Do Intense Perimetric Stimuli Saturate the Healthy Visual System?

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Purpose. A recent proposal for why glaucomatous perimetric sensitivities of approximately 15 to 19 dB or less are unreliable involves the idea that the neural response of normal retinal ganglion cells saturates for intense perimetric stimuli. A predicted consequence of this saturation is that the neural response for two different high intensity stimuli will be the same, leading to an inability to discriminate between them. We test that prediction.

Methods. We used a two-interval forced-choice method of constant stimuli (7 steps, 40 presentations/step) to measure the ability of four healthy observers to discriminate between different intensity Size III perimetric stimuli at 0°, 9°, and 21° eccentricity. The lower intensity stimulus for each discrimination was either 27, 23, 19, 15, or 11 dB (Humphrey Field Analyzer equivalents).

Results. Foveally, discrimination performance exceeded 90% for all observers provided the more intense stimulus was made sufficiently intense, even if the lower intensity stimulus in the pair was itself already intense ($\leq$19 dB). The shapes of the curves were similar across all lower intensity stimulus values investigated. At 21°, discrimination performance exceeded 90% in three of the four observers despite the lower intensity stimulus being 19 dB.

Conclusions. Observers can reliably discriminate between two different, but both very intense, perimetric stimuli, indicating that responses of the human visual system are not saturated by such stimuli. Therefore, the cause of high perimetric test–retest variability is not readily predicted from our current knowledge of how normal ganglion cells respond to high intensity stimuli.

Keywords: glaucoma, perimetry, saturation, variability, contrast discrimination

It is well established that perimetric sensitivities become increasingly variable in areas of glaucomatous visual field loss.[1–4] It has been argued recently that sensitivities less than approximately 15 to 19 dB cannot be measured reliably in glaucoma, and that retinal ganglion cell saturation is critical to this unreliability.[5] Briefly, it has been proposed that as stimulus intensity is increased within a location of severe visual field damage, the remaining ganglion cells reach response saturation before the stimulus can be detected reliably by cortical mechanisms monitoring the outputs of these ganglion cells.[5] Therefore, further increasing the stimulus intensity fails to increase the firing rate of the remaining cells and so the stimulus can never be detected reliably irrespective of how intense it is made. This form of absolute saturation described here, where increasing stimulus intensity fails to raise visual responses to threshold, should be distinguished from saturation used to describe when the relationship between background intensity and probe intensity starts to increase faster than some nominal behavior (e.g., Weber's law) but where probe thresholds still are reliably measurable; for example, see the study of Swanson et al.[6] Although a sensitivity cutoff of $\geq$19 dB has been recommended for research purposes,[5] it should be noted that this represents a somewhat arbitrary limit[5] as variability increases continuously as sensitivity decreases.[2]

The idea of response saturation being a candidate mechanism for perimetric variability was based on known responses in normal retinal ganglion cells, rather than on presumed changes to ganglion cell function as a result of glaucoma.[5] In particular, the semisaturation constant of retinal ganglion cells was assumed to be approximately 24 dB in perimetric terms (using the units of the Humphrey Field Analyzer [HFA; Carl Zeiss Meditec, Jena, Germany], or a contrast of 115%), as measured in nonhuman primates.[6] However, this constant applies only to ganglion cells within the magnocellular pathway. Cells within the parvocellular pathway measured in the same study showed little or no saturation even at the maximum contrast tested (500%). Therefore, it might be expected that remaining parvocellular cells should be able to continue to increase their firing and so allow reliable sensitivities to be measured, even if the responses from magnocellular cells become saturated. That parvocellular cells also are much more numerous in the retina also should increase the likelihood that some parvocellular cells are among the pool of cells remaining in areas of visual field loss.

Inherent in the idea that ganglion cell saturation underlies perimetric variability is that pooled responses from many ganglion cells are required for a stimulus to be detected reliably, even if some of the cells are firing at their maximum rates. Absent of this assumption, a single ganglion cell firing at its maximum rate would be sufficient for a stimulus to be detected. Makous et al.[7] measured responses to very tiny (0.75 minutes of arc) spots using adaptive optics so that over 50% of

the light was predicted to fall within the boundaries of a single cone. The area stimulated by such spots was over 1000 times smaller than a conventional Size III perimetric stimulus (0.43°). As spot intensity increased, the chance of detecting the stimulus increased to over 90%.[7] Assuming that perimetric thresholds are estimated as the stimulus intensity where the observer has a 50% chance of seeing the stimulus, this result implies that in the limiting case of one cone being sufficiently intensely stimulated, a perimetric stimulus may elicit a response from the observer. Although it is true that even a single cone will link to multiple ganglion cells, these results do show that responses from only a tiny fraction of the many ganglion cells stimulated by a Size III target are required for a stimulus to be reliably detected. That only a handful of cells must be stimulated to achieve reliable stimulus detection is in keeping with similar arguments made for cells in primary visual cortex.[8]

