

Visual Crowding in Glaucoma

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Submitted: July 1, 2018

Accepted: December 1, 2018

Citation: Ogata NG, Boer ER, Daga FB, Jammal AA, Stringham JM, Medeiros FA. Visual crowding in glaucoma. *Invest Ophthalmol Vis Sci*. 2019;60:538–543. <https://doi.org/10.1167/iovs.18-25150>

PURPOSE. Crowding refers to the phenomenon in which objects that can be recognized when viewed in isolation are unrecognizable in clutter. Crowding sets a fundamental limit to the capabilities of the peripheral vision and is essential in explaining performance in a broad array of daily tasks. Due to the effects of glaucoma on peripheral vision, we hypothesized that neural loss in the disease would lead to stronger effects of visual crowding.

METHODS. Subjects were asked to discriminate the orientation of a target letter when presented with surrounding flankers. The critical spacing value (s_{critical}), which was required for correct discrimination of letter orientation, was obtained for each quadrant of the visual field. s_{critical} values were correlated with standard automated perimetry (SAP) mean sensitivity (MS) and optical coherence tomography (OCT) retinal nerve fiber layer (RNFL) thickness measurements.

RESULTS. The study involved 13 subjects with mild glaucomatous visual field loss and 13 healthy controls. Glaucomatous eyes had significantly greater (worse) s_{critical} than controls (170.4 ± 27.1 vs. 145.8 ± 28.0 minimum of visual angle, respectively; $P = 0.007$). s_{critical} measurements were significantly associated with RNFL thickness measurements ($R^2 = 26\%$; $P < 0.001$) but not with SAP MS ($P = 0.947$).

CONCLUSIONS. In glaucoma patients, a pronounced visual crowding effect is observed, even in the presence of mild visual field loss on standard perimetry. s_{critical} was associated with the amount of neural loss quantified by OCT. These results may have implications for understanding how glaucoma patients are affected in daily tasks where crowding effects may be significant.

Keywords: glaucoma, visual crowding, visual function

In the peripheral visual field, objects that are clearly identifiable when shown in isolation become impossible to recognize when presented close together. For every location within the visual field, there is a critical spacing (s_{critical}) that must be exceeded for unimpaired recognition (i.e., if the objects are closer together than the s_{critical}) they are perceived as an unidentifiable jumble.^{1–5} This phenomenon is known as visual crowding and sets a fundamental limit on conscious visual perception. The phenomenon is illustrated in Figure 1, where one can easily perceive the target in isolation (the key on the left), but not in the presence of clutter (the key on the right). Crowding impairs the ability to recognize objects in clutter, and is therefore essential in explaining performance in a broad array of daily tasks, such as visual search and reading.¹

Previous work has shown that the loss of information in the periphery relative to the fovea goes much beyond issues of acuity.⁶ In fact, reduced peripheral acuity has only a modest effect on visual performance when compared with visual crowding.⁷ Crowding represents a bottleneck for recognizing objects in the periphery, and therefore its characterization may also offer insight into how object recognition works. However, despite the initial description in 1936³ and the recent progress in better understanding the crowding phenomenon, there is not a complete comprehension of its mechanisms.⁸ It appears that the phenomenon may be explained by a two-stage model in which the first stage involves detection of simple features in

cortical area V1, and the second stage involves the integration of features (as an object) at an area downstream of V1.^{8,9} In the periphery, these ‘integration receptive fields’ may be too large and, as a consequence, objects that are too close together are merged into a percept that is described as jumbled.⁹

Glaucoma is an optic neuropathy associated with progressive loss of visual field. The disease is a leading cause of blindness and visual impairment in the world.¹⁰ Loss of vision from glaucoma tends to disproportionately affect peripheral vision and may impact the ability to perform many daily tasks, such as visual search, reading, walking, and driving.¹¹ Despite the relevance of crowding to peripheral vision and the fact that glaucoma is the most common condition affecting the peripheral field, no study has yet investigated the effects of glaucomatous damage on visual crowding. Although crowding is recognizably a cortical phenomenon, loss of retinal ganglion cells in glaucoma may lead to change and reorganization of cortical receptive fields.^{12,13} Therefore, it is not unreasonable to speculate that the disease could potentially exert a significant effect on visual crowding in the periphery.

