Foveal crowding appears to be robust to normal aging and glaucoma unlike parafoveal and peripheral crowding

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Visual crowding is the inability to recognize a target object in clutter. Previous studies have shown an increase in crowding in both parafoveal and peripheral vision in normal aging and glaucoma. Here, we ask whether there is any increase in foveal crowding in both normal aging and glaucomatous vision. Twenty-four patients with glaucoma and 24 age-matched normally sighted controls (mean age = 65 ± 7 vs. 60 ± 8 years old) participated in this study. For each subject, we measured the extent of foveal crowding using Pelli's foveal crowding paradigm (2016). We found that the average crowding zone was 0.061 degrees for glaucoma and 0.056 degrees for age-matched normal vision, respectively. These values fall into the range of foveal crowding zones (0.0125 degrees to 0.1 degrees) observed in young normal vision. We, however, did not find any evidence supporting increased foveal crowding in glaucoma ($p = 0.375$), at least in the early to moderate stages of glaucoma. In the light of previous studies on foveal crowding in normal young vision, we did not find any evidence supporting age-related changes in foveal crowding. Even if there is any, the effect appears to be rather inconsequential. Taken together, our findings suggest unlike parafoveal or peripheral crowding (2 degrees, 4 degrees, 8 degrees, and 10 degrees eccentricities), foveal crowding (<0.25 degrees eccentricity) appears to be less vulnerable to normal aging or moderate glaucomatous damage.

Introduction

Visual crowding refers to an impaired ability to recognize a target in the presence of nearby items (Bouma, 1970; Pelli, Palomares, & Majaj, 2004; Whitney & Levi, 2011). Because the same target is recognizable when presented alone, visual crowding cannot simply be explained by reduced visual acuity or contrast sensitivity at a given retinal location. Crowding zone (i.e. the minimum spacing between a target and flankers required for reliable target identification), increases with increasing retinal eccentricity (Bouma, 1970; Pelli et al., 2004; Whitney & Levi, 2011). Thus, visual crowding is known to be more pronounced in the peripheral vision, whereas little crowding exists in the foveal vision (Coates, Jiang, Levi, & Sabesan, 2022; Coates, Levi, Touch, & Sabesan, 2018; Danilova & Bondarko, 2007; Flom, Weymouth, & Kahneman, 1963; Lev, Yehezkel, & Polat, 2014; Levi, Klein, & Hariharan, 2002; Pelli, Waugh, Martelli, Crutch, Primativo, Yong, Rhodes, Yee, Wu, Famira, & Yiltiz, 2016; Siderov, Waugh, & Bedell, 2013; Strasburger, Harvey, & Rentschler, 1991; Toet & Levi, 1992). However, some conditions, such as amblyopia, exhibit significantly increased foveal crowding (Bonneh, Sagi, & Polat, 2007; Flom et al., 1963; Hariharan, Levi, & Klein, 2005) compared to what is expected from normal vision.

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Here, we ask whether a common visual disorder called glaucoma is associated with increased foveal crowding. Glaucoma is one of the leading causes of irreversible blindness worldwide (Tham, Li, Wong, Quigley, Aung, & Cheng, 2014) and characterized by progressive death of retinal ganglion cells and optic nerve fibers. Studies have shown that patients with glaucoma exhibit increased crowding in both parafoveal and peripheral vision (Ogata, Boer, Daga, Jammal, Stringham, & Medeiros, 2019; Shamsi, Liu, & Kwon, 2022). For example, Ogata et al. (Ogata et al., 2019) reported that the crowding zone in the peripheral vision (10 degrees eccentricity) of patients with glaucoma was significantly greater than that of normally sighted controls. A recent study done by our group also demonstrated an enlarged crowding zone in the parafoveal vision (i.e. 2 degrees and 4 degrees eccentricities) of patients with glaucoma compared with age-matched healthy controls (Shamsi, Liu, & Kwon, 2022). Furthermore, comparing the crowding zone between the worse and the better eyes of patients with glaucoma indicated that eyes with more severe glaucomatous damage have a larger crowding zone, further highlighting the impact of glaucomatous damage on crowding.