Therefore, it is not clear what role ganglion cell saturation has in contributing to the variability inherent in estimating perimetric thresholds. Previous work found that sensitivity estimates below 15 to 19 dB were unreliable,[5] and so it would be expected that ganglion cells should show saturating responses for stimuli in or below this dB range should saturation be critically involved in this unreliability. If this were so, then contrast discrimination should be impaired at this stimulus intensity. Contrast discrimination requires a person to distinguish between two stimuli of differing luminous contrast; in this case, two perimetric stimuli with slightly different intensities, or dB values. To be perceptually different, the higher intensity stimulus must produce a visually significant increase in retinal ganglion cell responses compared to the lower intensity stimuli. If the stimulus of lower intensity already saturates ganglion cell responses, responses to the higher stimulus will be similarly saturated and discrimination should be impossible. Anderson and Vingrys[9] measured discrimination thresholds for small achromatic targets similar in size to perimetric targets, and presented on a similar background (4 cd/m^2), and found measurable contrast discrimination thresholds at contrasts equivalent to 19 dB. This suggests that at least some ganglion cells were not saturated at this dB level, but could further increase their response to signal an increase in target intensity. This is consistent with the action of local adaptation mechanisms in the visual system that are designed to prevent response saturation and so increase the dynamic range of the eye.[10] However, intensities greater than 19 dB were not explored by Anderson and Vingrys,[9] nor was an evaluation of how saturation might change with eccentricity. Local adapting mechanisms can be defeated by using very small adaptation fields, and these have been used to demonstrate saturating responses in the human visual system.[11,12] As eccentricity increases, perimetric targets become effectively smaller relative to ganglion cell receptive field sizes (although never smaller than the perceptive field indicated by Ricco's area at eccentricities used in 24-2 perimetry),[13–15] and so it may be that local adaptation mechanisms become less effective and that saturation, therefore, results.

We measured discrimination thresholds for pairs of perimetric stimuli differing only in intensity, to determine if the visual system saturates at stimulus intensities previously suggested. In addition, we examined the influence of stimulus eccentricity on saturation. Such experimental data is necessary to determine the likely role of ganglion cell saturation in causing variability in the measurement of perimetric sensitivity in glaucoma. We also performed experiments to investigate whether cues, such as change in the apparent size or duration of the stimuli, might explain our results.

Methods

Stimuli and Experimental Protocols

Experiment One. This experiment investigated contrast discrimination performance for a range of stimulus intensities. Stimuli were presented on an Octopus 900 perimeter (Haag-Streit AG, Koeniz, Switzerland) with a maximum projected stimulus intensity of 1273 cd/m^2 above the 10 cd/m^2 background. For convenience of comparison with other results in the literature, all stimulus intensities are expressed as HFA equivalents. We controlled the perimeter externally using a computer via the Open Perimetry Interface.[16] Stimuli were 0.43° diameter spots (Goldmann Size III) presented for 200 ms, with an interstimulus interval of 1.5 seconds. We measured luminous contrast discrimination using a two-interval forced choice (2-IFC) task. In one randomly selected interval, an increment of 27, 23, 19, 15, or 11 dB (contrasts of 63, 158, 396, 1000, or 2495%, respectively) was presented, which we refer to as the lower intensity stimulus. In the other interval, we presented a stimulus of higher intensity, using a method of constant stimuli. Participants were instructed to select the interval that contained the highest intensity stimulus by means of a button push (310 Gamepad controller; Logitech, Lausanne, Switzerland) connected to the driving computer. Auditory feedback, produced by the computer, indicated the correctness of each response. Stimuli were presented interleaved at 0°, 9° (temporal), and 21° (nasal) eccentricity. Seven intensities above each lower intensity stimulus were used.