In the present study, we performed an investigation of visual crowding in patients with glaucoma as compared with healthy subjects. In order to investigate the hypothesis that glaucomatous damage is associated with worsening of crowding effects in peripheral vision, we collected psychophysical measurements of visual crowding, along with structural assessment of



FIGURE 1. A real-world example of visual crowding. While fixating the middle of the keyboard, note the relative ease of detecting and identifying the key to the left (presented in isolation) versus the key on the right (presented with clutter).

nerve tissue loss by optical coherence tomography (OCT), and standard automated perimetry (SAP).

METHODS

The study included 13 subjects with glaucomatous visual field loss and 13 controls. Participants from this study were drawn from a prospective longitudinal study designed to evaluate functional impairment in glaucoma. The institutional review board approved all the methods, and written informed consent was obtained from all participants. The study adhered to the laws of the Health Insurance Portability and Accountability Act, and all study methods complied with the Declaration of Helsinki guidelines for human subject research.

All participants underwent a comprehensive ophthalmologic examination including review of medical history, visual acuity, slit-lamp biomicroscopy, IOP measurement using Goldmann applanation tonometry, corneal pachymetry, gonioscopy, dilated funduscopy examination using a 78-diopter lens, stereoscopic optic disc photography, SAP using the 24-2 Swedish Interactive Threshold Algorithm (SITA) Standard of the Humphrey Field Analyzer II, model 750 (Carl Zeiss Meditec, Inc., Dublin, CA, USA), and OCT. Only subjects with open angles on gonioscopy were included. Patients with coexisting retinal disease, uveitis, or nonglaucomatous optic disc neuropathy were excluded from the study.

Glaucoma was defined as the presence of two or more consecutive abnormal SAP tests at baseline, characterized by a pattern standard deviation (PSD) with $P < 0.05$ and/or glaucoma hemifield test results outside normal limits, and evidence of glaucomatous optic neuropathy based on masked assessment of stereo photographs. Healthy control subjects were recruited from the general population and had IOP of 21 mm Hg or less, SAP results within normality, and were required to have normal appearance of the optic disc on masked grading of stereo photographs.

Standard Automated Perimetry

Only reliable tests ($\leq 33\%$ fixation losses and false-negative results, and $\leq 15\%$ false-positive results) were included. Visual fields were reviewed and excluded in cases where other factors influenced the results, such as eyelid or lens rim artifacts, fatigue effects, inattention, or inappropriate fixation. Visual fields were also reviewed for the presence of abnormalities that could indicate diseases other than glaucoma. The worse eye of each patient was selected for testing, as indicated by the mean

deviation (MD). If SAP MD of the worse eye was ≤ -20 dB, the better eye was used. For each quadrant of the visual field we obtained a mean sensitivity (MS) value by obtaining the geometric average of the threshold sensitivities of the corresponding points.

Optical Coherence Tomography

Spectral-domain OCT (Spectralis SD-OCT, software version 5.4.7.0; Heidelberg Engineering, Heidelberg, Germany) was used to measure the retinal nerve fiber layer (RNFL) thickness in the present study. Details of the instrument have been published elsewhere.¹⁴ Peripapillary RNFL thickness measurements were obtained within a 3.45-mm circle scan centered on the optic disc. All images were reviewed to ensure good quality, with signal strength greater than 15 dB. RNFL thickness measurements were extracted corresponding to the quadrant areas determined by SAP using a previously described structure-function map.¹⁵

Visual Crowding Assessment

Assessment of visual crowding was based on quantifying the s_{critical} (i.e., the distance at which flankers degrade the performance in recognizing a target). The target was a letter T, which could be oriented up (“T”) or down (“⊥”), presented at 10° of eccentricity in each quadrant of the field of view as follows: temporal superior, nasal superior, temporal inferior, and nasal inferior. The target was surrounded by radial flanking distractors (letter “H”), presented at varying distances from the target during the experiment (Fig. 2). The experiment was performed using a 40-in LCD screen in a darkened room. The screen was centered at the subject’s eye level, at 43.3 in of distance, allowing the target to be positioned at 10° of eccentricity, with a fixed letter size corresponding to 1.3° of visual angle. All letters were presented in black on a white background and were of identical height and width.

