). In addition, the greater stimulus duration (200 ms) of the Humphrey would also be expected to reduce the spatial summation; the magnitude of the temporal influence on the degree of spatial summation cannot, however, be estimated due to lack of appropriate data.

Sensitivity profiles were determined for each of the five stimuli at 6-degree intervals out to an eccentricity of 30° using program 30-1 and at 12-degree intervals between 30 and 60° eccentricity using the Peripheral 30/60-1 program. Each subject attended a total of five sessions, each session consisted of an adaptation period of 10 min followed by two programs each separated by a 10-min rest period. The combination of stimulus size and test program was randomized within any one session.

Fixation was constantly monitored using the instrument telescope, and the head was steadied using the chin and head rests. Natural pupils were used; the group pupil diameter was 6.0 ± (SD) 0.60 mm.

The equations of Rovamo and Virsu [1979] were used to calculate the stimulus diameters at the measured eccentricities necessary to produce an isosensitivity profile across the visual field. The cortical representation (M_E) at each measured location along the

four principal meridians of the visual field was derived from the equations:

$$M_{E(nasal)} = (1 + 0.33E + 0.00007E_3)^{-1} M_0;$$
$$M_{E(superior)} = (1 + 0.42E + 0.00012E^3)^{-1} M_0;$$
$$M_{E(temporal)} = (1 + 0.29E + 0.000012E^3)^{-1} M_0;$$
$$M_{E(inferior)} = (1 + 0.42E + 0.000055E^3)^{-1} M_0,$$

where E is the given eccentricity and $M_0 = 7.99$ mm/degree.

The diameter of the stimulus size (L_E) at each eccentricity, necessary to evoke an equivalent cortical response to that of the smallest stimulus size at the fovea, was then calculated by $L_E = M_0/M_E \times L_0$, where L_0 is the angular subtent of the smallest stimulus size 0.108°. This latter value was selected to ensure that the calculated diameters lay within the range of the instrument. The sensitivity value corresponding to the calculated value of L_E was derived by linear interpolation using the measured data. The equations of Rovamo and Virsu [1979] were used since they have previously been utilized in relation to the interaction of spatial summation with cortical magnification [Rovamo and Raninen, 1984; Wood et al., 1986; Wild et al., 1986].

Results

The group mean sensitivity with peripheral angle as a function of stimulus size measured along the four principal meridians of the visual field of the right eye is shown in figure 1. The magnitude of the accompanying standard deviations increases with decrease in stimulus size and with increase in peripheral angle. The group mean sensitivity against the log stimulus size as a function of peripheral angle for the vertical meridian of the visual field of the right eye is shown in figure 2. The sensitivity values of the M-scaled stimulus diameters, derived by interpolation, for the four principal meridians of the visual field of the right eye are shown in figure 3.

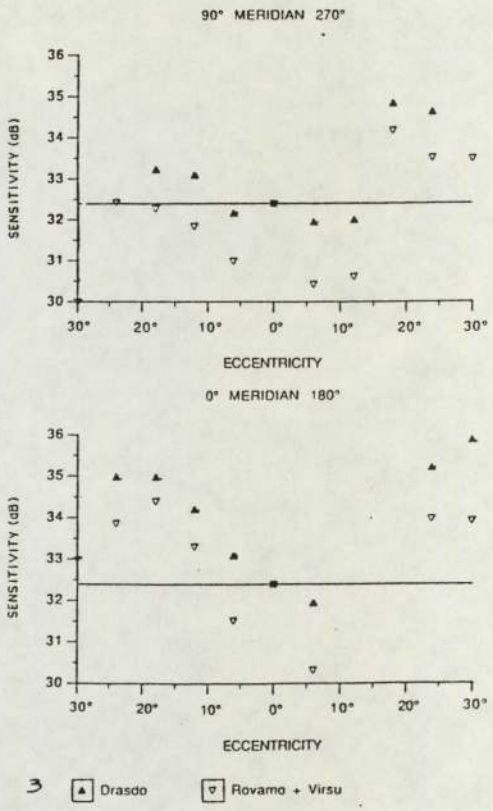

Fig. 3. M-scaled sensitivity values using the equations of Rovamo and Virsu [1979] and Drasdo [1977] relative to the foveal value for Goldmann target size I stimulating an equal area of cortex. The line parallel to the abscissa illustrates the expected isosensitivity profile. Top: vertical meridian. Bottom. horizontal meridian of the visual field of the right eye.

Discussion

The general relationship between differential light sensitivity and eccentricity as a function of stimulus size is in agreement with previous studies obtained under various states of parametric adjustment [Fankhauser

and Schmidt, 1958, 1960; Sloan, 1961; Johnson et al., 1978; Lie, 1980; Wood et al., 1986]. The sensitivity increases monotonically with increase in target size and with decrease in peripheral angle for all five stimuli. The rate of change of sensitivity, however, reduces as target size increases and is of least magnitude at the fovea. Indeed, there is no apparent difference in sensitivity between target sizes IV and V at the fovea. This saturation of sensitivity at the fovea for target sizes IV and V has not been reported at the lower adaptation level (4 asb) and shorter stimulus duration (100 ms) of the Octopus computer-assisted projection perimeter [Wood et al., 1986].

The increase in sensitivity with increase in target size at the periphery is most likely to arise due to the greater capacity for spatial summation exhibited by the peripheral regions which in turn has been related to the increase in receptive field size with eccentricity [Glezer, 1965]. Central saturation is likely to occur because the receptive fields within the central region are relatively small in primates [Glezer, 1965; Perry and Cowey, 1985], and, therefore, only a proportion of light energy contained within a larger stimulus will be summated to produce the concomitant increase in sensitivity.

The various profiles may be influenced to a greater or lesser extent by factors other than neural processing. The reduction in apparent pupillary area decreases the effective retinal illumination for all stimuli with increasing peripheral angle. The reduced retinal image projection, however, has been shown to compensate for this effect [Drasdo and Fowler, 1974], so that retinal illumination is approximately constant out to an eccentricity of 80° [Bedell and Katz, 1982; Koojiman, 1983]. Reductions in sensitivity for the smaller Goldmann targets arising from uncorrected errors of central refraction have been reported [Sloan, 1961; Fankhauser and Enoch, 1962], and it seems possible that the profiles for the smaller stimuli could be affected by off-axis optical effects. The mid-peripheral image quality of emmetropic observers, however, is believed to be more than adequate in relation to neural sampling despite the existence of oblique astigmatism [Jennings and Charman, 1981].

For all meridians, M scaling of perimetric sensitivity using the equations of Rovamo and Virsu [1979] does not result in an isosensitivity profile. Sensitivity decreases within an eccentricity of 12° for the superior and inferior meridians and within an eccentricity of 6° for the nasal and temporal meridians and then increases monotonically along all meridians to attain sensitivity values at the periphery which are of greater magnitude than that at the fovea. This finding is in contrast to that reported for the Octopus perimeter [Wood et al., 1986] in which the M scaling of stimulus size also failed to produce an isosensitivity profile but exhibited an increase in sensitivity with increase in peripheral angle at all eccentricities for all four principal meridians.

An underrepresentation of the central regions would seem to be revealed under the condition of reduced spatial summation. To test this hypothesis, the sensitivity data were additionally M scaled using the equations of Drasdo [1977] which are based upon a higher foveal representation, namely 11.5 mm/degree. The M-scaled results for Drasdo's equations (fig. 11) exhibit minimal paracentral reduction in sensitivity compared with the results for the Rovamo and Virsu [1979] values of M. Interestingly, Drum et al. [1986] demonstrated with the Tübingen perimeter

Table I. The eccentricities, determined by interpolation, at which the standard Goldmann targets would produce an isosensitivity profile and the corresponding M – scaled target diameters scaled using the equations of Rovamo and Virsu [1979] and of Drasdo [1977].

Meridian/ eccentricity degrees	Actual target diameter degrees	Rovamo and Virsu [1979] scaled target diameter degrees	Drasdo [1977] scaled target diameter degrees
Superior			
0	0.108	0.108	0.108
2.05	~~0.262~~ 0.216	0.201	0.246
5.00	0.431	0.336	0.443
15.9	0.862	0.881	1.264
26.3	1.724	1.536	2.120
Inferior			
0	0.108	0.108	0.108
2.35	~~0.262~~ 0.216	0.215	0.276
4.70	0.431	0.322	0.443
12.4	0.862	0.681	0.992
31.2	1.724	1.687	2.332
42.7	1.724	2.465	5.370

(bowl luminance 10 asb) that sensitivity could be made independent of eccentricity, if the stimulus diameter was scaled in proportion to the Macaque-corrected retinal ganglion cell density of Perry and Cowey [1985]. The disparity between the theoretical and obtained M-scaled profiles based upon 7.99 mm/degree can be further illustrated by calculation of the M-scaled target dimensions corresponding to the eccentricities at which the five Goldmann stimulus sizes produced equal sensitivities to that of the smallest stimulus at the fovea (table I).

Conclusions

The physiological implications from the data are that the foveal representation of 7.99 mm/degree is insufficient in the context of the processing of the spot stimuli used in clinical perimetry. Indeed, evidence for a two-stage magnification of the central field in macaque involving the retinogeniculate projections has been proposed [Cynader and Berman, 1972; Malpeli and Baker, 1975; Myerson et al., 1977; Perry and Cowey, 1985]. Conversely, Schein and de Monasterio [in press] have proposed that there is no further amplification of the central regions after the retina, but that central ganglion cell densities have been previously underestimated.

The perimetric implication from the data is that the use of the larger Goldmann stimuli, at the 31.5 photopic luminance generally employed in automated perimetry, saturates the central regions of the visual field and is, therefore, inappropriate to detect the earliest depression of sensitivity in this area. The enhanced representation of the central visual

field, relative to the periphery, at the visual cortex highlights the necessity to use stimuli scaled in inverse proportion to the decreased peripheral representation. Previous findings have suggested that the cortical representation of perimetric profiles depends upon the varying characteristics of the retinal ganglion cells across the retina, most notably spatial summation, in addition to ganglion cell receptive field density [Wild et al., 1986; Wood et al., 1986]. The current investigation endorses this hypothesis and, in addition, suggests that spatial summation is masking the underrepresentation of the fovea in the current human M-scaling equations. It is proposed that the use of perimetric routines incorporating target sizes adjusted in proportion to the increase in peripheral angle and based upon the physiological coverage factor of retinal ganglion cells (the product of cell density and receptive field area) would be a significant innovation in visual field examination.