Any (≥0.25 DC) astigmatic component in the participant's subjective refraction was fully corrected with a trial lens when testing in the perimeter bowl. A spherical lens also was added if required. Testing was monocular, with the untested eye occluded with an opaque patch. Participants removed the patch at the end of each run and room lights were switched on to avoid large differences in interocular adaptation occurring over the course of the experiment.[17] Testing was broken up into runs of 105 discrimination judgments, which took approximately 5 minutes each to complete and in which all combinations of intensities and eccentricities were presented interleaved. For each run, the computer generated 1000 potential random orders for the stimuli and then selected the order that minimized consecutive pairs of stimuli appearing at the same eccentricity. After an initial training run, participants performed 40 runs over the course of 4 or 5 test sessions, thereby giving a total of 40 presentations at each step in our method of constant stimuli.

Experiment Two. It might be thought that our contrast discrimination task is able to be performed on cues other than perceived stimulus intensity, such as alterations in the perceived size or duration of the stimulus. Indeed, it is known that changes in stimulus contrast can cause small changes in the apparent size of an object.[18] Therefore, this experiment investigated whether contrast discrimination for a fixed pair of stimulus intensities (11 vs. 15 dB) altered if duration or size of the stimulus was randomly altered (jittered). Introducing jitter is a well-established method in psychophysics to mask unwanted stimulus cues.[19–23] Specifically, as jitter magnitude increases, performance based on the stimulus dimension being jittered will tend toward chance (50% discrimination) in a 2-IFC experiment. If size or duration is an important cue for discrimination in our Experiment One, the addition of jitter should mask these cues and make them unreliable and so impair performance. We presented stimuli on a gamma corrected computer monitor (Cambridge Research Systems Display++, resolution 1920 × 1080, frame rate 75Hz, subtending 18° by 10°; Cambridge Research Systems Ltd, Kent, UK) to allow fine control of stimulus size and duration. The

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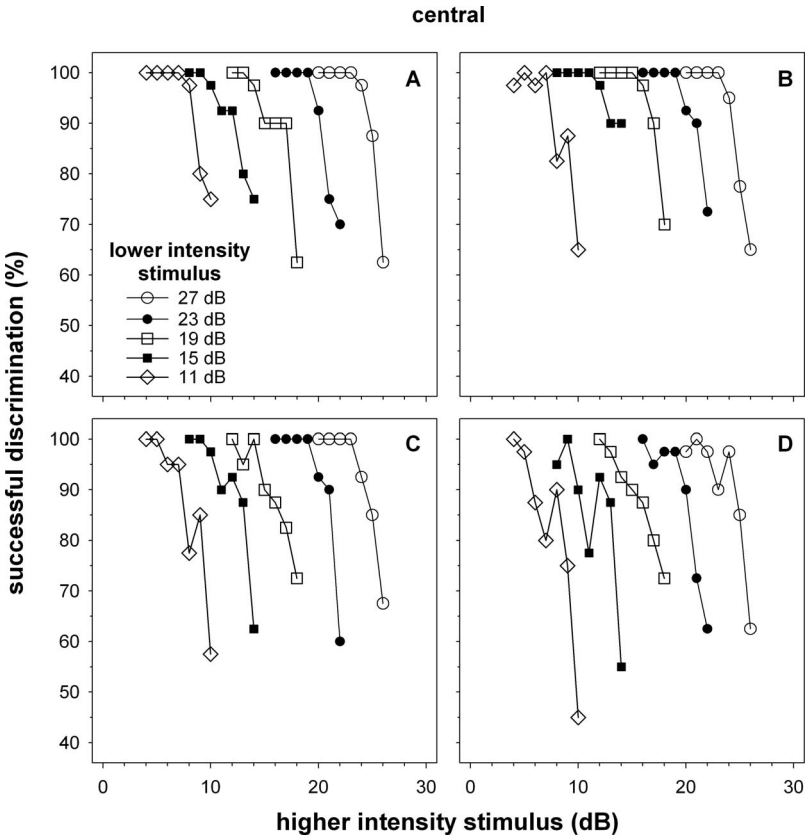

FIGURE 1. Discrimination functions for perimetric stimuli presented at fixation. The *key* gives the intensity of the less intense stimulus in each pair, expressed in HFA dB units. Panels show data from participants A through D. As an example, when Participant A (*top left*) attempted to discriminate a pair of stimuli consisting of a lower intensity stimulus of 23 dB (curve consisting of *filled circles*) and a higher intensity stimulus of 20 dB (*third datum* from the *right* on this curve), they could do so 93% of the time.