Subjects were instructed to fixate a central point before stimulus onset and to maintain central fixation during the trials. The target and flankers were presented for 240 ms and randomly interleaved by quadrant. The subjects were required to indicate whether they saw the upright or downright “T” by pressing the appropriate key on the computer keyboard, in a two-alternative forced choice task (2-AFC). Following the response, a new trial was started. No feedback was given. The experiment consisted of 12 blocks of 50 trials each, giving a total of 600 trials. Between blocks, the subjects received a short break to avoid fatigue. Within each block, the spacing between target and flankers was randomly intermixed. Spacing conditions appeared with equal probability (including a “target-only” condition where the target appeared without distractors). A test block of 50 trials with feedback was performed before the experiment, so that the experimenter was sure that the subject understood the procedure. Participants who were unable to maintain fixation were excluded from the study.

Crowding occurs when target-flanker spacing falls below a critical value and recognition of the target letter is reduced. We computed the s_{critical} value by fitting a logistic psychometric function to the data relating accuracy of target detection versus spacing between target and flankers. s_{critical} was considered as the spacing corresponding to 75% accuracy, as in a conventional 2-AFC experiment.¹⁶

In order to isolate the effect of crowding from that of simply missing the target due to visual field loss, it was important to ensure that subjects could see the target in isolation. Therefore, for each quadrant, we required subjects to have 90% accuracy in identifying the target when presented in