Despite the conventional view that the central vision remains intact until the end stages of glaucoma, recent neuroanatomic and behavioral evidence support the presence of glaucomatous damage in the central vision (Anctil & Anderson, 1984; Chien, Liu, Girkin, & Kwon, 2017; Elze, Pasquale, Shen, Chen, Wiggs, & Bex, 2015; Glen, Crabb, Smith, Burton, & Garway-Heath, 2012; Hood, 2017; Hood, Raza, de Moraes, Johnson, Liebmann, & Ritch, 2012; Hood, Raza, de Moraes, Liebmann, & Ritch, 2013; Hood, Slobodnick, Raza, de Moraes, Teng, & Ritch, 2014; Kwon, Liu, Patel, & Girkin, 2017; Medeiros, Lisboa, Weinreb, Liebmann, Girkin, & Zangwill, 2013; Ramulu, Swenor, Jefferys, Friedman, & Rubin, 2013; Roux-Sibilon, Rutgé, Aptel, Attye, Guyader, Boucart, Chiquet, & Peyrin, 2018; Shamsi, Liu, Owsley, & Kwon, 2022; Stievenard, Rouland, Peyrin, Warniez, & Boucart, 2021; Wang, Raza, de Moraes, Chen, Alhadeff, Jarukatsetphorn, Ritch, & Hood, 2015; Wang, Hood, Cho, Ghadiali, De Moraes, Zhang, Ritch, & Liebmann, 2009). Specifically, a number of retinal imaging studies have shown significant thinning of the retinal nerve fiber layer (RNFL) and the retinal ganglion cell plus inner plexiform layer (RGC+) even in the macular region of glaucomatous eyes (Hood et al., 2012; Hood et al., 2013; Hood et al., 2014; Shamsi, Liu, Owsley, et al., 2022; D. L. Wang et al., 2015). It has been reported that such macular damage occurs in up to 80% of patients with mild glaucoma (Blumberg, Liebmann, Hirji, & Hood, 2019; Hood et al., 2014). Consistent with the structural damage, behavioral studies have also shown impairments of various central visual functions, such as foveal contrast sensitivity (Bambo, Ferrandez, Güerri, Fuertes, Cameo, Polo, Larrosa, & Garcia-Martin, 2016; Chien et al., 2017; Hawkins, Szlyk, Ardickas, Alexander, & Wilensky, 2003; Horn, Martus, & Korth, 1995; Ichhpujani, Thakur, & Spaeth, 2020; Lahav, Levkovitch-Verbin, Belkin, Glovinsky, & Polat, 2011; Wilensky & Hawkins, 2001), reading (Burton, Crabb, Smith, Glen, & Garway-Heath, 2012; Kwon et al., 2017; Mathews, Rubin, McCloskey, Salek, & Ramulu, 2015; Ramulu et al., 2013; Ramulu, West, Munoz, Jampel, & Friedman, 2009; Smith, Glen, Mönter, & Crabb, 2014), and object (Lenoble, Lek, & McKendrick, 2016) and face recognition (Glen et al., 2012; Roux-Sibilon et al., 2018) in patients with glaucoma. For example, Lahav et al. (Lahav et al., 2011) found that foveal contrast sensitivity was significantly lower in glaucomatous eyes under both photopic (i.e. daylight) and mesopic (i.e. dim light) conditions. Although photopic visual acuity appears to remain relatively intact in early stages of glaucoma (Kwon et al., 2017; Xiong, Kwon, Bittner, Virgili, Giacomelli, & Legge, 2020), the acuity of patients with glaucoma under low luminance condition was shown to be substantially compromised (Bhorade, Perlmutter, Wilson, Kambarian, Chang, Pekmezci, & Gordon, 2013; Blumberg et al., 2019). Whereas reading is considered to be one of the most common central vision tasks, surprisingly, reading problems have been cited as one of the main complaints among patients with glaucoma (Crabb, Smith, Glen, Burton, & Garway-Heath, 2013; Duke-Elder, 1969; McKean-Cowdin, Wang, Wu, Azen, Varma, & the Los Angeles Latino Eye Study Group, 2008; Nelson, Aspinall, & O'Brien, 1999). Consistent with patients' subjective reports, Kwon et al. (Kwon et al., 2017) found significantly slower reading speed even in patients with early or moderate glaucoma (i.e. nearly 20% reduction) and the observed decrease in reading speed covaried with a shrinkage of the visual span (i.e. the number of letters reliably recognizable at one glance), which is known to be largely limited by visual crowding (Legge, Cheung, Yu, Chung, Lee, & Owens, 2007; Liu, Patel, & Kwon, 2017; Pelli & Tillman, 2008).