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Induced intraocular light scatter and the sensitivity gradient of the normal visual field*

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Abstract. The influence of intraocular light scatter on the perimetric sensitivity profile of the normal eye was investigated using a series of light-scattering cells containing 0.01%, 0.02% and 0.025% concentrations of 500 nm diameter latex beads. The degree of induced intraocular light scatter was quantified by measuring contrast sensitivity using the Nicolet CS2000 system in the presence and absence of both wide- and narrow-angel glare light. Perimetric sensitivity out to an eccentricity of 30° was assessed, using the Octopus 201 and the Dicon AP3000 automated perimeters, with the three light-scatter cells and in the cell-free control condition. The results for both functions were expressed at the difference between the control response and that recorded under the particular experimental condition. Perimetric attenuation increased with increase in intraocular light scatter; the extent of the attenuation varied with stimulus type, bowl luminance and eccentricity

Introduction

The degree of visual function in the presence of media opacities has traditionally been assessed clinically using conventional visual acuity measurements. More recently, contrast sensitivity (Hess and Woo 1978) and hyperacuity (Williams et al. 1984) have been advocated. Furthermore, the introduction of glare light in the measurement of letter and ring acuity (Miller et al. 1972; Le Claire et al. 1982; van der Heijde et al. 1985) and of contrast sensitivity (Paulsson and Sjostrand 1980; Griffiths et al. 1984, 1986, Abrahamsson and Sjostrand 1986) has also been shown to provide a reliable indication of visual function in cataractous patients since the level of forward intraocular light scatter can be calculated to provide an index of the level of media turbidity.

The effect of cataract on the visual field profile determined by manual kinetic perimetry has been shown to include a contraction of the isopters, pseudodefects of amplification of existing field loss (Lyne and Phillips 1969; Bigger and Becker 1971; Kolker and Hetherington 1976; Radius 1978; Greve 1979) whilst in manual static perimetry a general reduction in sensitivity occurs, with the central field being depressed more than the periphery (Greve 1973, 1979).

Computer-assisted perimetry has fundamentally altered the approach to the measurement of the differential light threshold. The technique is now accepted as a rapid and effective means for assessing the integrity of the neurovisual pathways and plays an important role in the early and differential diagnosis of many ocular and neurological conditions. The method has minimized the errors previously associated with the perimetrist, but those which are associated with the patient response and which are inherent in the psychophysical assessment of any threshold still remain. Furthermore, the influence of physiological factors such as age, refractive correction and pupil size on the sensitivity gradient determined by automated perimetry still have to be fully ascertained. In particular, the perimetric attenuation arising from changes in the ocular media, as opposed to those of a neural origin, needs to be separated and quantified. Indeed, this latter problem is likely to become more apparent clinically with the current trend towards an increasingly elderly population.

In any psychophysical investigation of visual processing in eyes with advanced media disturbances, the integrity of the visual system behind the opacity cannot be determined with certainty. As a result, various cataract simulations have been employed in front of the normal eye, e.g. petroleum jelly spots distributed across a glass surface (Zuckerman et al. 1973), ground glass (Williams et al. 1984; Heuer et al. 1987), orthoptic occluders (Niesel et al. 1978; Niesel and Wiher 1982; Urner-Bloch 1987), and neutral density filtres (Eichenberger et al. 1987).

The purpose of the present study was to investigate the relationship in the normal eye between induced intraocular light scatter and the associated attenuation of the computer-assisted perimetric response. Two different conventional perimetric stimulus configurations (projected stimuli and light-emitting diode stimuli) were utilized to determine the relative sensitivity of each to image degradation from the intraocular light scatter.

Materials and methods

The sample comprised 12 clinically normal, age-matched subjects (mean age 24.1 years; SD 2.9 years) experienced in automated perimetry and in psychophysical techniques in general. Visual acuity was 6/5 or better in each eye. Subjects taking ocular or systemic medication were excluded from the study. Two of the subjects were ametropes with a refractive error within 5.00 dioptres sphere and 2.00 dioptres cylinder. Intraocular light scatter was induced

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by suspending various solutions of latex beads (0.01%, 0.02% and 0.025%) in cells before the eye. The cells were constructed with front and back surfaces of plano-powered CR39 optical lenses in order to minimize optical distortion contributing to the scatter. A bead diameter of 500 nm was selected since it has been demonstrated that the diameter of the protein aggregates in human (Bettelheim and Siew 1982) and calf (Delaye et al. 1982) cataractous lenses is between 300 nm and 500 nm. Different concentrations of beads were utilized since it has also been demonstrated (Bettelheim and Siew 1982) that interparticle separation is another important parameter in intraocular light scatter. The cells were suspended as close as possible to the subject's eye.

Intraocular light scatter was assessed using the Nicolet CS2000, an automated contrast sensitivity apparatus. Vertical sine wave gratings were presented on a monitor 3 m from the subject. A spatial frequency of 1 cycle/deg was selected in order to avoid optical attenuation arising due to blur (Campbell and Green 1959), and the gratings were counterphased at 2 cycle/deg. The screen luminance was 94.4 cd/m^2 and was calibrated at the start of each session. A circular rear illuminated diffusing screen provided a surround of the same mean luminance as the gratings. Wide- and narrow-angle glare light was generated by two circular fluorescent rings concentric with, and suspended between, the screen and the subject and which subtended 30° and 3.5° at the eye, respectively. Contrast sensitivity was measured, using the method of increasing contrast, in normal and under both glare conditions. The technique has been reported in fully by Griffiths et al. (1984, 1986).

The visual field was measured with two computer-assisted perimeters, the Octopus 201 which uses projection stimuli, and the Dicon AP3000, which employs LED stimuli. For the Octopus perimeter, a stimulus diameter of 0.431° (Goldmann size III) was presented out to an eccentricity of 30° over the central field using a sqaure stimulus grid of 6° interstimulus separation (Octopus Program 31). Stimulus presentation time was 100 ms, the bowl luminance 4 asb and the maximum stimulus intensity 1000 asb. A random double staircase strategy was employed with a final increment of 1 dB. For the Dicon perimeter, differential light sensitivity was measured at two bowl luminances of 10 asb and 45 asb, for eccentricities of 7.5°, 20°, 27.5° along the 85° and 265° meridians of the visual field using the Meridional Threshold Profile program and for 0°, 1°, 3°, 5° eccentricities along the vertical meridian using the Macula Threshold program. The light-emitting diode stimuli subtended 0.28° at the eye; the peak wavelenght was 570 nm. The stimulus presentation time was 400 ms, the interstimulus duration 1 s and the maximum stimulus intensity 10000 asb. The thresholding strategy was an ascending method of limits with a final increment of 2 dB.

Optimum distance correction was used where necessary. Natural pupils were used throughout since the procedure was intended for clinical application. Interestingly, Abrahamsson and Sjostrand (1986) applied a correction factor of 1.4 for a pupil variation of 3–4 mm during their intraocular light-scatter measurements. Vos (1983), however, demonstrated that pupil size did not significantly influence his glare results. The role of pupil size during visual field examinations has been shown to be clinically insignificant (Greve 1993; Bedwell and Davies 1977; Fankhauser 1979; Mikelberg et al. 1987).

Using these procedures, contrast sensitivity and visual fields were measured for the right eye of all subjects both with and without the various simulating cells. The contrast sensitivity and the Dicon examinations were conducted at one session and the Octopus examination on a subsequent occasion. The order of the examinations in the first session and between the two sessions were randomized.

The intraocular light scatter factor, with and without the various simulating cells, was calculated for each subject for both wide- and narrow-angle glare light using the equation of Paulsson and Sjostrand (1980):

$$\mu = L/E(M_2/M_1 - 1)$$

where μ = the intraocular light scatter factor, L = the screen luminance, E = the illuminance of the glare source and M_2 and M_1 are the contrast thresholds with and without the glare source, respectively. The difference between the scattering factor in the presence and absence of a given simulating cell was plotted for each subject against the corresponding difference in perimetric sensitivity at a given eccentricity. In the case of the Octopus, the difference in perimetric sensitivity was expressed as a mean of the results from the four locations at a given eccentricity along the four principal meridians; for the Dicon the difference was expressed as the mean of the two stimulus locations at a given eccentricity along the superior and inferior meridians.

Results

The attenuation of perimetric sensitivity for the projected target of the Octopus with variation in intraocular light scatter for wide- and narrow-angle glare light at fixation and at 30° eccentricity is shown in Fig. 1. At fixation, attenuation of sensitivity increases approximately linearly with increase in both wide- and narrow-angle intraocular light scatter. Attenuation increases monotonically but with a decreasing gradient for both glare sources at 30° eccentricity. The intraocular light scatter arising from the wide-angle glare source is less than that for narrow-angle glare light. The perimetric attenuation is lower centrally and of greater magnitude at the more eccentric location.

Perimetric attenuation for the Dicon at fixation and at 27.5° eccentricity also demonstrates a similar non-linear relationship with increasing narrow (Fig. 2) and increasing wide-angle intraocular light scatter measured at the 10 asb and 45 asb background luminances. The attenuation is greatest at the lower bowl luminance for both narrow- and wide-angle glare sources.

Attenuation is greater for the Dicon (10 asb bowl luminance) at fixation than for the Octopus with increase in both narrow- and wide-angle intraocular light scatter, whereas at more peripheral locations the Octopus produces a greater loss of sensitivity than the Dicon (Fig. 3).