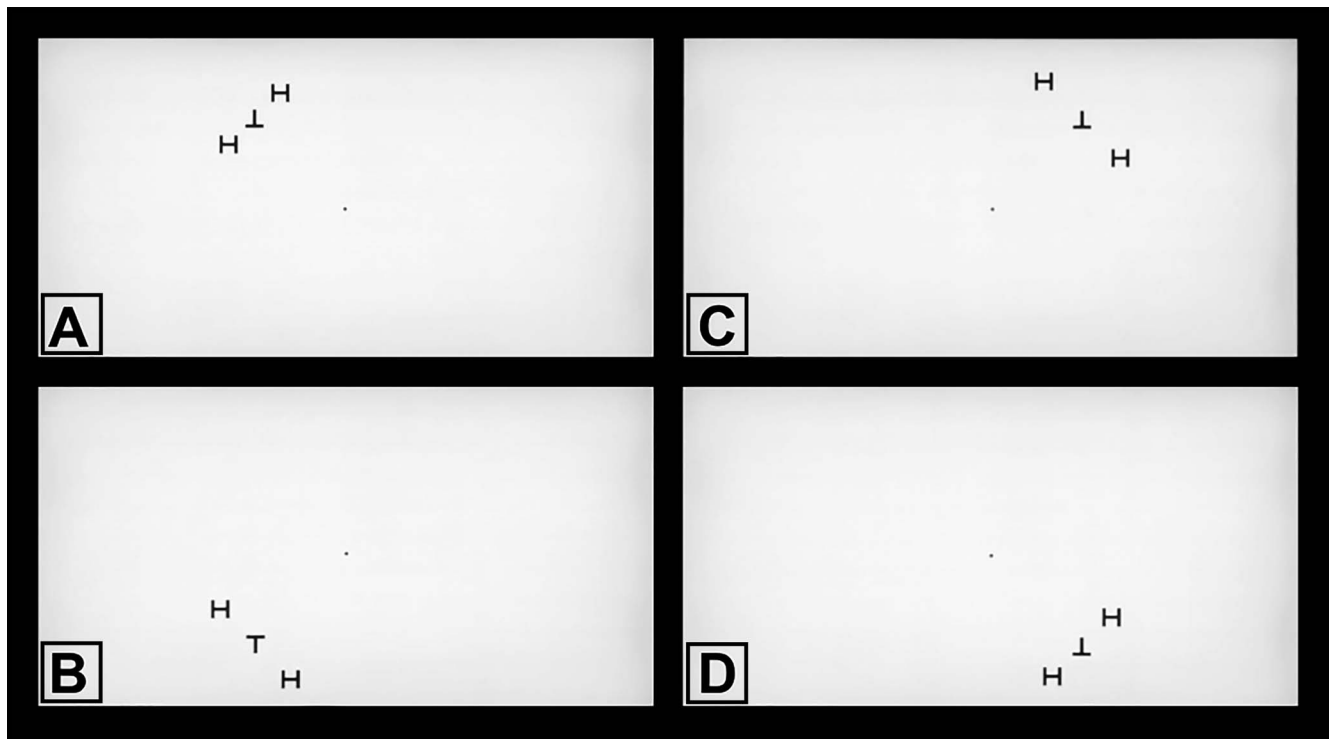


FIGURE 2. Screenshots of the visual crowding test. While fixating the center dot, subjects were required to identify the visual target stimulus (either upright or downright letter “T”) surrounded by radial flanking distractors (letter “H”). Target stimuli were presented at 10° of eccentricity, one quadrant at a time, in random order: (A) upper left quadrant, (B) lower left quadrant, (C) upper right quadrant, and (D) lower right quadrant. Note the variable spacing between the target and the flankers. The distance at which flankers degraded the performance in recognizing the target was considered the critical spacing.

isolation.^{8,17} If 90% accuracy was not achieved for a particular quadrant, calculations of s_{critical} were not performed for that quadrant and the quadrant was excluded from further analyses.

Statistical Analysis

Descriptive statistics included mean and SD. Normality assumption was assessed by inspection of histograms and using Shapiro-Wilk tests. Student’s *t*-tests were used for group comparison for normally distributed variables and Wilcoxon rank-sum tests for continuous nonnormally distributed variables.

We initially ran univariable models investigating the relationship between OCT RNFL thickness and s_{critical} . Subsequently, multivariable models were used, adjusting for potential confounding factors such as age, sex, and race. Generalized estimating equations (GEE) with robust sandwich variance estimators were used to adjust for potential correlations between measurements obtained in the same individual.

s_{critical} were obtained using Matlab software (MathWorks Inc., Natick, MA, USA). The psychometric curves for illustration purposes were obtained using OriginPro (OriginLab Corporation, Northampton, MA, USA). All other statistical analyses were performed with commercially available software (Stata, version 14; StataCorp LP, College Station, TX, USA). The α level (type I error) was set at 0.05.

RESULTS

Demographic and clinical characteristics are summarized in Table 1. There were no statistically significant differences in age, sex, or race between the groups. As expected, glaucoma eyes had significantly thinner global OCT RNFL thickness than

healthy subjects (66.2 ± 12.2 vs. 77.2 ± 10.8 μm ; $P = 0.027$) as well as significantly higher SAP PSD (4.7 ± 3.6 vs. 2.6 ± 2.0 dB; $P = 0.038$). Glaucoma eyes had lower SAP MD compared with controls, although the difference did not reach statistical significance (-3.0 ± 3.1 vs. -1.3 ± 2.5 dB; $P = 0.130$).

For the visual crowding task, subjects performed a total of 15,600 trials. In 35 quadrants of 20 subjects, the 90% accuracy cutoff for seeing the target in isolation was not achieved and, therefore, these quadrants were not used in calculations of s_{critical} , leaving 69 quadrants from 26 subjects for analysis. For these 69 quadrants, there was no statistically significant difference in SAP MS by quadrant in glaucomatous versus healthy eyes (28.2 ± 2.1 vs. 29.3 ± 2.5 dB; $P = 0.514$; GEE), reflecting the requirement that subjects had still relatively preserved vision in each quadrant to see the target in isolation. However, for these quadrants, glaucomatous eyes had significantly greater s_{critical} compared with healthy eyes (170.4 ± 27.1 vs. 145.8 ± 28.0 minimum of visual angle; $P = 0.007$; GEE), indicating a significantly worse crowding effect in glaucoma.