background luminance was reduced slightly (to 7.5 cd/m^2) from that in Experiment One to allow high incremental contrasts to be presented. The stimulus was a square of width 0.38°, thereby giving a stimulus area matched to a conventional Size III perimetric target. We used a 2-IFC discrimination task and a 1.5-second interstimulus interval, with targets presented monocularly at 9° eccentricity for a nominal duration of 200 ms. We collected 60 presentations for each of the three manipulations (size jitter alone, duration jitter alone, and simultaneous size and duration jitter) in separated experiments, interleaved in a counterbalanced design with 60 control trials (no manipulation applied). Binocular light adaptation was restored in between each run of 30 judgments.[17] For size jitter, the stimulus size on each interval was altered by a random amount of up to ±10% (sampled from a uniform distribution). For comparison, the Weber fraction for size discrimination thresholds is approximately 5%.[24] For duration jitter, the duration of the stimulus for each interval was altered by either 0 to 2 additional display frames of 13.3 ms each (i.e., up to a total of 13% longer). For comparison, the Weber fraction for interval duration discrimination thresholds is approximately 5%.[25]

Curve Fitting and Statistical Analysis

We used a maximum likelihood estimation method to fit cumulative Gaussian distributions to the frequency-of-seeing curves generated from our discrimination experiment in Experiment One.[26] For such fits, it is necessary for the change being discriminated to be expressed in such a way that an infinitely small change appears at minus infinity on a log axis. This is not achieved by our data expressed in raw perimetric dB values as presented in Figures 1 through 3, and so fitting conventional frequency-of-seeing curves to data presented in such a way is inappropriate. As such, the independent variable for the fit was the log increase in Weber contrast for each stimulus pair, that is $\log([L_2 - L_1]/L_1)$, with L_x reflecting the luminance of the appropriate stimulus, ignoring the 10 cd/m^2 background of the perimeter bowl. False-positive and lapsing probabilities were incorporated using Abbott's formula,[26] with false-positive probabilities fixed at 0.5 due to the forced-choice nature of the experiment. We analyzed differences in slopes, thresholds, and lapsing probabilities as a function of eccentricity using a 2-way repeated measures ANOVA.

Participants

Four healthy observers (aged 44, 45, 29, and 29; observers A through D) participated in Experiment One. As noted in the Introduction, the idea of response saturation being a candidate mechanism for perimetric variability is based on known responses in normal retinal ganglion cells, rather than on presumed changes to ganglion cell function as a result of glaucoma.[5] As such, it is only possible to test this theory by investigating responses in healthy observers: measuring contrast discrimination in observers with glaucoma would not allow the theory proposed by Gardiner et al.[5] to be tested.

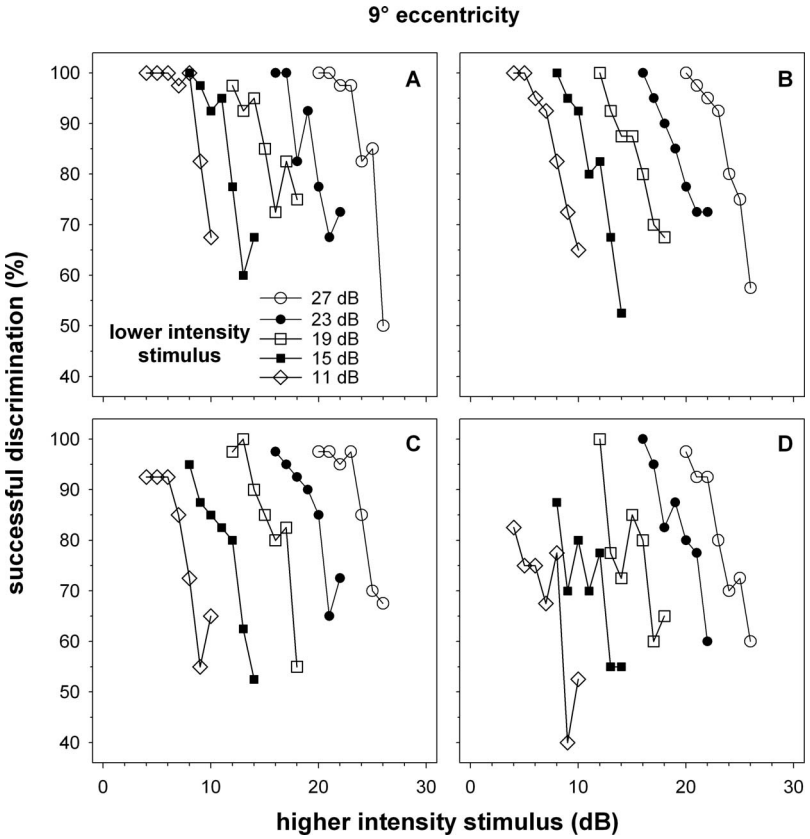

FIGURE 2. Discrimination functions for stimuli presented at 9° eccentricity. Remaining details are as given in the legend for Figure 1.