Discussion

Perimetric attenuation measured with the conventinal projected Goldmann III target and with the LED stimulus increases with increase in intraocular light scatter. This finding is in general agreement with the results of Guthauser and Flammer (1987) who demonstrated that the extent of visual field changes measured with Program G1 on the Octopus was highly correlated with the degree of media opacity quantified by means of the Scheimpflug principle. The

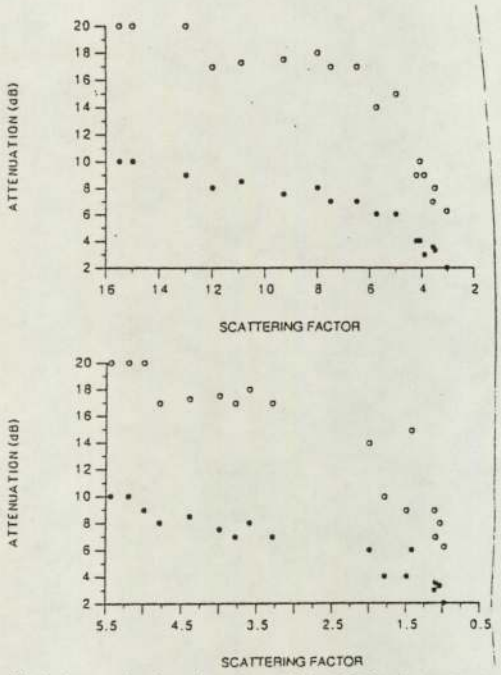

Fig. 1. Attenuation in perimetric sensitivity (dB) for the projected Goldmann size III target of the Octopus against intraocular light scatter measured for narrow-angle (*top*) and wide-angle (*bottom*) glare light as a function of eccentricity (°) (closed circles 0°; open circles 30°)

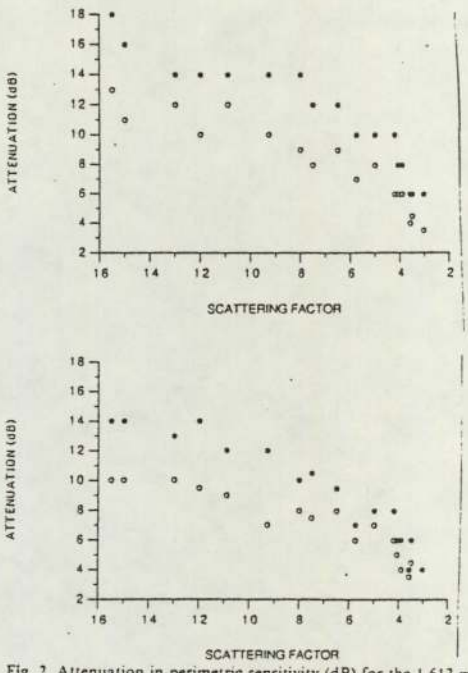

Fig. 2. Attenuation in perimetric sensitivity (dB) for the 1.613 mm diameter LED target of the Dicon against intraocular light scatter measured for narrow-angle glare light at 10 asb (*top*) and at 45 asb (*bottom*) bowl luminances as a function of eccentricity (°) (closed circles 0°]; open circles 27.5°)

intraocular scattering factors derived in the presence of wide-angle glare light are consistantly smaller than those from narrow-angle glare light and arise from the form of the line spread function of the eye. The wide-angle glare light may be the more representative measure of lenticular light scatter (Griffiths et al. 1986).

The greater attenuation at the background luminance of 10 asb compared with that of 45 asb for all eccentricities is in accord with the effect on perimetric attenuation arising from neutral density filters reported in manual static perimetry (Greve 1973) and in automated static perimetry (Klewin and Radius 1986; Baldwin and Smith 1987). This has been found to be greater at lower background luminances and has been attributed to the logarithmic change in Webers fraction at the lower photopic luminances. It should be noted, however, that natural pupils have been used for these studies.

The LED stimuli of the Dicon produce greater attenuation centrally that the projected targets of the Octopus; at peripheral locations, however, attenuation is greatest for the Octopus. The magnitude of the attenuation with increase in scattering factor, as a function of eccentricity, for each type of perimetric stimulus is illustrated by the nomograms (Fig. 4) constructed from second-order polynomial regression equations ($r = \geq 0.96$).

The difference between the two profiles arises, in part, from the difference in size of the two types of stimuli. The combination of the larger projected target and lower bowl luminance of the Octopus produces a flatter sensitivity profile than the Dicon at either bowl luminance because the central area is saturated in terms of incident light energy (Wood et al. 1986) compared with more peripheral locations, and the fovea is thus relatively insensitive to small changes in light intensity. The introduction of intraocular light scatter effectively steepens the sensitivity profile of the Octopus. This steepening has also been demonstrated with increasing age, as measured with Octopus Program 32 out to an eccentricity of 30° (Jaffe et al. 1986). Conversely, the sensitivity profile for the LED stimuli demonstrates the classical flattening reported in the literature (Greve 1973, 1979) for subjects with media changes, namely a greater reduction in sensitivity centrally compared to the periphery. This arises because the LED stimuli of the Dicon, like the targets used in conventional manual perimetry, are relatively small and do not saturate the central area, which is therefore more responsive to reductions in the light intensity of these stimuli. It is recognized that the attenuation measured for the Dicon may also be influenced by the LED stimuli being mounted in black holes – a feature unique to the Dicon.

The underlying mechanism which produces light scatter in media opacities is unknown; however, it is generally be-

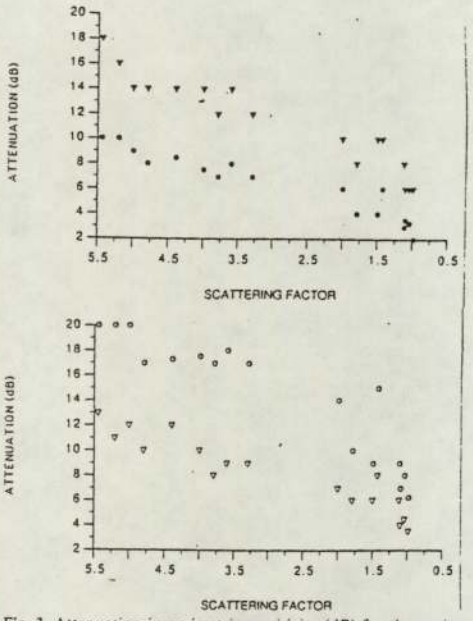

Fig. 3. Attenuation in perimetric sensitivity (dB) for the projected target of the Octopus (*circles*) and for the LED target of the Dicon (10 asb bowl luminance) (*triangles*) against wide-angle intraocular light scatter as a function of eccentricity (°). (*Top*: fixation; *bottom*: 30° and 27.5°, respectively)

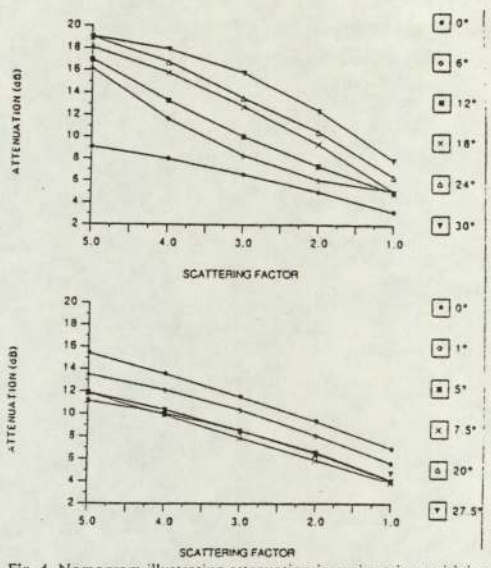

Fig. 4. Nomogram illustrating attenuation in perimetric sensitivity (dB) for the projected target of the Octopus (*top*) and for the LED target of the Dicon (10 asb bowl luminance((*bottom*) against wide-angle intraocular light scatter as a function of eccentricity (°)

lieved to be of a similar nature to Rayleigh scatter, such that light scatter is inversely proportional to the wavelength of incident light raised to the fourth power. Based on this assumption, the Dicon LEDs with peak wavelength of 570 nm would be expected to produce less light scatter than white targets of the same size, since the former contain a smaller proportion of short wavelength light. It can be inferred from the results that a combination of a relatively high background luminance lying within the linear range of Weber's law and a large ensuring minimal image degradation would be most resistant to perimetric attenuation arising from intraocular scatter.

In common with any simulation of intraocular light scatter, or more specifically simulated cataract, the plane of the simulating body must, for obvious practical reasons, be situated anterior to the corneal plane. Indeed, Baraldi et al. (1987) have suggested that greater retinal image degradation occurs as the position of the opacity becomes more posterior. The measurement of intraocular light scatter provides an assessment of the forward light-scattering characteristics of the media opacity regardless of density and position. Geometric considerations, together with absorption and blurring characteristics, would suggest that the qualitative relationship between light scatter and perimetric attenuation established for the simulation would be valid for any given media opacity; the quantitative aspects fo the relationship, however, would be expected to differ.

The results demonstrate that it is possible to predict perimetric attenuation from the measurement of intraocular light scatter and that the form of the attenuation varies with the type of perimetric stimulus.

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FACTORS AFFECTING THE NORMAL PERIMETRIC PROFILE DERIVED BY COMPUTER - ASSISTED STATIC THRESHOLD LIGHT EMITTING DIODE PERIMETRY. I. PUPIL SIZE.

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ABSTRACT

The relationship between pupil size and perimetric sensitivity was investigated in a group of clinically normal emmetropic subjects using the Dicon AP3000 computer - assisted perimeter at bowl luminances of 10 asb and 45 asb. Pupil size was modified with the miotic thymoxamine 0.5% and the mydriatic phenylephrine 10%; saline was used as the control. Perimetric sensitivity increased with an increase in pupil size, the effect being greatest for peripheral locations. The fluctuations in perimetric sensitivity increased with peripheral angle and with decrease in pupil size for both bowl luminances.

INTRODUCTION

The introduction of computer - assisted perimetry has permitted standardisation of the testing conditions under which the examination is conducted and has minimised the influence of the perimetrist on the measurement of the visual field. Factors associated with the subjective nature of the threshold response, however, still modify the data and confound accurate analysis. These factors contribute to the short - and the long - term fluctuations; the former representing the variation in threshold measured at a specific stimulus location within a single examination, whilst the latter is the additional variation in threshold at a specific stimulus location from one examination to another. In addition, factors such as age (Haas et al 1986; Jaffe et al 1986), fatigue (Heijl and Drance 1983), prior perimetric experience (Wood et al [a] In press) and clarity of the ocular media (Wood et al [b]; [c] In press) are known to influence the magnitude of both the threshold response and the short - and long - term fluctuations.

Pupil size affects certain psychophysical functions but the role in the determination of the perimetric response remains equivocal. Leibowitz (1952) using grating targets, demonstrated that increase in pupil size resulted in a concomitant increase in visual acuity which peaked for a pupil size of 2.77 mm and then decreased for the larger pupil sizes. This is in general agreement with the findings of Campbell and Green (1965) who reported that an increase in pupil size greater than 2 mm depressed contrast sensitivity, particularly at the high spatial frequencies. Furthermore, it has been reported that the naturally occurring pupil diameter is optimum for visual resolution (Campbell and Gregory 1960) and that the optimum decreases with increase in ambient illumination (Leibowitz 1952; Woodhouse 1975).