Table 2 summarizes the relationships between s_{critical} and several predictor variables. A significant association was found between s_{critical} and the corresponding OCT RNFL thickness in each quadrant ($R^2 = 26\%$; $P < 0.001$; Fig. 3). However, the correlation between s_{critical} and SAP MS values per quadrant was not found to be significant ($R^2 = 0\%$; $P = 0.947$; Fig. 4). Additionally, there were no statistically significant relationships between s_{critical} and visual acuity, age, sex, or race in this sample. In a multivariable model adjusting for age, race, and sex, RNFL thickness maintained its significant association with s_{critical} . Each 10 μm lower RNFL thickness was associated with an increase in s_{critical} of 6.63 minimum of visual angle (95% CI: 3.84–9.42 min of visual angle; $P < 0.001$). Figure 5 illustrates

TABLE 1. Demographic and Clinical Characteristics of Subjects Included in the Study

	Healthy Control (<i>n</i> = 13)	Glaucoma (<i>n</i> = 13)	<i>P</i> Value
Age, y	69.7 ± 9.2	72.0 ± 9.3	0.518*
Sex, female (%)	8 (61.5)	6 (46.2)	0.695†
Race, African American (%)	3 (23.1)	2 (15.4)	1.000†
Eye tested, left eye (%)	6 (46.2)	5 (38.5)	1.000†
Visual acuity, 10 logMAR	-0.2 ± 1.1	0.0 ± 1.5	0.700‡
SAP 24-2 MD, dB	-1.3 ± 2.5	-3.0 ± 3.1	0.130‡
SAP 24-2 MS, dB	29.3 ± 2.5	28.2 ± 2.1	0.514§
SAP 24-2 PSD, dB	2.6 ± 2.0	4.7 ± 3.6	0.038‡
Global RNFL thickness, μm	77.2 ± 10.8	66.2 ± 12.2	0.027‡
<i>s</i> _{critical} , minimum of visual angle	145.8 ± 28.0	170.4 ± 27.1	0.007§

Values are presented as mean ± SD, unless otherwise noted.

* Student's *t*-test.

† Fisher's exact test.

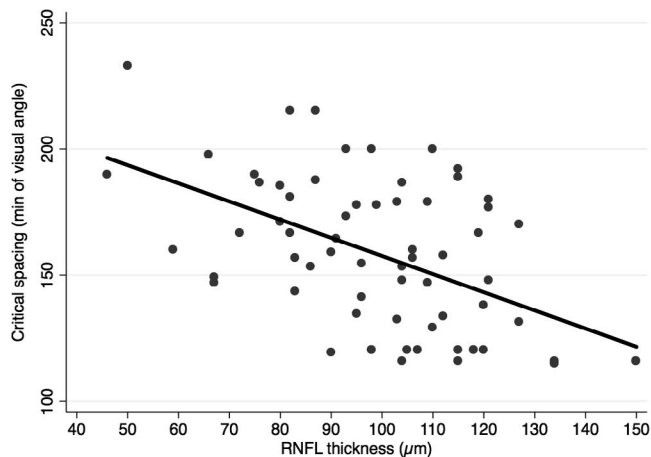
‡ Wilcoxon rank-sum test.

§ Generalized estimating equation.

psychometric functions for determining *s*_{critical} obtained from a normal and a glaucoma subject, along with SAP and OCT results. And Figure 6 illustrates the smallest (best), the typical and the largest (worst) critical spacing results from each group.

DISCUSSION

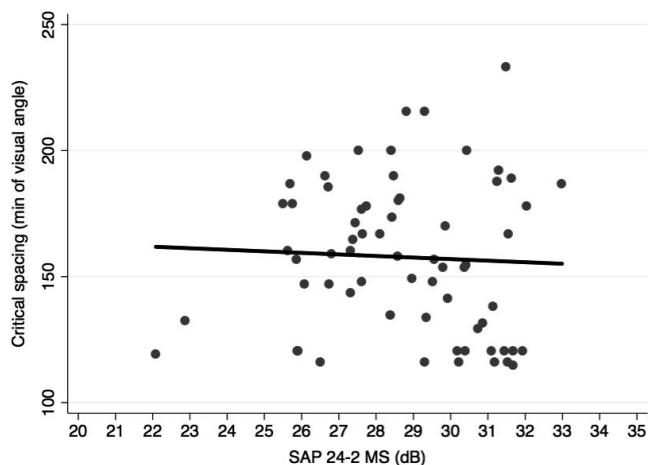
In this pilot investigation, we showed that glaucoma patients experienced a significantly greater effect of visual crowding compared with healthy subjects. The magnitude of the crowding effect, in terms of *s*_{critical}, was significantly correlated to the amount of nerve tissue loss as measured by OCT. Although patients with glaucoma were able to see and correctly discriminate target orientation when presented in isolation, they had significantly more trouble than healthy subjects in recognizing the target under crowded conditions. This result suggests that tests of visual crowding place demands on the visual system that may reveal neural losses in glaucoma earlier than identification/discrimination tasks involving isolated targets.

