# Perimetric sensitivity and response variability in glaucoma with single-stimulus automated perimetry and multiple-stimulus perimetry with verbal feedback

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**ABSTRACT.**

***Purpose:*** **To measure perimetric sensitivity and response variability of glaucomatous patients with single-stimulus automated perimetry (SSAP) and multiple-stimulus perimetry (MSP) with verbal feedback.**

***Methods:*** **Frequency-of-seeing (FOS) data were collected from the same four visual field locations (normal and reduced sensitivity) in one eye of 10 glaucoma patients, using SSAP and MSP. The SSAP technique was similar to that used in routine clinical perimetry while the MSP technique required the patient to verbally report the positions of the seen stimuli (0–4, with no more than 1 in each quadrant) after each presentation. At each test location, stimuli (0.5°, 200 ms) were repeatedly presented at five or more intensities around the estimated threshold. FOS curves (logistic) were determined using a maximum likelihood method and the threshold sensitivity (50% seen) and response variability (20–80% seen range) were compared between the two perimetric techniques.**

***Results:*** **There was an increase in sensitivity (mean = 1.9 dB, $P < 0.01$, Wilcoxon) and reduction in variability (mean range reduced from 3.7 to 2.5 dB, $P < 0.01$, Wilcoxon) with MSP. The increase in sensitivity with MSP varied between patients ($P < 0.001$, one-way anova) with the mean MSP–SSAP sensitivity per eye ranging from 0.1 to 4.8 dB.**

***Conclusion:*** **Patients have a higher sensitivity and less variability in their visual field when tested with MSP with verbal feedback than with SSAP. These differences vary between patients and a likely explanation is the better maintenance of attention with MSP and verbal feedback. This finding demonstrates how the variability found in routine clinical perimetry can be reduced through changes to the way in which the stimuli are presented and the way in which the patient responds.**

**Key words:** glaucoma – perimetry – psychophysics – visual attention – visual field

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## Introduction

Currently, the detection and management of primary open-angle glaucoma is based upon intraocular pressure (IOP), the appearance of the optic nerve head and the results of a visual field test. Of all the methods available, visual field assessment is one of the most important because it is a direct measure of visual function, the preservation of which is the main purpose of treatment.

Although enormous advances have been made in perimetry, the currently used techniques still suffer from a large amount of variability. This variability is particularly problematic in areas of visual field loss, because of the strong relationship between sensitivity and variability (Heijl et al. 1989; Weber & Rau 1992; Chauhan et al. 1993; Henson et al. 2000). Reducing the amount of variability is an important and challenging topic: it would reduce the amount of change necessary to detect progressive loss (Spry & Johnson 2002).

Variability in the visual field is dependent upon a number of cognitive factors including attention, learning effect (Werner et al. 1988; Heijl et al. 1989; Wild et al. 1989, 1991), fatigue (Wild et al. 1989) and response bias (Kutzko et al. 2000). While recent work has demonstrated that these cognitive factors can have a considerable effect upon the results of a visual

field examination (Kutzko et al. 2000; Wall et al. 2004), the frequency and impact of lapses of attention during a visual field examination have not been quantified.

Most of the current clinical visual field tests use single-stimulus automated perimetry (SSAP), in which the patient is given a fixed time interval to give a positive response following each exposure. This technique is demanding of the patient, and it is not unusual for them to report periods during the test when they found it difficult to maintain their attention. Temporary lapses of attention are likely to be associated with a raising of the threshold that, when factored in with periods of normal attention, will both reduce the overall sensitivity and increase response variability (Wall et al. 2004).

In the 1950s, Harrington & Flocks (1954) introduced multiple-stimulus perimetry (MSP) for the purpose of rapid screening; under this procedure, between two and four stimuli are presented at each exposure. The patient is asked to verbally report the number and, when stimuli have been missed, the location of the seen stimuli. Previous studies have suggested that verbal reporting is one of the parameters that helps to maintain patient attention and reduce variability (De Jong et al. 1985; Henson & Anderson 1989).

Variability in the visual field is well defined by the slope of the psychometric function $[\psi(x;\ \alpha,\beta,\gamma,\lambda) = \gamma + (1 - \gamma - \lambda)F(x;\ \alpha,\beta)]$, where $\alpha$ and $\beta$ give the shape of the function (displacement and slope), $\gamma$ and $1-\lambda$ give the lower and upper boundaries of the function and $F(x;\alpha,\beta)$ is typically a sigmoid two-parameter function that ranges from 0 to 1, such as the Weibull, logistic or cumulative normal function.