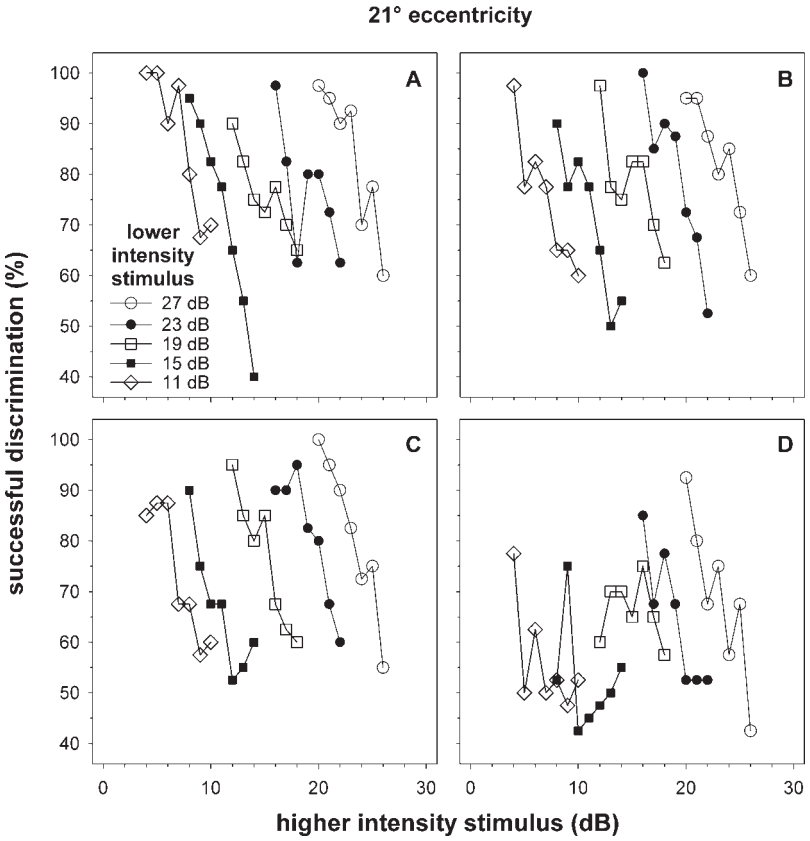

FIGURE 3. Discrimination functions for stimuli presented at 21° eccentricity. Remaining details are as given in the legend for Figure 1.

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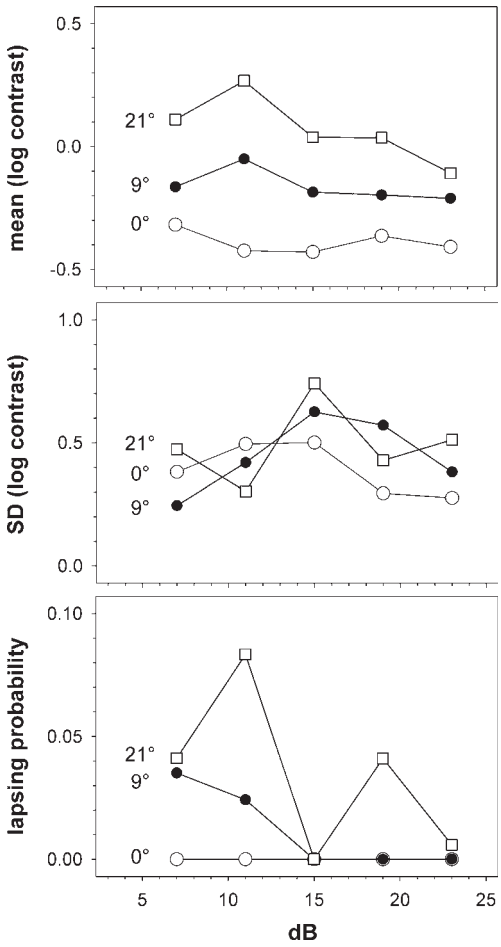

FIGURE 4. Median fit parameters for cumulative Gaussian (or cumulative normal) distributions fit to the psychometric function data in Figures 1 through 3. Mean (*upper*), the mean of the cumulative Gaussian, with increasing values corresponding to a rightward translation of psychometric function; SD (*middle*), the standard deviation of the cumulative Gaussian, with increasing values corresponding to a flattening of the psychometric function slope; Lapsing probability (*lower*), how far away the upper asymptote of the psychometric function is away from 1.0 (i.e., perfect performance in discriminating large contrast differences).