Alpern and Spencer (1953) reported that critical flicker fusion frequency (CFF) was higher at the fovea than at the periphery for fixed pupils, whereas for natural pupils CFF increased in the periphery. These results were explained in terms of changes in the retinal illumination. Pupil size also has an effect on the colour stereoscopic phenomenon. Sundet (1972) reported that with small pupils subjects perceived a red field to be behind a green field, whereas for large pupils the reverse effect was found. Interestingly, pupil size has not been found to be a significant parameter in the measurement of either the pattern electroretinogram (Karpe and Wulfing 1969; Holder and Huber 1984) or the flash visual evoked response (Skalka and Holman 1986) although miosis has been reported to increase the latency and decrease the amplitude of the pattern visual evoked response (Hawkes and Stow 1981).

Empirical clinical observations with manual perimetry have suggested that the inter - individual differences in pupil size encountered within the normal clinical range have a negligible effect on the kinetic visual field threshold (Aspinall 1967; Drance et al 1967; Williams 1983; McCluskey et al 1986). Similarly, using static automated perimetry, it has been demonstrated that in normal eyes, pupil size does not significantly influence mean sensitivity (Brenton and Phelps 1986) nor the magnitude of the short - term fluctuations (Flammer et al 1984).

Drug induced miosis produces isopter contraction measured by manual kinetic perimetry within the central visual field out to an eccentricity of 30° (Day and Scheie 1953) and also across the full field (Engel 1942; Harrington 1981; Shields 1982; Kolker and Hetherington 1983). Furthermore, pupillary constriction has been shown to simulate glaucomatous field loss and to increase the area of existing glaucomatous field defects by effectively reducing retinal illumination (Engel 1942; Forbes 1966). The effect of miosis has been quantified by McCluskey et al (1986) who demonstrated that a change in pupillary area for diameters of less than 2 mm was significantly correlated to the change in kinetic isopter area. These workers also stated that the effect of pupillary miosis on perimetric sensitivity was of greatest magnitude for the smaller stimuli such as the Goldmann I-2_e.

Greve (1973) using the Friedmann Visual Field Analyser (FVFA I) demonstrated that a reduction in pupil diameter from 6 mm to 2 mm, modified by illuminating the non - examined contralateral eye, depressed the sensitivity profile out to an eccentricity of 25° by approximately 0.2 log units. Similarly, Bedwell and Davies (1977) using the FVFA I reported that a change in pupil diameter of between 3.5 mm and 9.5 mm, induced by 0.2% thymoxamine and 5% ephedrine respectively, produced a maximum change in sensitivity of 0.14 log units. Induced pupillary constriction has also been shown to produce a reduction in sensitivity within the central 30° using the Goldmann III projection stimuli of the Octopus automated perimeter: Fankhauser (1979) reported a 0.2 log units depression in the mean threshold with 3% pilocarpine induced miosis whilst Mikelberg et al (In press) found a good correlation between pupil area (modified by thymoxamine 0.5%) and mean sensitivity.

Several authors have proposed that the isopter constriction resulting from pupillary miosis arises as a direct consequence of reduced retinal illumination (Scott 1956; Forbes 1966). The visibility of perimetric stimuli is believed, however, to be dependent upon Weber's law, where the ratio between the stimulus

luminance, ΔL, and the background luminance, L, is a constant (Aulhorn and Harms 1972; Greve 1973). From Weber's law it is predicted that if pupil size is varied, even though both the stimulus and background luminance will change, the Weber ratio will be maintained; hence the differential light sensitivity should remain unaltered. Thus, unless the retinal illumination levels fall within the mesopic range, where Weber's law is no longer operative, changes in retinal illumination due to variations in pupillary size should not affect perimetric sensitivity. McCluskey et al (1986), however, have conjectured that factors such as diffraction may reduce perimetric sensitivity when the pupil is miotic.

The absence of quantitative data relating changes in pupil size to perimetric sensitivity mitigates against the use of normative data for comparison purposes for patients whose pupil size lies outside the normal range. This occurs, for example, in patients taking medications which modify the pupil size or in whom ocular disorders have compromised the motor or neuronal function of the pupil. Furthermore, the use of serial field analysis to determine the efficacy of treatment and to monitor visual field retention is confounded if pupil size variations are introduced. This may arise if medication is altered or if the period between drug instillation and field examination varies.

The purpose of the investigation was to quantify the influence of changes in pupil size on perimetric sensitivity as a function of eccentricity. The influence of pupil size on the spread of values associated with the measurement of sensitivity at a given location was further investigated to determine whether natural variations in pupil size contribute to the variation in perimetric response measured during a single examination.

METHODS

The investigation was conducted at two background luminances in order to test the hypothesis that the effect of pupil size on perimetric sensitivity is independent of background luminance (Aulhorn and Harms 1972; Greve 1973) assuming that Weber's fraction is constant for the adaptation levels employed in computer assisted perimetry. The Dicon AP3000 was selected to assess perimetric sensitivity in the investigation since it provides the facility to vary bowl luminance.

The Dicon AP3000 is a computer - assisted perimeter employing light emitting diode stimuli with a peak wavelength of 570 nm at a viewing distance of 33 cm. Threshold is determined by an ascending method

of limits. The sensitivity scale measured in dBs is referenced to the maximum absolute stimulus luminance of 10,000 asb. Sensitivity is measured to an accuracy of 2 dB.

The mydriatic phenylephrine 10% and the miotic thymoxamine 0.5% were used to modify pupil size. Thymoxamine and phenylephrine both act on alpha adrenoreceptors present on the smooth muscle of the dilator pupillae. In addition, both agents act on the ciliary body vasculature but interference with ciliary muscle function is, for young subjects, unlikely to affect the sustained accommodative response (Mordi et al 1986) required for fixation at the perimetric viewing distance of 33 cm. Thymoxamine induces pupillary miosis as a result of antagonist action on alpha receptors; phenylephrine induces pupil mydriasis as a result of agonist action on alpha receptors.

The sample comprised 10 clinically normal, age - matched,emmetropic subjects (3 females, 7 males; mean age 23.45 years, SD 2.84 years). The subjects were free from any ocular or systemic medication and were experienced in automated perimetric routines and in psychophysical techniques in general. Informed consent was obtained from all subjects prior to their involvement in the study and following a full explanation of the experimental procedures.

The pupil size of each eye was modified using one drop of 0.5% thymoxamine for miosis and one drop of 10% phenylephrine for mydriasis; 0.9% saline was used as a control. All drugs employed in this study were obtained from Smith and Nephew single - dose applicators ("minims"). The instillations were made with a precision micro - pipette such that each instillation comprised 25 μl of drug. Prior to the administration of the drug, one drop of benoxinate hydrochloride 0.4% was instilled into each eye to inhibit reflex tearing of the cornea.

Perimetry was undertaken 30 minutes after drug instillation. Perimetric sensitivity was determined for each of two bowl luminances, 10 asb and 45 asb, at eccentricities of 10°, 12.5°, 20°, 30°, 35°, 40° and 50° along the 265° meridian of the inferior visual field of the right eye using the Meridional Threshold program of the Dicon AP 3000 and at eccentricities of 0°,1°, 3° and 5° along the vertical meridian of the inferior field using the Macular Threshold program. Sensitivity at each location was measured three times and was represented as the mean of these measurements. The stimulus duration was 100 msec and the interstimulus duration was 1 sec.

Each subject attended a total of three sessions within a maximum period of three weeks. At each session one drop of benoxinate hydrochloride was instilled into each eye followed by the instillation of one of the two active agents or the control solution; the period between the two instillations was five minutes. The washout period between each session was a minimum of 2 days. The order of the drug instillation was randomised for each subject and a double blind protocol was employed such that neither the examiner nor subject were aware of which agent had been used.

Pupil size was measured immediately prior to perimetric examination and thereafter at 5 minute intervals using the scaled axes on the video monitor of the perimeter. The pupil size could be measured to an accuracy of 0.5 mm. The value for pupil diameter was represented as the mean of the measurements taken throughout the examination; the duration of the perimetric examination was approximately 30 minutes. The order of bowl luminance and of perimetric program at a given bowl luminance was randomised throughout the sample. Each subject underwent an adaptation period of 10 minutes to the appropriate bowl luminance.

RESULTS AND ANALYSIS

Table 1 indicates the group mean pupil size and standard deviation for each combination of drug and adaptation level.

Figure 1 illustrates the relationship between group mean perimetric sensitivity and eccentricity for each combination of drug and adaptation level.

Figure 2 illustrates the relationship between group mean perimetric sensitivity and pupil size for each combination of drug and adaptation level as a function of eccentricity.

Figure 3 represents the group mean proportionate change in perimetric sensitivity relative to the saline control for each combination of drug and adaptation level.

Table 2 shows the linear regression characteristics of group mean proportionate change in sensitivity against group mean proportionate change in pupil area relative to the saline control at the 10 asb and 45 asb background luminances as a function of eccentricity.

Figure 4 illustrates the group mean range of sensitivity values measured at each eccentricity for each combination of drug and adaptation level.

DISCUSSION

The decrease in sensitivity with increase in peripheral angle (Figure 1) is in accord with previous findings obtained with both manual (Fankhauser and Schimdt 1960; Aulhorn and Harms 1972; Johnson et al 1978) and automated static perimetry (Wood et al 1986; Wild et al In Press). The standard deviation was, on average, 2dBs. It was reasonably constant out to an eccentricity approaching 12.5° beyond which the magnitude increased with increase in peripheral angle for each drug condition. The increase in variance with increase in peripheral angle is in accord with that previously reported in automated projection (Wood et al 1986; Wild et al In press) and LED perimetry (Flanagan et al In submission).

Increase in pupil size (Figure 1) has the effect of reducing the rate of decay in sensitivity with increase in peripheral angle, i.e. a flattening of the sensitivity profile, such that the sensitivity of the more peripheral regions is elevated with respect to that obtained with the smaller pupil size. The reason for this finding is unclear. Flattening of the sensitivity profile has been reported in automated perimetry with increase in size of projected stimuli at adaptation levels of both 4 asb and 31.5 asb (Wood et al 1986; Wild et al In Press) and with LED stimuli for decrease in adaptation level (Barnes et al 1985) and for increase in intraocular light scatter (Wood et al [b]; [c] In Press). The steepening of the profile has been demonstrated with projected stimuli for increase in age (Jaffe et al 1986) and for increase in intraocular light scatter (Wood et al [b]; [c] In Press).