**FIGURE 3.** Scatterplot illustrating the relationship between critical spacing and retinal nerve fiber layer (RNFL) thickness.**TABLE 2.** Univariable Analysis for Relationships Between Critical Spacing and Possible Predictor Variables

Characteristic	Univariable Model	
	Coefficient (95% CI)	<i>P</i> Value
RNFL, per 10 μm lower	6.60 (3.80 to 9.40)	<0.001
SAP 24-2 MS, per dB lower	0.13 (-3.79 to 4.06)	0.947
Diagnosis, glaucoma	25.55 (6.89 to 44.21)	0.007
Visual acuity, per logMAR lower	20.37 (-79.15 to 119.89)	0.688
Age, per year younger	0.17 (-1.05 to 1.38)	0.788
Sex, female	10.89 (-10.07 to 31.86)	0.309
Race, African American	7.77 (-23.86 to 39.40)	0.630

In order to isolate the effect of crowding on target orientation discrimination, it was important to ensure that glaucoma subjects were actually able to see the target when presented in isolation. As in previous studies investigating visual crowding,⁸ we required subjects to accurately discriminate at least 90% of isolated targets, in each of the quadrants. As a consequence, we were only able to investigate crowding effects in quadrants that had relatively mild or undetectable field loss on standard perimetry. Despite this fact, visual crowding effects were still prominent, with glaucoma subjects exhibiting a significantly larger *s*_{critical} than healthy individuals. Importantly, the magnitude of *s*_{critical} was significantly associated with RNFL thickness measurements obtained by OCT, as illustrated in Figure 3. Each 10-μm thinner RNFL was associated with 6.6 minimum of angle increase in the *s*_{critical}. This finding suggests that assessment of visual crowding may provide a sensitive measure of visual function that corresponds well to the degree of neural tissue loss in glaucoma, even before substantial visual field loss is apparent on SAP.

Despite the widespread belief that peripheral vision is most strongly limited by its relatively low acuity compared with the fovea, the drop off in performance for visual crowding is decidedly more severe. Indeed, the slope of the decline in performance between retinal eccentricity and *s*_{critical} is much steeper than that found between eccentricity and visual acuity,⁷ which indicates that crowding exerts a much more limiting impact than acuity on the capacity of peripheral vision. As an example of this phenomenon, Anstis⁶ showed that even quite far in the periphery, visual acuity is sufficient to read isolated letters. Increasing letter density, however, made

**FIGURE 4.** Scatterplot illustrating the relationship between critical spacing and standard automated perimetry (SAP) 24-2 mean sensitivity (MS).