The converging evidence of structural damage and functional deficits in the central vision of patients with glaucoma, in combination with increased parafoveal and peripheral crowding observed in glaucomatous eyes, hints at the possibility of increased crowding in the central vision of patients with glaucoma. Thus, here, we examined the effect of glaucoma on foveal crowding in glaucomatous vision. To this end, we evaluated foveal crowding in patients with glaucoma ($n = 24$) and age-matched healthy controls ($n = 24$) in comparison with that of young adults with normal vision published in previous studies (Coates et al., 2018; Danilova & Bondarko, 2007; Flom et al., 1963; Marten-Ellis & Bedell, 2021; Pelli et al., 2016; Siderov et al., 2013; Toet & Levi, 1992; Wolford & Chambers, 1984) that allowed

us to evaluate both glaucoma-related (glaucoma vs. age-matched normal vision) and age-related (old normal vision vs. young normal vision) changes in foveal crowding.

Foveal crowding was measured with Pelli's foveal crowding paradigm (Pelli et al., 2016), in which an observer is asked to identify Pelli font digits (see details in the Methods section) with and without flankers. Foveal crowding was defined as the minimum spacing between two target digits (i.e. the spatial extent of crowding) that yields a criterion recognition accuracy of 70% using the QUEST adaptive procedure (Watson & Pelli, 1983). In this adaptive procedure, as both the size of digits and the center-to-center spacing between digits were updated together according to the observers' response, it was important to make sure that any observed difference in the extent of crowding (if any) is not simply due to the difference in visibility limited by an observer's reduced acuity or contrast sensitivity. For this very reason, we also examined the correlation between the extent of foveal crowding and either visual acuity or contrast sensitivity to see if decreased foveal acuity or contrast sensitivity plays a role in increased foveal crowding (if any). We also examined the relationship between foveal crowding and the severity of glaucoma indicated by standard visual perimetry (i.e. the Humphrey Field Analyzer 24-2 or 10-2 test).

Note that the current study was undertaken to explore whether there is an increased foveal crowding in patients with glaucoma that likely impacts everyday visual activities, such as reading or visual search. Because everyday visual tasks are often performed under binocular viewing, our crowding, acuity, and contrast sensitivity measurements were all done binocularly. To the best of our knowledge, this is the first study that investigates the extent of foveal crowding in patients with glaucoma and older adults with normal vision in relation with young adults with normal vision.

Methods

Participants

A total of 48 subjects participated in this study: 24 patients with primary open-angle glaucoma (mean age = 65.21 ± 7.40 years) and 24 age-matched normally sighted older adults (healthy controls) (mean age = 60.08 ± 8.07 years). The study participants were recruited from either Callahan Eye Hospital Clinics at the University of Alabama at Birmingham (UAB) or the UAB campus. Patients with glaucoma, whose diagnosis was validated through medical records, met the following inclusion criteria: (i) glaucoma specific changes of optic nerve or nerve fiber layer defect, the presence of the glaucomatous optic nerve was defined by masked review of optic nerve head photographs by glaucoma specialists using previously published criteria (Sample, Girkin, Zangwill, Jain, Racette, Becerra, Weinreb, Medeiros, Wilson, De León-Ortega, Tello, Bowd, & Liebmann, 2009); (ii) glaucoma-specific visual field defect; a value of the Glaucoma Hemifield Test from the Humphrey Field Analyzer (HFA) must be outside normal limits; and (iii) no history of other ocular or neurological disease or surgery that caused visual field loss.