The eccentricity - dependent alteration to the profiles is further illustrated in Figure 3: a 4 - way analysis of variance indicated that eccentricity ($p < 0.025$) and drug ($p < 0.001$) both significantly affected proportionate change in sensitivity. At both adaptation levels, the eccentricity effect is negligible within approximately 10° but at eccentricities greater than 10°, an increase in pupil size produces an increase in sensitivity. With smaller pupils, sensitivity decreased beyond a peripheral angle of 10°. The eccentricity - dependent change in sensitivity may relate to the fact that the effective illumination for all stimuli is reduced with increasing peripheral angle. This arises because the available area of the pupil decreases more slowly than the cosine of the angle of eccentricity (Spring and Stiles 1948; Jay 1962). The reduced retinal image

projection in the periphery, however, has been shown to compensate for this effect (Drasdo and Fowler 1974) so that retinal illumination is approximately constant out to an eccentricity of 80° (Bedell and Katz 1982; Koojiman 1983). The increase in peripheral sensitivity with increase in pupil size may alternatively arise because the increased pupil aperture permits greater peripheral aberrations which increases the intraocular light scatter. The greater capacity for spatial summation of the peripheral regions relative to the central regions will allow this scattered light to be preferentially utilised and thus may facilitate the increased peripheral sensitivity.

The influence of pupil size change on perimetric sensitivity is similar at both adaptation levels and suggests that Weber's law is a constant over the range of adaptation levels employed in the study. This is in contrast to the findings of Baldwin and Smith (In press) who demonstrated that the reduction in retinal illuminance (using neutral density filters) produced a greater depression in perimetric sensitivity at a bowl luminance of 3.15 asb compared to that of 31.5 asb. They attributed this result to changes in Weber's fraction at the lower luminances; pupil size, however, was not controlled in the study.

At both adaptation levels, linear regression of proportionate change in sensitivity against proportionate change in pupil area as a function of eccentricity exhibited an increasing gradient with increase in peripheral angle (Table 2). The magnitude of the correlation coefficient generally increased in a similar manner with the values being statistically significant beyond approximately 30°. Second order regression gave similar results.

Mikelberg et al (In Press) using Program G1 of the Octopus automated perimeter have reported that reduction in absolute pupil diameter induced by thymoxamine 0.5% showed no statistically significant change in the visual field indices (Flammer et al 1985) such as mean sensitivity and mean defect. A highly significant positive relationship was found, however, between change in both proportionate pupil diameter and area and proportionate change in mean sensitivity. The use of the mean sensitivity index, however, provides a measure of the overall sensitivity of the field which is independent of test location and also short - term fluctuation. The index will thus mask any eccentricity effect; moreover Octopus Program G1 only determines threshold out to an eccentricity of 26°.

Some indication of the short - term fluctuation in perimetric sensitivity can be obtained from the group mean range of sensitivity at each eccentricity (Figure 4). The range increases with increase in peripheral

angle for both adaptation levels and with decrease in pupil size. This finding is in contrast to that of Flammer et al (1984) who found that pupil size did not influence the magnitude of the short term fluctuation obtained in normal subjects for the larger projected Goldmann III stimulus of the Octopus. These workers did report, however, that a decrease in pupil size increased the magnitude of the short - term fluctuations in a series of glaucomatous subjects.

CONCLUSION

The effect of pupil size, modified by thymoxamine 0.5% and phenylephrine 10%, on perimetric sensitivity and a measure of the accompanying fluctuations at the two adaptation levels of 10 asb and 45 asb is greatest at peripheral angles larger than 10°. The proportionate change in sensitivity for any drug condition reaches a maximum value of approximately 3dBs beyond 35° eccentricity with the effect reaching approximately 7dBs for a pupil size difference of 3.7 mm.

It has been recently suggested that perimetry undertaken at an adaptation level of 315 asb facilitates the detection of early glaucomatous and neuro - ophthalmological lesions (Paige 1985). In addition, dark - and light - adapted automated perimetry has been shown to facilitate the separation of patients with retinitis pigmentosa into appropriate subgroups (Jacobson et al 1986). The use of perimetric examinations over a range of adaptation levels provide the opportunity to examine differential sensitivity over a further dimension (Barnes et al 1985). The results from this investigation demonstrate that the effects of proportionate change in pupil size induced by such large changes in adaptation level must be controlled in order that meaningful results may be obtained. Furthermore, pupil size must also be considered in the serial analysis of the visual fields of patients whose therapeutic regime changes to one producing a significant modification of pupil diameter.

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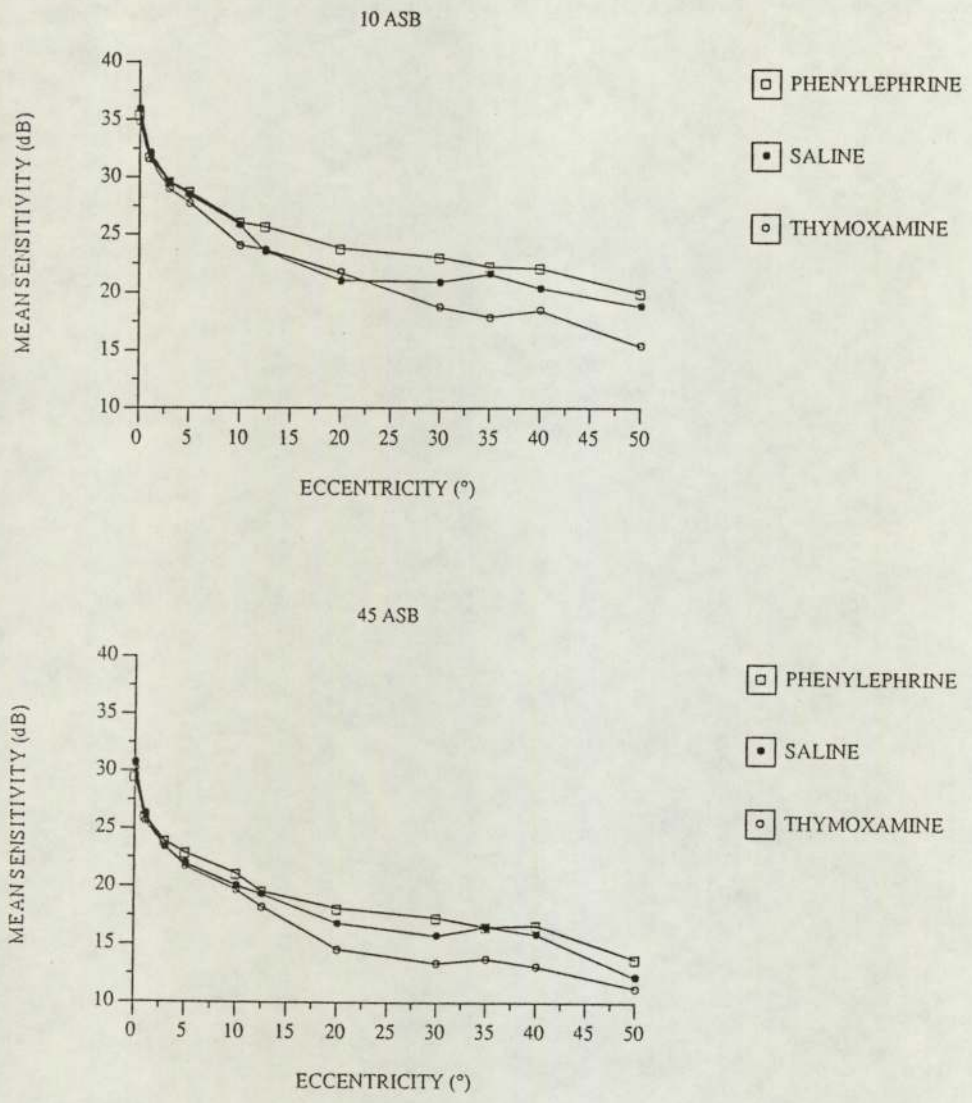

Figure 1. Group mean perimetric sensitivity against peripheral angle as a function of pupil size modified by thymoxamine 0.5% and phenylephrine 10% (top) and for the 45 asb (bottom) background luminances.

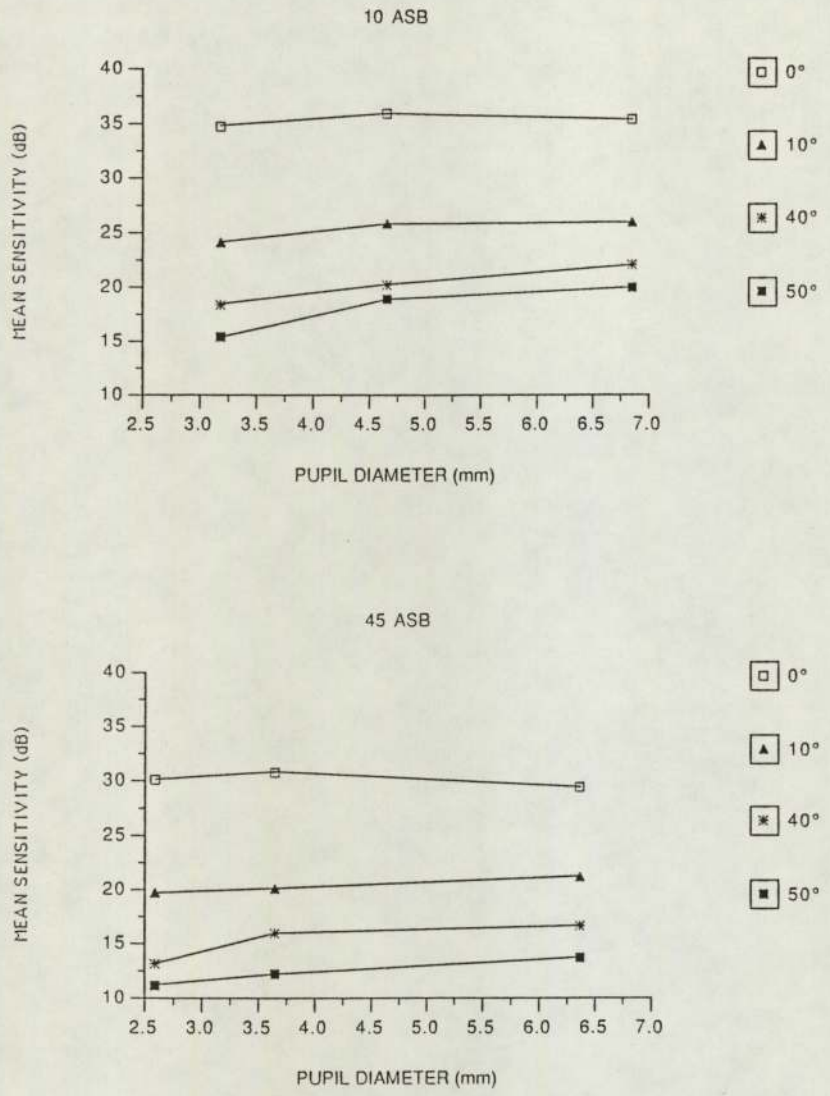

Figure 2. Group mean perimetric sensitivity against pupil size modified by thymoxamine 0.5% and phenylephrine 10% as a function of eccentricity for the 10 asb (top) and for the 45 asb (bottom) background luminances.