The aim of this study was to establish whether there were differences in sensitivity and variability between SSAP and MSP strategies using the psychometric function, and indirectly to establish the impact of lapses of attention upon response variability in clinical perimetry.

# Materials and Methods

### Patients

Patients were recruited from the Manchester Royal Eye Hospital glaucoma clinics according to the following criteria: previous experience with SSAP; visual acuity (VA) ≥ 0.3 logMAR (6/12); refractive error within ±5.00 D sphere and <3.00 D cylinder; no ocular comorbidity other than early lens changes or prior cataract surgery; and absence of advanced visual field loss (involving more than 25% of the central visual field). The patients did not have prior experience of MSP with verbal feedback.

The study was approved by the Stockport Research Ethics Committee and follows the tenets of the Declaration of Helsinki. Informed consent was obtained from each patient after explanation of the nature and possible consequences of the study.

### Data collection

Frequency-of-seeing (FOS) data were collected from one eye of each patient using a Henson Pro perimeter (Sheen Instruments, Surrey, UK) with custom software. The same four visual field test locations (one per quadrant) were used for SSAP and MSP (randomized order). Based on previous visual field data (collected within the preceding 6 months), locations with severe loss and those that were close to the border between damaged and normal areas were avoided; truncation effects would make it difficult to fit a psychometric function to areas of severe loss, and locations close to a border would be sensitive to small eye movements (Henson et al. 1996). At least one location was chosen to be in an area of reduced sensitivity (Pattern Deviation <−5 dB), and another one in an area of normal sensitivity. At the onset of the test, 3–5 responses were collected at intensities that straddled the previously recorded threshold estimate for each test location. During the test, the experimenter was provided with continuous feedback on the patient's responses (number presented and seen at each test intensity). Throughout the test, the experimenter's task was to adjust the number of presentations and the range of intensities to ensure that: (1) the response range approached 0 and 100% seen; (2) data were collected at a range of at least five intensities (minimum step size 1 dB); and (3) the data were concentrated at the shoulder regions of the FOS curve. Adjustments could be made at any time and did not require an interruption to the test.

With SSAP, the patients were asked to press a button every time they saw a stimulus (quadrant- and intensity-randomized); with MSP, the patients were asked to verbally report the number and location (using clock hours or top, bottom, left, right) of the stimuli they saw [quadrants, intensity and number of stimuli (1–4) randomized]. In both cases, the instructions to the patients were designed to give a similar response bias (Kutzko et al. 2000).

Broad spectrum LED stimuli (540–590 nm) subtending 0.5º for 200 ms, with an intensity range of between 63 cd/m$^2$ (12 dB) and 0.25 cd/m$^2$ (36 dB), were presented on a background intensity of 3.15 cd/m$^2$. A break was given during and between each test.

### Data analysis

FOS curves (logistic) were fitted to the psychometric data using MatLab (MathWorks, Inc., Natick, MA, USA) and the toolbox psignifit, version 2.5.6 (see http://bootstrap-software.org/psignifit/), which implements the maximum-likelihood method described by Wichmann & Hill (2001a). This software allows the upper and lower bounds of the function to vary within defined limits (0.95–1.00 and 0.00–0.05 in this study). Confidence intervals were determined using a bootstrap method based on 5000 Monte–Carlo simulations (Wichmann & Hill 2001b).

Threshold sensitivity (defined as the inverse of the detection function $F(x,\alpha,\beta)$ at the 50% seen level) and variability (defined as the range between the 20% and 80% seen levels) were compared between SSAP and MSP using Wilcoxon signed rank test for zero median (paired test). A one-way anova was performed to determine the influence of patient characteristics on the sensitivity difference between MSP and SSAP.

# Results

A total of 40 sets of data were obtained. Data from test locations where the performance (measured from the fitted FOS curve) did not exceed the 50% level seen with either the SSAP ($n$ = 3), MSP ($n$ = 1) or both ($n$ = 3) were excluded. These

curves corresponded to areas of more advanced sensitivity loss and were subject to truncation effects brought about by the limited range of intensities available with the equipment (Fig. 1D).

On average, the MSP test took longer to perform than the SSAP test (5.4 min/100 presentations in MSP; 4.3 min/100 presentations in SSAP). The number of test exposures was also larger in the MSP strategy (552 ± 64 in MSP; 489 ± 27 in SSAP).

Figure 1 shows four examples of fitted FOS curves. Each example gives the result from a single test location tested with SSAP and MSP.