The visual field test was performed with standard automated perimetry (SAP) using both the Swedish interactive testing algorithm (SITA) standard 24-2 and 10-2 tests with a Humphrey Field Analyzer (Carl Zeiss Meditec, Inc., Jena, Germany). The Humphrey Field Analyzer 24-2 (HFA 24-2) test measures 24 degrees temporal and 30 degrees nasal visual field. A mean deviation (MD) value obtained from HFA 24-2 test is commonly used for evaluating the severity of glaucoma. The Humphrey Field Analyzer 10-2 (HFA 10-2) test is designed to evaluate the central visual field and it, thus, measures 10 degrees temporally and nasally. Goldmann size III targets with a diameter of 0.43 degrees were presented for 200 ms at one of 54 (HFA 24-2) or 68 (HFA 10-2) locations in a grid on a white background (10 cd/m^2). The average mean deviation obtained from the HFA 24-2 test in glaucoma patients was –5.33 ± 7.14 dB for the better eye and –11.37 ± 9.83 dB for the worse eye.

The average mean deviation obtained from the HFA 10-2 test in patients with glaucoma was –2.19 ± 4.81 dB for the better eye and –8.12 ± 9.44 dB for the worse eye. According to the Hodapp-Anderson-Parish glaucoma grading system (Hodapp, Parrish, & Anderson, 1993), the majority of our patients with glaucoma were in either early or moderate stages of glaucoma (21 of 24).

Visual acuity, the ability to resolve fine details, was measured binocularly using Early Treatment Diabetic Retinopathy Study (ETDRS) charts and reported in logarithm of the minimum angle of resolution (logMAR). In this chart, 10 Sloan letters are arranged in 14 lines with five letters in each line. The letter size successively decreases by a factor of 0.1 log units. The visual acuity is determined based on the number of letters on the last line that the subject reported correctly (each correct letter improves visual acuity by 0.02 log units). The mean binocular visual acuity for patients with glaucoma was –0.05 ± 0.08 logMAR (or approximately 20/20 Snellen equivalent). Contrast sensitivity, the ability to distinguish objects from background, was measured binocularly using the Pelli-Robson contrast sensitivity chart. In this chart, 10 Sloan letters with constant size (spanned about 3 degrees of visual angle at the viewing distance of 1 meter) are arranged in 16 triplets over eight lines and the contrast of these triplets (all letters in each triplet

have the same contrast levels) successively decreases. Each triplet represents an increment of 0.15 log units (0.05 per each letter) and the contrast sensitivity ranges from 0 to 2.25 log units. The contrast sensitivity is measured by determining the lowest contrast letter that the subject reported correctly. The mean binocular log contrast sensitivity of patients with glaucoma was 1.72 ± 0.15 log units. Normal binocular vision of all glaucoma subjects was confirmed through Worth four dot and Stereo Fly vision tests, which were in the normal range, except for one subject whose left eye was prosthetic. Note that our patients with glaucoma did not have any other ocular pathologies (except for mild cataract or a history of cataract surgery) as well as neurological disorders. Three patients corrected their vision through cataract surgery. At the time of the study, only two patients had nuclear sclerotic cataracts (NSCs) in both eyes of mild to moderate severity (1+ to 2+). Their visual acuity values were 0.04 and 0.02 logMAR (approximately 20/20 Snellen equivalent), which are in the normal range. Only one of them had reduced Pelli-Robson contrast sensitivity (1.5 log units) whereas the other one had normal contrast sensitivity (2.1 log units).