Observers A and B were authors, with observers C and D being naïve to the specific hypotheses of the experiment. All participants had monocular visual acuities of 6/6 or better, and no known eye disease or systemic conditions known to affect vision, such as diabetes, uncontrolled hypertension, or active migraine. Participants had their intraocular scatter measured using an Oculus (Wetzlar, Germany) C-Quant straylight meter (Software version 2.73r19), as well as refractive error at 0°, 9°, and 21° eccentricity measured using a Shin-Nippon (Tokyo, Japan) SRW-5000 Natural Vision Auto Refractometer. During these latter measurements, participants viewed a pin target at a radial distance approximately matched to where the Octopus perimeter bowl would be. As expected from their age, observers A and B had the highest intraocular scatter measures of the group: only these observers participated in Experiment Two. The study complied with the tenets of the Declaration of Helsinki, and was approved by the authors' institutional ethics committee, with participants giving informed consent before participating.

RESULTS

Figure 1 shows the discrimination performance in Experiment One for the four observers when viewing the stimuli foveally, expressed as frequency-of-seeing curves. For all observers, discrimination success exceeded 90% provided the intensity of the more intense stimulus in the pair was sufficiently great. This held true even if the less intense stimulus was already $\leq$19 dB. Typically, pairs of stimuli were highly discriminable when differing by as little as 4 to 5 dB. The shapes of the curves were similar for the range of less intense stimulus intensities investigated. A similar result was obtained for stimuli presented at 9° (Fig. 2), although curves typically were translated to the left (reflecting an increase in discrimination thresholds) and Participant D did not reach discrimination performance above 90% for the two most intense stimuli we presented. Participant D did, however, still achieve performance in excess of 75%, being a point on the 2-IFC frequency-of-seeing curve equivalent to a 50% threshold in perimetry (i.e., in a yes/no task).

The horizontal translation of the frequency of seeing curves continued when stimuli were presented at 21° (Fig. 3). For Participants A through C, discrimination performance still exceeded 90% for sufficient intense stimuli, save for one exception (Participant C, lower intensity stimulus of 11 dB, 85% discrimination success for most intense stimulus). For Participant D, however, curves were shifted sufficiently to the left that reliable discrimination could not be achieved except when the least intense stimulus in the pair was low (27 dB).

To quantify the trends seen in Figures 1 through 3, we fitted cumulative Gaussian curves to the data, expressed as increments in Weberian contrast (see Methods). Fit parameters are shown in Figure 4, using the median value from the observers to provide robustness against instances where our data would be poorly fit in a single observer (e.g., Fig. 3, observer D). Consistent with the leftward shift in our data with eccentricity seen in Figures 1 through 3, the mean of the fitted cumulative Gaussian curves increases as eccentricity increases (Fig. 4, upper panel). The mean changes little as a function of the lower intensity stimulus, however. The standard deviation of the cumulative Gaussian (middle panel) relates to the slope of the frequency of seeing curve, and there is no apparent systematic change in this parameter as a function of either the lower intensity stimulus or of eccentricity. The lapsing probability is less than 0.1 for all conditions, indicating that the fitted psychometric functions reached discrimination probability of >0.9 at their upper asymptotes. A 2-way repeated measures ANOVA on the fit parameters confirmed that the mean of the cumulative Gaussian significantly increased with eccentricity ($F[2, 24] = 5.34$, $P = 0.047$), but that there was no significant alteration in the remaining parameters (all other $P > 0.05$).

The results of Experiment Two are shown in Figure 5. For all three manipulations (jittered size, jittered duration, simultaneous size and duration jitter), discrimination performance was not significantly altered, suggesting that none of these cues was being used to perform the discrimination task. This is consistent with the perceptual observations from both subjects, who reported that the targets differed in their apparent luminance.

All participants had straylight values less than the average age expected value,[27] indicating lower than average levels of intraocular scatter (see Table). Off-axis refractive error changes were less than 1.00 diopter (D) when expressed as spherical equivalents, with less than 2.00 DC cylindrical component (see Table).