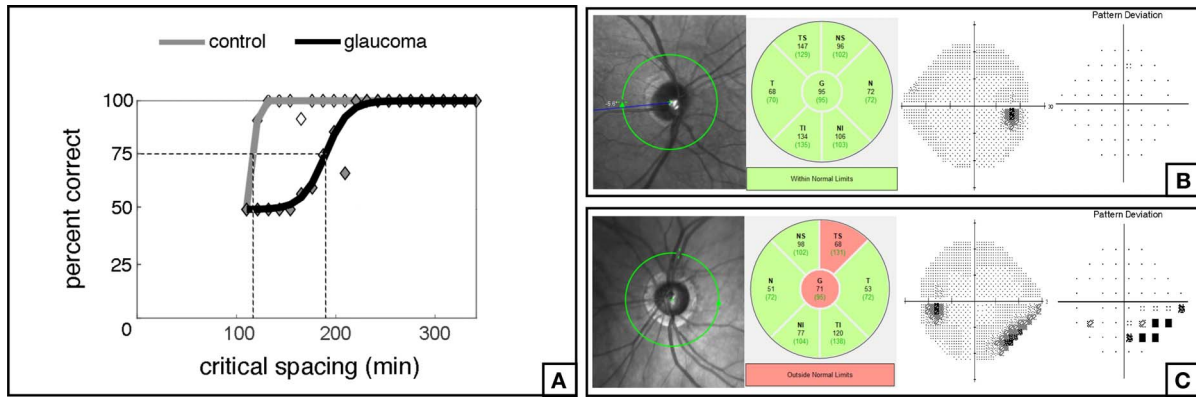


FIGURE 5. Examples of psychometric functions (A) obtained in the inferior nasal quadrant of the visual field from a normal patient (B) and a glaucoma patient (C) with their respective SAP and OCT results.

identification of single letters significantly more difficult; this accounts for why it is so difficult to read text in the periphery. As we live in a cluttered world, crowding limits the ability to perform many daily tasks, such as finding car keys on a cluttered desk (see Fig. 1), for example. Crowding impairs not only discrimination of object features, but also the ability to respond appropriately to objects in clutter. When driving, a hazard that would be clearly detected in isolation may not be recognized and acted upon if presented in a cluttered situation. Because neural losses in glaucoma appear to be associated with stronger crowding effects, our findings may have important implications for how glaucoma patients perform several daily tasks. Future studies could attempt to quantify crowding magnitude in glaucoma patients for tasks that impact safety (e.g., driving) and quality of life (e.g., reading speed).

The mechanisms underlying visual crowding are still not completely understood. It is known that crowding is a cortical

phenomenon,¹⁸ although the precise locus is unknown. This can be demonstrated by showing that significant crowding effects occur when the target and flankers are presented to each eye separately.^{19,20} It appears that cortical areas responsible for integrating object features make the features appear indistinct if they are within an “integration receptive field.”¹³ Larger integration fields occur in more eccentric regions of the peripheral vision, which would appear to explain why crowding effects are worse with eccentricity. In terms of why neural loss in glaucoma would result in worse crowding effects, previous studies have shown that retinal ganglion cell loss in glaucoma is associated with expanded regions of visual integration.^{12,13,21,22} This would likely lead to a summation of sorts, where features of objects in the periphery would be lost, in favor of simple detection. Glaucoma patients exhibit enlarged areas of summation in the periphery as shown by Redmond et al.,¹³ who found that loss of sensitivity could be completely compensated for by