Normal vision was defined as better than or equal to 0.2 logMAR best-corrected visual acuity in each eye with normal binocular vision (confirmed through Worth four dot and Stereo Fly vision tests) and with no history of ocular or neurological disease other than cataract surgery. The mean binocular visual acuity for healthy control subjects was –0.08 ± 0.09 logMAR (or 20/15 Snellen equivalent) and the mean binocular log contrast sensitivity was 1.92 ± 0.12. All participants were native or fluent English speakers without known cognitive or neurological impairments, confirmed by the Mini Mental State Examination (≥25 MMSE score, for those aged 65 years and over). The experiments were conducted with binocular viewing, except for one patient with glaucoma whose left eye was prosthetic and who performed all tests using the right eye. Proper refractive correction for the viewing distance was used. The experimental protocols followed the tenets of the Declaration of Helsinki and were approved by the Internal Review Board at UAB. Written informed consents were obtained from all participants prior to the experiment, after explanation of the nature of the study.

Measuring pelli's foveal crowding and acuity

Stimulus and apparatus

We used the experimental paradigm proposed by Pelli et al. (Pelli et al., 2016) to measure the extent of foveal crowding. This paradigm involves identifying targets under crowded and uncrowded conditions (hereafter we refer to uncrowded condition as the acuity condition). The stimuli consisted of two alternating targets repeated over the display for the crowded condition or a single target at the center of the display for the acuity condition (Figure 1B). All targets were randomly drawn from a set of nine Pelli font digits: "1, 2, 3, 4, 5, 6, 7, 8, 9" (the digits have an aspect ratio of 5:1 and the stroke is 1/2 of the width; see Figure 1A; see Pelli et al., 2016 for details about the Pelli font digits). In the crowding condition, as the two alternating digits cover the whole display, the

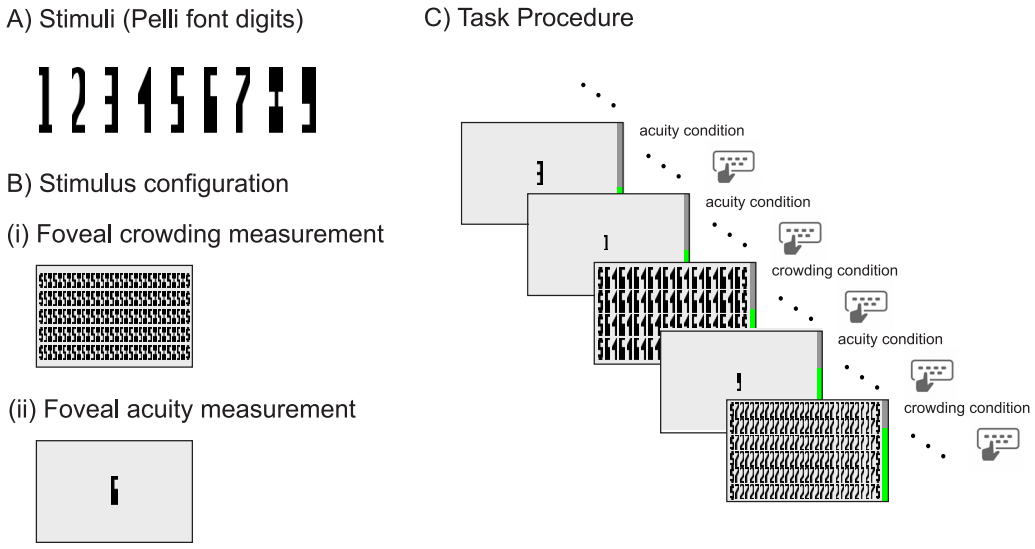

Figure 1. (**A**) Stimuli (Pelli font digits). Note that digit "0" was not used in the experiment. (**B**) Stimulus configurations for (i) foveal crowding and (ii) foveal acuity conditions. (**C**) Task procedure. For crowding trials, subjects were instructed to report two digits (in any order) and for acuity trials, they reported a single digit. The green bar shows the progress of the experiment.