Figure 2 gives the MSP and SSAP sensitivity and variability for all included data sets ($n$ = 33) grouped according to patient number. Variability is represented by the difference between the 20% and 80% seeing levels on the psychometric function – i.e. 60% of the responses should fall within the variability range. This index was chosen, rather than gradient of the function, to give a measure of variability in more clinically meaningful units (dB).

In almost all cases, the sensitivity estimate derived with MSP was higher ($P < 0.01$ Wilcoxon test) than that for SSAP and the variability lower ($P < 0.01$ Wilcoxon test).

Figure 3 gives the mean, maximum and minimum difference between MSP and SSAP for each patient. This figure highlights that while some patients have very little difference between their MSP and SSAP threshold sensitivities (e.g. patients 2, 6 and 8), others have a large difference that is consistent across all their test locations. A one-way ANOVA shows a significant ($P < 0.001$) patient effect.

Figure 4 shows the relationship between sensitivity and response variability for MSP and SSAP. Variability is seen to increase as sensitivity reduces; the combined data are well described ($r^2 = 0.40$) by the equation $\log_{10}$(variability) = A*sensitivity + B, where A and B are −0.0493 and 1.62, respectively. The lines drawn on Fig. 4 connect data collected with SSAP and MSP from the same test location and highlight how switching to MSP both increases the sensitivity and reduces the variability.

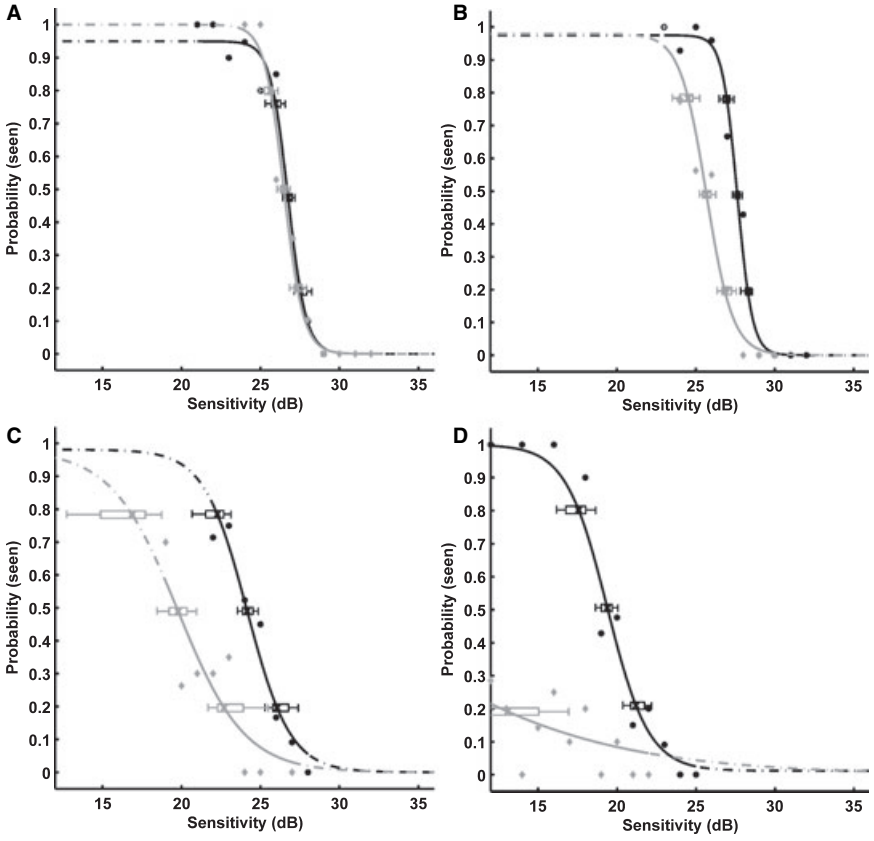


**Fig. 1.** Four examples of data obtained from the multiple-stimulus perimetry (MSP) (black) and single-stimulus automated perimetry (SSAP) (grey) strategies. Each example gives the data from a single test location. Confidence limits are represented by the horizontal box plots [box ± 1 standard deviation (SD), whiskers ± 2 SD] at 0.2, 0.5 and 0.8 probability levels. (A) An example where MSP and SSAP give almost identical results. (B) A more typical result with SSAP having a lower sensitivity and increased variability. (C) A test location with lowered sensitivity where there is again a difference between SSAP and MSP. (D) Results from a location that was excluded from the analysis because the SSAP data did not reach 0.5 probability.