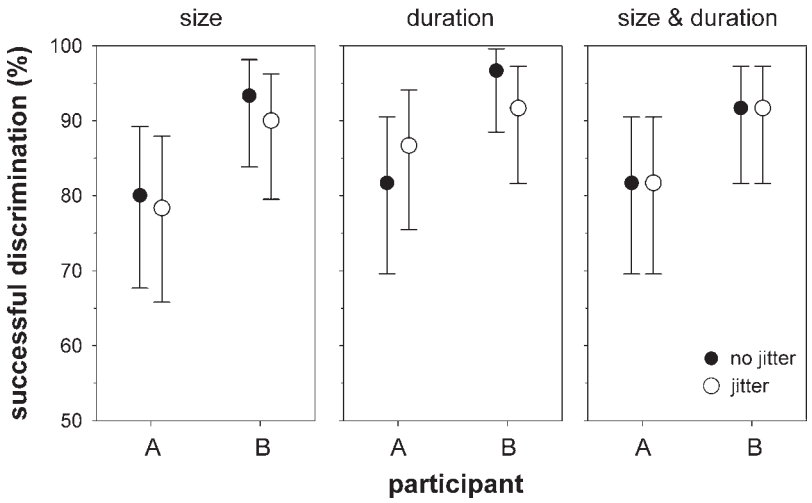

Figure 5. Effect of stimulus jitter on discriminating an 11 dB from a 15 dB stimulus. Size jitter was randomly selected from a uniform distribution of ±10%, with duration jitter being randomly selected to be from zero to two additional display frames (i.e., up to +13%). Stimuli were presented at 9° eccentricity. *Error bars*: 95% confidence intervals.[38]

Discussion

We find no evidence for saturation of the visual system with intense perimetric stimuli when measuring contrast discrimination for central targets and with targets located at a moderate eccentricity of 9°. Increases in stimulus intensity could be detected reliably by our participants even for stimuli above those believed to cause ganglion cell saturation (Figs. 1, 2).[5] As visual perception is necessarily mediated through retinal ganglion cells, our results indicated that the more intense stimulus in our experiments produced a perceptually significant increase in ganglion cell firing for at least some cells relative to the less intense stimulus. Jittering the size and duration of the stimulus had no influence on performance, indicating that alterations in the perceived size or duration of the stimulus were not cues being used to perform the contrast discrimination task. Although performance typically was poorer when targets were presented at larger eccentricities closer to the edge of a 24-2 visual field, discrimination performance always exceeded 80% correct and commonly exceeded 90% even when both stimuli were intense, for three of our four observers (Fig. 3).

The ganglion cell responses to perimetric stimuli measured by Swanson et al.[6] were from cells between 5° and 15° eccentricities, and so should most closely reflect ganglion cell processing underlying our stimulus at 9°. Why, then, is there almost no sign of response saturation seen in our data? As noted in the introduction, although magnocellular cells may saturate for perimetric stimuli of approximately 15 to 19 dB, parvocellular cells likely do not. The theory proposed by Gardiner et al.[5] is based on the response properties of magnocellular cells only. Semisaturation constants for parvocellular cells exceeded the maximum contrast tested by Swanson et al.[6] (25 dB for all cells, and up to 18 dB in a subset of cells) and so were poorly constrained by their experimental data. Kaplan and Shapley[28] similarly found no evidence of saturation for parvocellular cells, albeit using a lower maximum contrast of 64% (27 dB). As the receptive fields of different ganglion cell classes overlap, even if one cell class saturates there is the opportunity for another cell class to detect the stimulus. This redundancy for detecting stimuli is likely further enhanced by there being an estimated 20 distinct classes of retinal ganglion cells, with each class perfectly tiling the retina and so being able to respond to specific characteristics of a stimulus located anywhere in the visual field.[29] Therefore, trying to predict overall visual function based on the response characteristics of a single ganglion cell class may well be impossible. There also is the possibility that ganglion cell responses measured in anesthetized nonhuman primates do not fully reflect ganglion cell functioning in awake human observers. Different anesthesias can differently alter electrophysiologic responses from the retina.[30] Anesthesia also abolishes eye movements and, therefore, stabilizes retinal images, and it is known that stabilizing retinal images in humans results in a marked increase in thresholds over a broad range of spatial frequencies.[31] Furthermore, stimuli typically