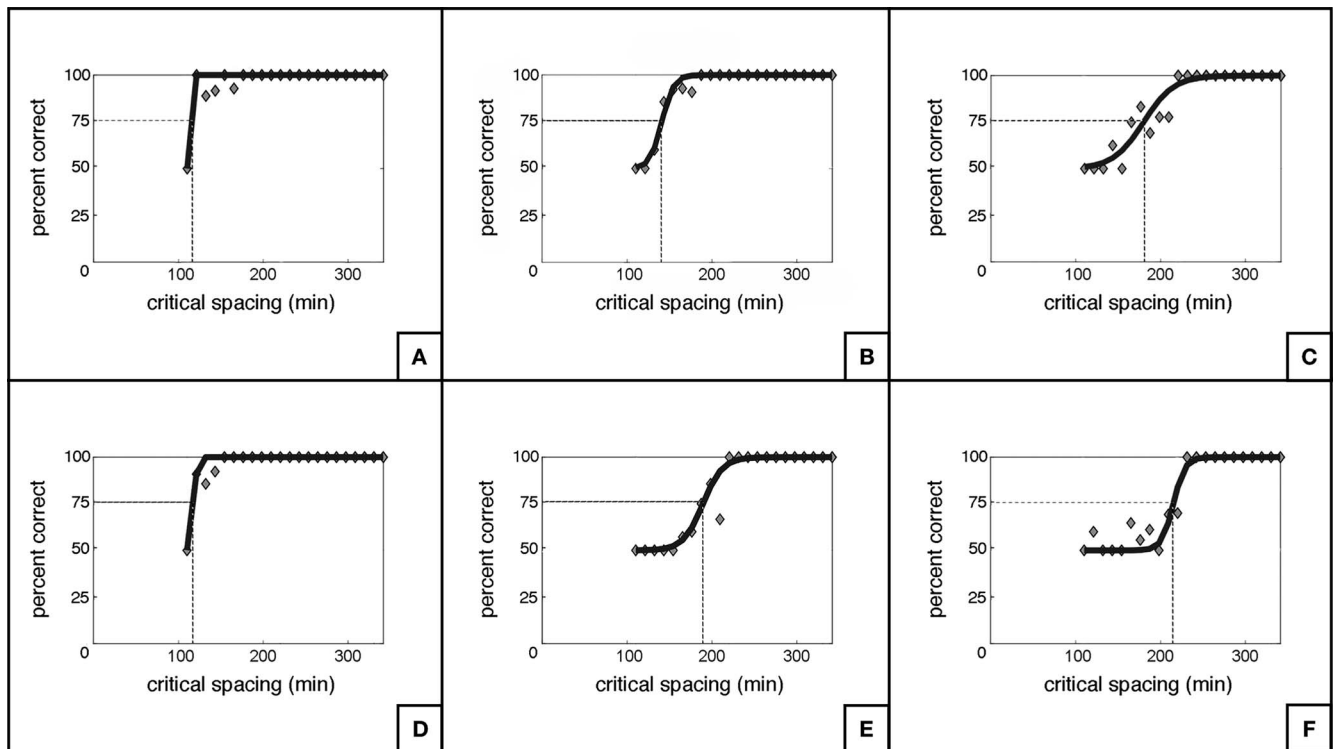


FIGURE 6. Illustration of the smallest/best (A), the typical (B), and the largest/worst (C) critical spacing results from the normal group, and the respective curves for the glaucoma group (D-F).

this neural adaptational change. Behaviorally, this idea is supported by the fact that crowding depends strongly on target/flanker similarity—the decreased sampling caused by retinal ganglion cells loss could affect feature distinction and make otherwise differentiating features appear similar when seen through glaucomatous eyes. The significant negative correlation between RNFL thickness and S_{critical} determined in the present study provide anatomic and behavioral data to support this hypothesis.

In the current study, we used a fixed letter size to study crowding effects. As the letter was of relatively small size, the requirement that it would have to be seen in isolation essentially eliminated subjects with moderate or advanced visual field loss. However, for subjects with worse field losses, crowding effects would have likely been quantifiable if targets of different sizes had been used. In terms of stimulus conditions for testing visual crowding, previous studies have shown that radially oriented flankers induce more crowding than tangentially oriented ones; this informed our choice of stimulus configuration in the present study.⁸ However, to determine fully the impact of different patterns on visual performance in crowding, future studies should investigate different stimulus configurations at different eccentricities in glaucoma patients.

Although the present study included a relatively small sample of subjects, those who participated underwent exhaustive psychophysical testing. Our results should be viewed as a pilot investigation of the relationship between visual crowding and glaucomatous damage—additional investigations with larger samples and different testing conditions are needed to help further elucidate this relationship. The development and validation of a psychophysical test that could quickly assess visual crowding in glaucomatous patients may provide a useful tool to assess functional performance in this population.

In conclusion, we demonstrated that visual crowding effects were significantly worse in glaucoma patients compared with healthy subjects. Additionally, the severity of visual crowding was significantly associated with the amount of neural loss quantified by OCT. Our findings suggest that visual crowding in glaucoma may be due to increased areas of peripheral receptive field integration, and may have implications for understanding how glaucoma patients are affected in daily tasks where crowding effects may be significant, such as driving, reading, visual search, and object identification. Lastly, tests of visual crowding may provide a clinical means for use in diagnosis and monitoring neural loss in glaucoma.

Acknowledgments

Supported in part by National Institutes of Health/National Eye Institute (Bethesda, MD, USA) Grant EY025056 (FAM) and EY021818 (FAM).

Disclosure: **N.G. Ogata**, None; **E.R. Boer**, None; **F.B. Daga**, None; **A.A. Jammal**, None; **J.M. Stringham**, None; **F.A. Medeiros**, None

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