# Discussion

In this study, we have found that visual field sensitivity is improved and variability reduced when patients with glaucoma are tested with MSP rather than SSAP. Furthermore, the improvement in sensitivity was found to be patient-dependent. While in some patients there was a small difference between MSP and SSAP, in others the difference was much larger.

Greve (1972), in a carefully conducted trial, could find no difference in either sensitivity or variability between SSAP and MSP. Greve's methodology differed from that used in this study, in that he collected data from both strategies within a single experimental session, a technique that would have masked any differences in cognitive factors (such as attention) between MSP and SSAP.

Henson & Anderson (1989) measured threshold sensitivities and variability with MSP and SSAP in a group of 18 subjects drawn from university students and staff. Their study, which separated the MSP and SSAP sessions, found that MSP had a higher sensitivity (0.95 dB) and reduced variability compared to SSAP. They also reported on a SSAP two-alternative forced-choice technique where the subjects were forced to report if the stimulus was in either the upper or lower visual field. With this strategy they found a small improvement in the threshold sensitivity, above that of the conventional SSAP but still below that of MSP.

Henson & Anderson (1989) ascribed the difference between SSAP and MSP to a number of factors including the better maintenance of the patients' attention throughout the period of the examination. Temporary lapses of attention during a visual field

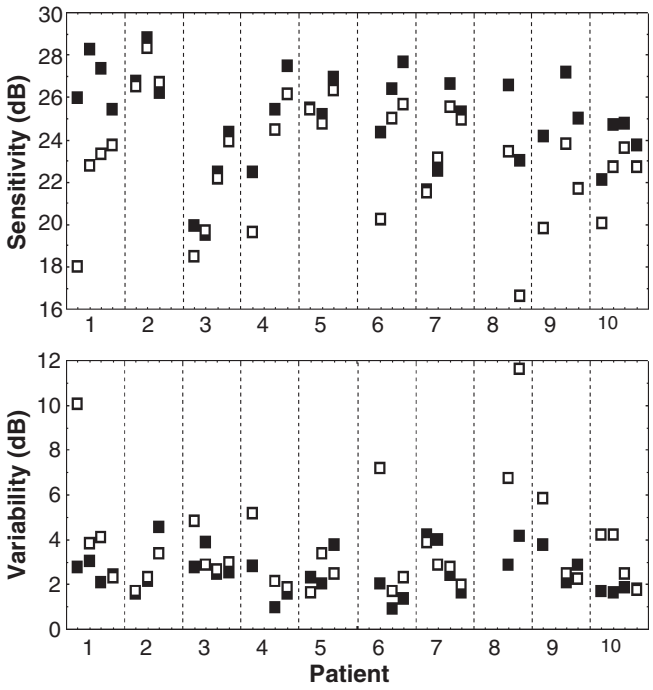


**Fig. 2.** Sensitivity (upper plot) and variability (lower plot) taken from the best-fitting psychometric function for each included test location ($n$ = 33). Variability is the difference between the 20% and 80% seeing levels. Symbols: (■), data from the multiple-stimulus strategy; (□), data from the single-stimulus strategy. Data are grouped according to patient number.

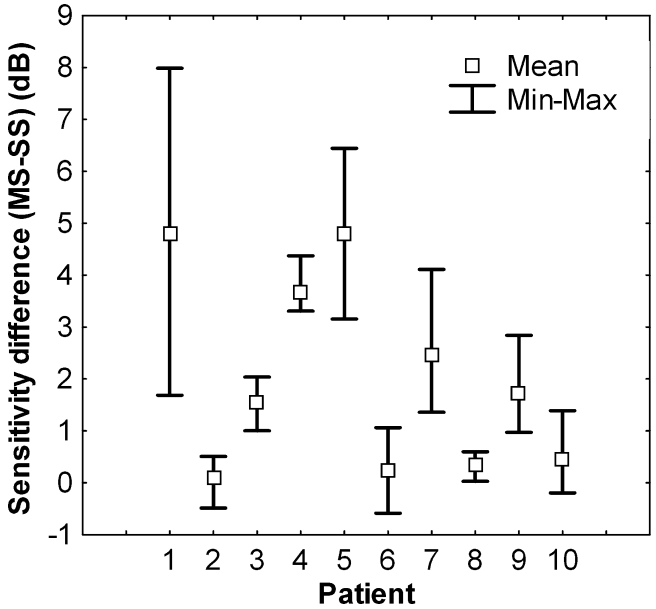


**Fig. 3.** The mean, minimum and maximum differences between the multiple-stimulus perimetry (MSP) and single-stimulus automated perimetry (SSAP) thresholds for each patient.

examination are likely to be associated with temporary reductions in sensitivity that, when factored in with periods of normal sensitivity, will lower the overall measure of sensitivity and increase response variability. The extent will be dependent upon the duration and number of lapses, and is likely to be patient-dependent.