Table. Straylight Values and Peripheral Refractive Errors for Each Participant

Participant	Straylight Value, log(s) (±SE)	Change in Refractive Error			
		Spherical Equivalent (±SE)		Cylinder (Absolute) (±SE)	
		9°	21°	9°	21°
A	0.92 (±0.00)	0.09 (±0.16)	−0.27 (±0.27)	1.42 (±0.23)	1.88 (±0.48)
B	0.92 (±0.00)	−0.08 (±0.04)	−0.92 (±0.13)	0.35 (±0.21)	1.53 (±0.12)
C	0.64 (±0.03)	0.11 (±0.12)	−0.14 (±0.28)	1.15 (±0.15)	1.79 (±0.12)
D	0.68 (±0.02)	−0.03 (±0.11)	−0.56 (±0.11)	0.38 (±0.34)	0.81 (±0.11)

Straylight values are the average of three reliable measurements, with reliability determined automatically by the C-Quant (= esd ≤ 0.08 and Q ≥ 0.5). Changes in refractive error are calculated from the difference in obliquely crossed spherocylindrical autorefraction results taken centrally and eccentrically, with negative spherical equivalent values indicating more myopic peripheral refractions. Values represent the average of four pairs of measurements.

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are arranged to cover the entire receptive field being measured in electrophysiology experiments, whereas in natural vision, receptive fields underlying the stimulus edge may be only partly stimulated. Overall, we believe that the presence of multiple ganglion cell classes is likely to be the principal reason why a single class of cell may be shown to saturate, whereas responses from the entire visual system do not.

Given that we find little evidence for response saturation in healthy eyes, how are we to interpret the results of Gardiner et al.?[5] One explanation would be that ganglion cells become dysfunctional before death in glaucoma and that a manifestation of this dysfunction is that cell responses saturate at lower stimulus intensities. Previous behavioral evidence has suggested that the response of retinal ganglion cells may be impaired before cell death.[32,33] Such dysfunction might reflect direct damage to cells, as in the dendritic shrinkage noted in animal models of glaucoma,[34] or may reflect surrounding cell death altering the normal lateral inhibition that shapes a cell's response.[35,36]

Although the physical contrasts of our perimetric stimuli are well described, it is possible that scattered light reduces the effective retinal contrast and, therefore, the potential for saturation. Our participants were all aged less than 50, and age-related increases in scatter are small below this age.[37] Furthermore, our participants had measured intraocular scatter values below the average value expected based on age-matched normative data,[37] and had visual acuities of 6/6 or better. Therefore, we are confident that any effect of scatter on our results is lower than that seen in clinical investigation where increased perimetric variability—and, therefore, presumed ganglion cell saturation—has been demonstrated.[1–4] This reduced light scatter in our participants would predict that there should be an increase in saturation seen in our results relative to previous clinical investigations, which is the opposite of our findings. Spread of light on the retina due to optical defocus would be expected to act similarly to light-spread due to scatter. Our protocol fully corrected any cylindrical component in the participant's subjective refraction, and so we are confident that any influence of a blur-induced reduction in retinal image contrast is smaller than in clinical investigations where small cylindrical corrections are ignored. Indeed, our protocol should have completely removed any blur for our targets presented at the fovea, which again should have increased the amount of saturation in our data, yet no evidence of response saturation was found. Our participants did, however, show increasing amounts of off-axis astigmatism as eccentricity increased (see Table). It should be noted that the electrophysiologic investigation of retinal ganglion cell responses themselves used stimuli imaged by the optics of the eye and so were presumably subject to normal levels of intraocular scattering and uncorrected off axis-astigmatism.[6] Because of this, these factors alone do not represent a reason for why electrophysiologic measures in animals might differ from behavioral measures in humans. Importantly, the results of our Experiment Two showed that any alteration in the apparent size of the stimulus that might arise from light spread was not a necessary cue to reliably perform our contrast discrimination task.

In summary, we showed an increase in the intensity of already very intense perimetric stimulus can be reliably discriminated in most situations, indicating that responses of the human visual system are not saturated by such stimuli. Although it is undisputed that perimetric sensitivities less than approximately 19 dB in glaucoma must be interpreted with caution due to their high variability, the cause of this variability is not readily predicted by our current knowledge of how normal ganglion cells respond. As such, our results challenge the validity of the mechanism to explain sensitivity variability in damaged field locations recently proposed by Gardiner et al.[5] that is based on response characteristics of normal ganglion cells.

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