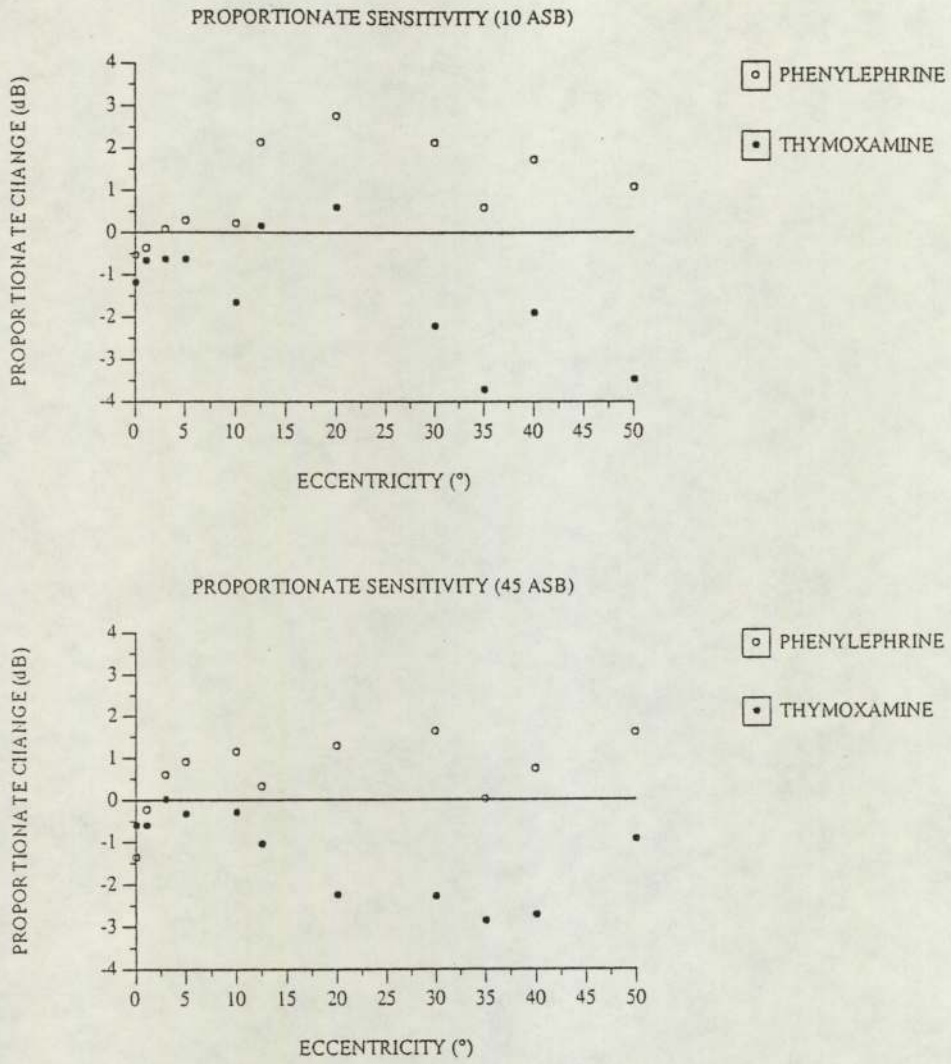

Figure 3. Group mean proportionate change in sensitivity relative to the saline control for miosis and for mydriasis at the 10 asb (top) and 45 asb (bottom) background luminances against peripheral angle.

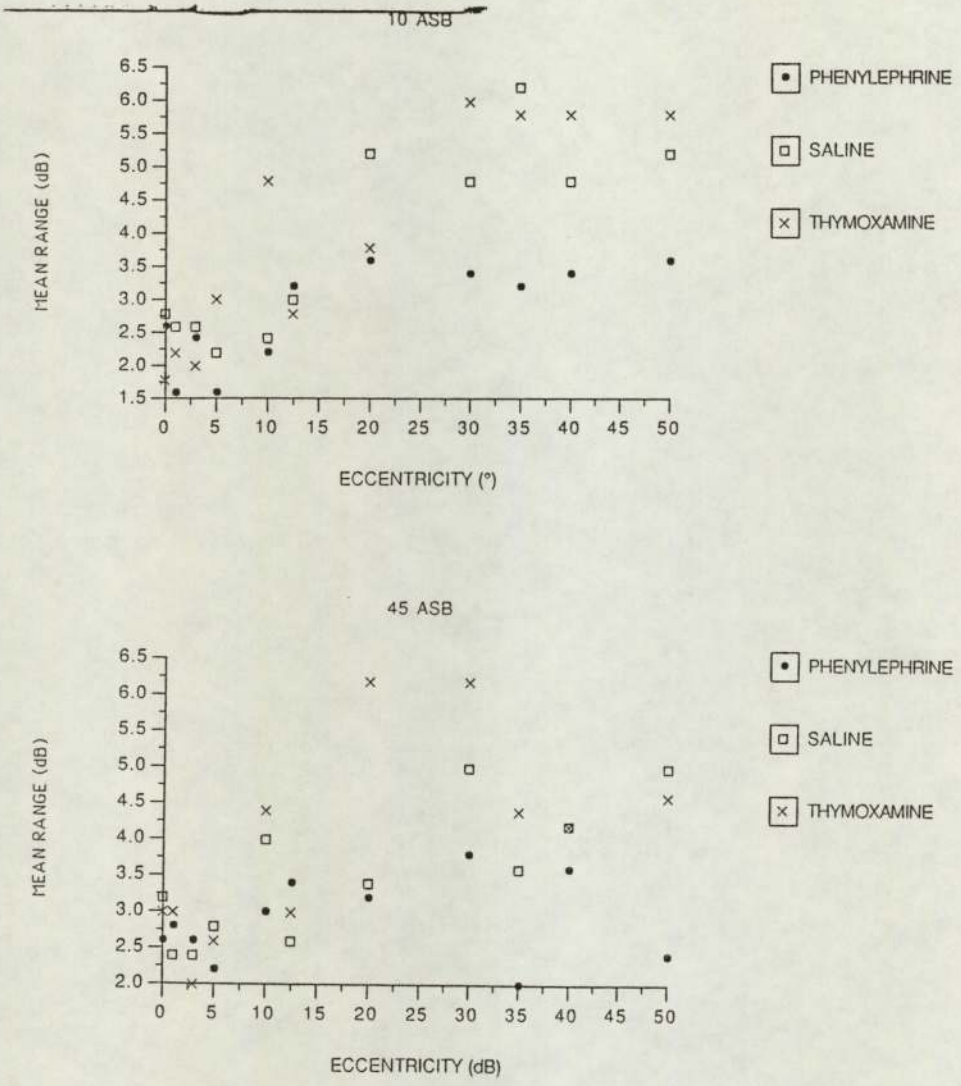

Figure 4. Group mean range of sensitivity against eccentricity as a function of pupil size modified by thymoxamine 0.5% and phenylephrine 10% for the 10 asb (top) and for the 45 asb (bottom) background luminance.

Adaptation Level	Phenylephrine 10%	Saline 0.9%	Thymoxamine 0.5%
10 asb	6.85 (0.67)	4.65 (0.62)	3.18 (0.56)
45 asb	6.37 (0.55)	3.65 (0.55)	2.59 (0.34)

Table 1. Group mean pupil size modified by thymoxamine 0.5% and phenylephrine for the 10 asb and for the 45 asb background luminances.

	ECCENTRICITY	SLOPE	INTERCEPT	CORRELATION	PROBABILITY VALUE
	0	0.02	-0.96	0.19	0.44
	1	0.01	-0.58	0.11	0.65
	3	0.03	-0.47	0.37	0.10
	5	0.025	-0.34	0.25	0.14
	10	0.07	-1.13	0.40	0.08
10 asb	12.5	0.07	0.73	0.49	0.03
	20	0.06	1.33	0.30	0.15
	30	0.14	-0.84	0.63	0.003
	35	0.13	-2.33	0.45	0.05
	40	0.10	-0.65	0.50	0.02
	50	0.12	-1.90	0.40	0.09
	0	-0.03	-0.78	0.14	0.57
	1	0.02	-0.53	0.12	0.60
	3	0.02	0.125	0.20	0.41
	5	0.05	-0.13	0.46	0.04
	10	0.05	-0.02	0.45	0.05
45 asb	12.5	0.04	-0.71	0.26	0.15
	20	0.13	-1.62	0.59	0.006
	30	0.13	-1.41	0.58	0.007
	35	0.09	-2.15	0.46	0.04
	40	0.12	-1.98	0.59	0.006
	50	0.11	-0.60	0.51	0.022

Table 2. The linear regression of the group mean proportionate change in sensitivity with group mean proportionate change in pupil area relative to the saline control at the 10 asb and 45 asb background luminances as a function of eccentricity.

FACTORS AFFECTING THE NORMAL PERIMETRIC PROFILE DERIVED BY COMPUTER - ASSISTED STATIC THRESHOLD LIGHT EMITTING DIODE PERIMETRY. II. ACCOMMODATIVE MICROFLUCTUATIONS.

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ABSTRACT

The relationship between accommodative fluctuations and perimetric sensitivity was investigated in a group of 10 clinically normal, emmetropic, subjects using the Dicon AP3000 computer - assisted perimeter at a bowl luminance of 10 asb. Accommodative microfluctuations were attenuated with the antimuscarinic drug cyclopentalate HCl 1% and the concomitant mydriasis was matched on a separate trial using the sympathomimetic phenylephrine HCl 10%. Saline 0.9% was used as the control. Accommodative microfluctuations were found to play a minor role in determining the magnitude of sensitivity out to an eccentricity of 5°; between 5° and 27.5°, this effect was masked by the influence of pupil size produced by the drugs used in the study. The range of sensitivity values at a given location were reduced when accommodative fluctuations were minimised.