The nature of the MSP test used in this study led to more stimuli being presented than with SSAP. Increasing the number of presentations is likely to improve the precision of the fitted FOS curves but not the parameters of the curve. While the increased duration of MSP may have increased patient fatigue, it is not believed that this had a major effect upon the results; any such effect would have reduced the difference between the two strategies rather than increased it.

The total test time for each strategy, which included breaks, was approximately 25 min. The mean number of exposures (MSP = 552, SSAP = 489) is less than that experienced by a patient having both eyes tested with the standard SITA strategy [339/eye (Bengtsson & Heijl 1998)]. The level of fatigue experienced during the collection of the FOS data, and any time-dependent effects upon attention, are therefore likely to be similar to those experienced in clinical perimetry when both eyes are tested.

In accordance with previously published data (Heijl et al. 1989; Weber & Rau 1992; Chauhan et al. 1993; Henson et al. 2000), this study found that variability increases as sensitivity reduces. The earlier results from Henson et al. (2000) showed that the relationship could be well described ($r^2$ = 0.57) by linear model between log(variability) and sensitivity. The results from this study also show that the relationship can be well described ($r^2$ = 0.40) by such a relationship [$\log_{10}$(variability) = 1.62−0.0493*Sensitivity]. The smaller $r^2$ value is likely to be because of the smaller range of sensitivity values (16–29 versus 10–36 dB).

The patients who participated in this study were not selected on the basis of their prior visual field results, other than ensuring that they did not have advanced loss, and are felt to be representative of those attending a major eye hospital for the management of their glaucoma. Within the group of 10 patients, four showed very little change (< 0.5 dB) in their sensitivity when switching from SSAP to MSP presentations, two showed a moderate shift (> 0.5–2 dB) and four showed a large shift (> 2 dB). While the sample size is insufficient to make any judgment of proportions, these findings demonstrate that significant reductions in variability can be obtained with strategies that differ from those widely used in clinical perimetry.

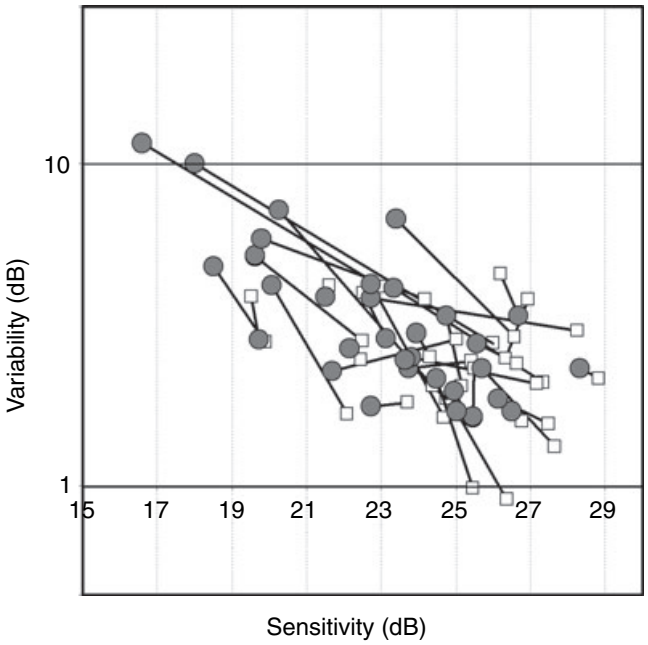


**Fig. 4.** Variability (20–80% seen of best-fitting psychometric function) versus sensitivity for single-stimulus automated perimetry (SSAP) (●) and multiple-stimulus perimetry (MSP) (□). The lines represent the change in variability and sensitivity when switching from SSAP to MSP presentations.

# Conclusions

Variability continues to be a problem in clinical perimetry that hampers both the detection and monitoring of this condition. The state of attention is just one of several cognitive factors that are likely to have an effect upon variability. This study has found that patients have a higher sensitivity and less variability in their visual field when tested with MSP rather than SSAP. These differences were found to vary between patients and are most likely caused by better maintenance of attention with MSP and verbal feedback. This finding highlights the role of attention as an important cause of response variability in a large number of patients undergoing clinical perimetry. Better control of attention during clinical perimetry will reduce variability and the amount of change necessary to detect progressive loss.

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