INTRODUCTION

The steady - state accommodation response to a visual stimulus exhibits microfluctuations (Campbell et al 1959; Campbell and Westheimer 1960; Bour 1981; Denieul 1982). The amplitude of these microfluctuations is approximately 0.10D with a frequency bandwidth ranging from 0 to 6 Hz (Campbell et al 1959; Denieul 1982). Accommodative microfluctuations are not considered to be a product of muscular noise (Campbell 1960) but are thought to be under central nervous system control. Furthermore, microfluctuations provide a continuous monitoring of the quality of the retinal image (Millodot 1968; Charman and Tucker 1978). Studies have demonstrated that microfluctuations in accommodation increase with increasing accommodative effort (Campbell et al 1959; Denieul 1982; Johnson et al 1984; Bullimore et al 1986), in the presence of small pupils (Campbell et al 1959) and when the image quality is poor (Denieul 1982).

Foveal visual functions are sensitive to sustained optical defocus, although the magnitude of this effect is dependent upon the type of stimuli employed. Contrast sensitivity, measured with sinusoidal grating stimuli, for example, is depressed by defocus of the retinal image (Campbell and Green 1965; Charman 1979; Kay and Morrison 1987) and the tolerance to defocus increases with decrease in both spatial frequency and pupil size (Campbell and Green 1965; Charman 1979). Similarly, visual resolution measured with high contrast Snellen letters is markedly depressed by optical defocus (Borish 1970; Westheimer 1979). The rate of degradation of hyperacuity with optical defocus is, however, significantly slower than that of both stereoacuity and Snellen visual acuity (Westheimer 1979). Critical flicker frequency fusion (CFF) has been shown to be independent of variations in the steady state accommodative response (Berger and Mahneke 1953) and in defocus of the retinal image (Hylkema 1944).

The influence of defocus on peripheral vision is dependent upon the particular visual function under

investigation. Functions such as motion thresholds (Johnson and Leibowitz 1974) and absolute thresholds (Ronchi 1971) are sensitive to blur, whereas the influence of optical attenuation on peripheral visual acuity is uncertain (Green 1970; Frisen and Glansholm 1975; Millodot et al 1975).

The influence of sustained defocus on the perimetric thresholds is well documented and the effect is dependent upon the parametric adjustment under which sensitivity is measured. Optical blur constricts the Goldmann II/2 kinetic isopters measured manually (Serra 1983) and depresses manual static thresholds out to an eccentricity of 30° for Goldmann stimulus size I (Fankhauser and Enoch 1962) and for Goldmann stimuli I and II (Sloan 1961). Using automated static perimetry, optical defocus depresses sensitivity more at fixation than in the periphery for stimulus size III (Benedetto and Cyrlin 1985) and increases the mean defect determined with stimulus size III (Goldstick and Weinreb 1987).

Little is known about the influence of accommodative microfluctuations on perimetric sensitivity. The relationship between transient defocus, due to variations in the accommodative response, and perimetric sensitivity has, however, been discussed by several workers. Tate (1985) reported that both accommodative spasm and accommodative fatigue can depress foveal sensitivity, the former being common in young uncorrected hyperopes and the latter in undercorrected presbyopes. Greve (1973) reported that accommodative fatigue may result in progressively decreasing light sensitivity which is manifested as a spiralling kinetic visual field and increased variation in threshold measurements. Miotics have also been reported to depress perimetric sensitivity due to the pseudo - myopia resulting from the accommodation spasm (Greve 1973).

The aims of the study were, therefore, twofold: firstly to investigate whether the transient blurring of the perimetric stimuli due to accommodative microfluctuations influences the magnitude of perimetric sensitivity and secondly to assess whether these microfluctuations contribute to the variability of the threshold response at a given test location measured during a single visual field

examination.

MATERIALS AND METHOD

The subjects for the study consisted of 10 clinically normal, emmetropes (3 females, 7 males) aged between 21 and 29 years (mean age 23.72 years, SD 3.53 years) with visual acuity of 6/5 or better. All subjects were free from any ocular or systemic medication and were experienced observers in automated perimetry and in other psychophysical techniques of investigation. Informed consent was obtained from all subjects prior to their involvement in the study, following a full explanation of the experimental procedures.

The ciliary smooth muscle activity was modified on separate occasions with either cyclopentolate HCl 1% or phenylephrine HCl 10%; saline 0.9% was employed as a control solution. Cyclopentolate is a muscarinic antagonist which produces marked cycloplegia and attenuation of the accommodative microfluctuations (Campbell et al 1959; Johnson et al 1984) together with mydriasis and abolition of the direct and indirect pupillary light response. Phenylephrine acts on alpha adrenoreceptors present on the smooth muscle of the dilator pupillae leaving both the direct and indirect pupillary light response relatively unaffected. It was employed to match the pupillary mydriasis of cyclopentolate without markedly affecting the sustained accommodative response. In this way, the influence of accommodative microfluctuations on perimetric sensitivity could be separated from the influence of changes in pupil size.

Each subject attended a total of three experimental sessions within a maximum period of three weeks. At the beginning of each session one drop of benoxinate hydrochloride was instilled into each eye to inhibit reflex tearing. This was followed by two 25 µl instillations, each made with a precision micro - pipette, of either one of the two active agents or of the control solution; the period

between the two instillations within a given session was five minutes. All drugs employed in the study were obtained from Smith and Nephew single - dose applicators ("minims"). The wash-out period between sessions was a minimum of 2 days. The order of instillation of the active drug and of the control drug was randomised for each subject.

Twenty five minutes following the instillation of the benoxinate hydrochloride the monocular amplitude of accommodation was measured under normal room illumination using a standard clinical technique namely, the RAF rule. The measurement was repeated at the end of the experimental session, immediately following the visual field examination. The marked cycloplegic effect induced by cyclopentalate necessitated the use of a +3 D auxillary lens to measure the amplitude of accommodation.

Following initial measurement of the amplitude of accommodation, the influence of the pharmocological agents was further assessed by measuring the accommodative response to a target at a stimulus vergence of -3 D using the Canon R-1 autorefractor. The Canon R-1 is a commercially available infra-red optometer which has been used in other studies of accommodative function (McBrien and Millodot, 1986; Bullimore et al 1986) and is capable of producing an accurate measure of refractive status at approximately 1 s intervals. The target consisted of a matrix of numbers equivalent to N5. The subject was instructed to focus on the central number within the matrix while a series of 30 consecutive readings were taken under normal room illumination. The standard deviation of the measured accommodative response is considered to be an index of the magnitude of the microfluctuations of accommodation but not a measure of their absolute amplitude (Johnson et al 1984; Bullimore et al 1986).

Perimetry was undertaken using the Dicon AP3000 30 minutes after drug instillation. This perimeter, in common with most other automated perimeters, has a fixation distance of 33 cm, and thus requires a relatively high level of accommodative effort to be sustained throughout the

examination. The LED stimuli subtend a visual angle approximately equivalent to that of the Goldmann II and may be more sensitive to optical degradation than the standard Goldmann III used in automated projection perimeters. These properties facilitate investigation of accommodative microfluctuations since the magnitude of the microfluctuations increases in proportion to the accommodation exerted (Campbell et al 1959; Denieul 1982; Johnson et al 1984; Bullimore et al 1986). The Dicon AP3000 used in this study was also used to assess the effect of variations in pupil size on perimetric sensitivity; an account of this investigation is given in the accompanying paper (Wood et al In submission).

The differential light sensitivity of the right eye was measured at eccentricities of 0°, 1°, 3° and 5° using the Macular Threshold program and at eccentricities of 7.5 °, 10°, 15°, 20°, 25° and 27.5° along the 265° meridian using the Meridional Threshold program. The order of perimetric program was randomised throughout the sample. Stimulus duration was 100 ms with an interstimulus duration of 1 s. Each subject underwent a 10 minute adaptation period to the bowl luminance of 10 asb. A bowl luminance of 10 asb was used since this provides the greatest dynamic range with which to assess sensitivity. The threshold for each location was measured five times in order to obtain a measure of the variability of the threshold perimetric response during a single session. During the cyclopentolate 1% session, a +3 D lens was suspended in front of the eye using the lens holder of the perimeter.

The size of the pupil was measured immediately prior to perimetric examination and thereafter at 5 minute intervals using the scaled axes on the video monitor of the perimeter. Pupil size could be measured to an accuracy of 0.5 mm. The value for pupil diameter was represented as the mean of the measurements taken during the examination; the duration of the perimetric examination was of the order of 30 minutes.

RESULTS

Table 1 indicates the group means and one standard deviation for the various aspects of accommodative function investigated. Data relating to pupil size is included and indicates that the mydriatic responses to cyclopentalate and phenylephrine were similar. The microfluctuations in accommodative response are represented in terms of the group range of the standard deviations of the accommodative response obtained for each drug. A 50% reduction in the accommodative microfluctuations was obtained with cyclopentolate compared with that for phenylephrine and for saline.

Figure 1 illustrates the relationship between group mean perimetric sensitivity and eccentricity for each drug. Sensitivity decreases with increase in peripheral angle for all trials and is consistent with the results of the accompanying study (Wood et al In submission). The standard deviation ranged from 0.95 dB to 2.66 dB and was on average 2.0 dB. It was fairly constant out to an eccentricity approaching 12.5° beyond which the magnitude increased with increasing eccentricity for each drug trial.

Figure 2 illustrates the group mean proportionate change in perimetric sensitivity with eccentricity for each drug relative to the saline control. For eccentricities less than 5°, proportionate sensitivity decreased for both active drugs; beyond this eccentricity both drugs induced an increase in proportionate sensitivity.

An estimate of the influence of accommodative microfluctuations on the short - term fluctuations in perimetric sensitivity may be derived by plotting the group mean range of sensitivity values (which, given the software limitations of the Dicon perimeter system, are an indication of the short - term fluctuation in perimetric sensitivity) as a function of eccentricity for each drug (Figure 3). A

reduction in the range in sensitivity values was observed with both of the active drugs relative to the control. The mean range of perimetric sensitivity was of least magnitude for the cyclopentolate trial. The reason for the large mean range of perimetric sensitivity values at 7.5° for the saline trial is unclear. This was not, however, found in the accompanying study in which the subject group was taken from the same population (Wood et al In submission).

DISCUSSION

The amplitude of accommodation measured with the RAF rule was relatively unaffected by phenylephrine, but was profoundly reduced by cyclopentolate in all subjects (Table 1). This finding in agreement with previous reports (Garner et al 1983; Ward and Charman 1986; Mordi et al 1986). The accommodative response to a -3 D target was also depressed by cyclopentolate in all subjects, relative to the saline trial (Table 1). Interestingly, although the effect of phenylephrine on the accommodative response to the -3 D stimulus was small compared with that of cyclopentolate 1%, it did reduce the amplitude of accommodation slightly and supports the findings of Garner et al (1983) and Mordi et al (1986). The apparent accommodative microfluctuations present with cyclopentolate can be attributed to the measurement error of the Canon R - 1.

The decrease in perimetric sensitivity with increasing eccentricity (Figure 1) is in accord with the findings for projection perimetry (Wood et al 1986; Wild et al 1986) and for LED perimetry (Flanagan et al In submission).

The proportionate change in sensitivity (Figure 2) for both cyclopentolate and phenyleprine is depressed for eccentricities out to 5°, and has a maximum depression of 1.5 and 0.75 dB, respectively, at the fovea. Interestingly, proportionate sensitivity for both phenylephrine 10% and thymoxamine 0.5% has been shown to be depressed relative to saline within the central regions

when pupil size alone is varied (Wood et al In submission). The findings reported here would appear to be due to changes in pupil size rather than in accommodative microfluctuations. Phenylephrine exhibited a higher proportionate sensitivity than cyclopentolate at all eccentricities.

An elevation of proportionate sensitivity for both cyclopentalate and phenylephrine occurs between eccentricities of 5° and 27.5° (Figure 3) and is probably the result of the eccentricity - dependent increase in sensitivity with increased pupil size. This is in agreement with the findings of Wood et al (In submission) where the sensitivity of the peripheral regions was found to be more dependent on changes in pupil size than for central regions. As pupil size increases from 4.87 mm to 7.48 mm, peripheral locations (between 5° and 27.5°) exhibit an increase in mean perimetric sensitivity of the order of 1.5 dB. It is important to note, however, that although the mean pupil size for cyclopentolate is slightly larger than that for phenylephrine (7.48 mm compared to 7.25 mm respectively), the sensitivity with the latter drug is greater. This may arise because of the discomfort experienced by the observers due to a reduced amplitude of accommodation following instillation of cyclopentolate. In addition, the use of a supplementary lens for perimetry in the cyclopentolate trial may have resulted in depression in sensitivity due to the reduction in light transmission and the prismatic effects induced by the ophthalmic lens. The prismatic effects of ophthalmic lenses can be ignored during static perimetry for lens powers up to ±10 D, whilst the light transmission of ophthalmic lenses is of the order of 92% (Atchison and Johnston 1979).

The values of mean range of perimetric sensitivity (which is a correlate of the short - term fluctuations) recorded at each location (Figure 3) are greatest for saline and least for cyclopentolate. This difference may arise from the differences in pupil size. The greater mean range in sensitivity for the phenylephrine trial relative to the cyclopentolate trial, where pupil size with the two drugs is very similar, would, however, tend to discount this explanation. It is possible, therefore, that the reduction in accommodative microfluctuations due to the cyclopentolate may account for the reduction in mean range of perimetric sensitivity. The mean range in sensitivity is greatest at

stimulus locations beyond 5° for all three trials. This may arise because the fixation target employed for the meridional program requires less accurate accommodation than for the supplementary fixation target of the macula threshold program due to their relative angular subtense. Indeed, the mean range in sensitivity is attenuated by cyclopentolate for stimulus locations beyond 5°.

CONCLUSIONS

The findings suggest that although accommodative microfluctuations play a minor role in determining the magnitude of sensitivity within the central 5°, their importance in the periphery is superceded by factors such as the pupil size produced by the drugs used in the study. Nevertheless, the range in perimetric sensitivity values measured at a specific location, were reduced when accommodative fluctuations were minimised. This suggests that when relatively high levels of accommodation must be sustained, accommodative microfluctuations are a minor component of the short - term fluctuations in perimetric sensitivity. In clinical perimetry these effects can largely be discounted.

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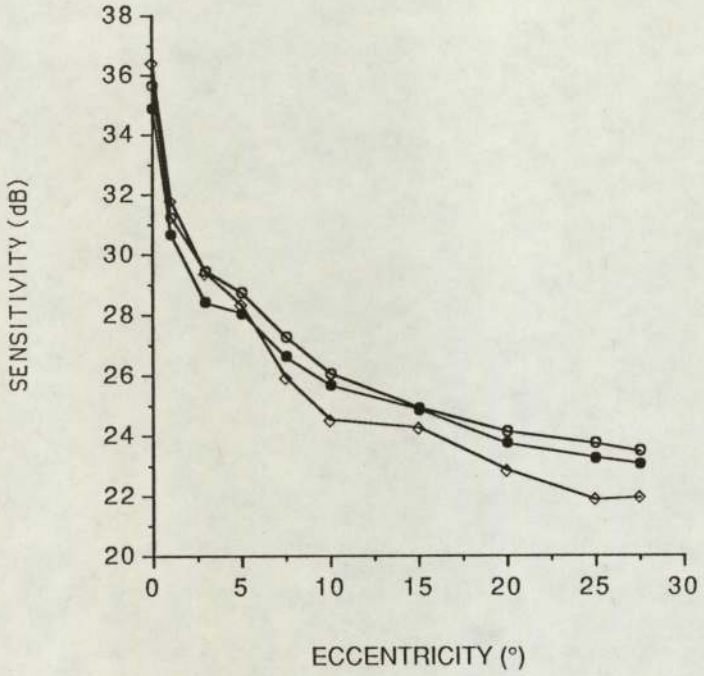

Figure 1 Group mean perimetric sensitivity against eccentricity for phenylephrine 10% (open circles), cyclopentolate 1% (filled circles) and saline 0.9% (open diamonds).

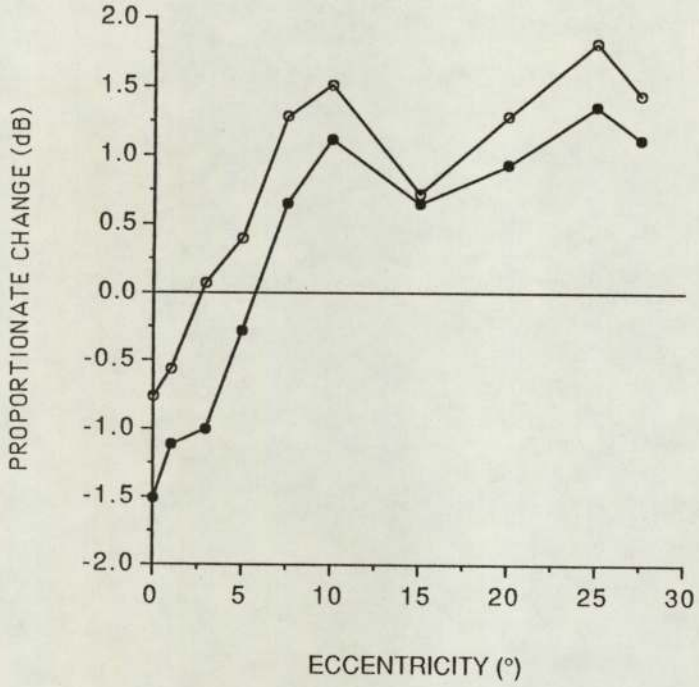

Figure 2 Mean proportionate change in perimetric sensitivity relative to the saline control against eccentricity for phenylephrine 10% (open circles) and cyclopentolate 1% (filled circles).

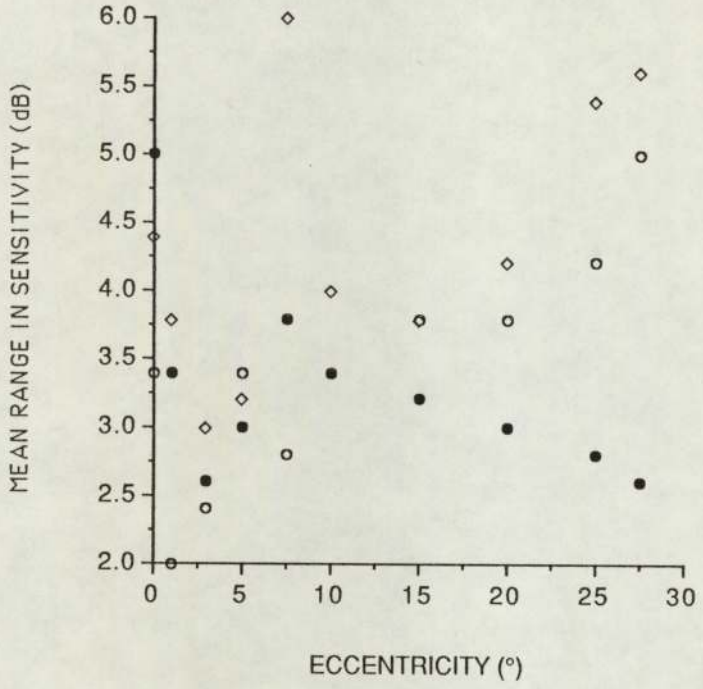

Figure 3 Group mean range in perimetric sensitivity values for five threshold determinations against eccentricity for phenylephrine 10% (open circles), cyclopentolate 1% (filled circles) and saline 0.9% (open diamonds).

		Cyclopentolate 1%	Phenylephrine 10%	Saline 0.9%
Amplitude of accommodation (D)	(mean)	1.06	8.10	9.60
	(S.D.)	0.58	1.22	1.72
Accommodative response (-3D) stimulus (D)	(mean)	0.16	2.49	2.52
	(S.D.)	0.48	0.12	0.17
Accommodative microfluctuations (D)	(range)	0.05-0.11	0.10-0.20	0.13-0.21
Pupil size (mm)	(mean)	7.48	7.25	4.87
	(S.D.)	0.47	0.55	0.72

Table 1 Group means and one standard deviation for each drug condition for the amplitude of accommodation; the level of accommodation in response to a -3D target; and the pupil diameter; together with the interindividual range of standard deviations in the accommodative response.

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