targets will be placed on the subjects' fovea regardless of their gaze position. All stimuli were generated and controlled using *CriticalSapaing.m* software (https://github.com/denispelli/CriticalSpacing/) implemented in MATLAB (version 8.3) and Psychophysics Toolbox extensions (version 3; Brainard & Vision, 1997; Pelli & Vision, 1997) for Windows 7, running on a PC desktop computer (model: Dell Precision Tower 5810). Stimuli were presented on a liquid crystal display monitor (model = Asus VG278HE; refresh rate = 144 Hz; resolution = 1920 × 1080; display size = 52.7 × 29.7 cm). The measurements were conducted at a viewing distance of either 400 or 600 cm. The display subtended 7.5 degrees × 4.2 degrees visual angle at the viewing distance of 400 cm and 5 degrees × 2.8 degrees visual angle at the viewing distance of 600 cm. The minimum measurable center-to-center spacing was 0.031 degrees and 0.021 degrees for 400 and 600 cm distance, respectively. Note that the viewing distance for subjects was determined based on preliminary vision tests. Limited by the spatial resolution of the display monitor, the viewing distance was adjusted to render the smallest possible angular size of digits and spacing on the display screen that accommodates each subject's foveal acuity threshold.

Task procedure

The extent of foveal crowding was measured as the horizontal spacing threshold between the two target digits. The threshold horizontal spacing was defined as the horizontal center to center distance, which resulted in 70% target recognition accuracy. Similar recognition accuracy criterion was considered to determine the threshold vertical size of single digits (acuity condition). Whereas both crowding trials and acuity trials were interleaved within a block, two independent QUEST adaptive procedures (Watson & Pelli, 1983), one for the crowding task and the other for the acuity task, were run simultaneously to adjust stimulus properties based on the subject's responses. For crowding trials, the center-to-center spacing between digits was updated based on the subject's responses. However, as the ratio of spacing over digit size (width) was fixed (1.4:1), both the spacing and the digit size covaried for crowding trials. For acuity trials, the QUEST adaptive procedure only updated the digit size based on the subject's response. The number of trials was set to 20 for each task. Each presentation of the crowding task was counted as two trials as subjects had to report two digits, whereas each presentation for the acuity (single target) task was considered as one trial. Note that in the crowding task, the response for each of the two digits was considered as one trial. Therefore, if for a given trial, the subject only reported one letter correctly (and the other one incorrectly), one correct and one incorrect response was recorded for the corresponding spacing size. Each 20 trials of the same tasks were used to estimate the threshold value (horizontal spacing or vertical size) for the corresponding condition. The subjects were instructed to report two digits (in any order) for the crowding task and a single digit for the acuity task and the experimenter entered the subject's responses using a keyboard. Once the response was given, the typed number was echoed by the computer, followed by a beep for the correct responses. Then, the next stimulus appeared on the screen. A green bar on the screen was used to show the progress of the task (see Figure 1C). Due to the novelty of Pelli font digits used in the experiment, digits were printed on a paper and provided to subjects during the tasks. For more details about the experiment paradigm and software, see Pelli et al., 2016 and https://github.com/denispelli/CriticalSpacing/.

Data analysis

The Pelli's foveal acuity measure computed the threshold vertical size of the Pelli font digits. In the current study, we, however, converted the foveal acuity based on the threshold vertical size into horizontal size using the aspect ratio of Pelli font (5:1), so that it becomes comparable with the extent of foveal crowding based on the threshold horizontal spacing.

We performed the two-sample *t*-test to see if there was any significant difference in Pelli's foveal crowding, foveal acuity, Pelli-Robson contrast sensitivity, and HFA visual field sensitivity between glaucoma and age-matched healthy controls. We also performed correlation analysis to examine the relationship between foveal crowding zone and the aforementioned visual functions. Note that the HFA 24-2 and HFA 10-2 test results were only available for a subset of patients with glaucoma (22 of 24) and healthy controls (18 of 24). The MD value from HFA 24-2 test was used as an indicator of the severity of glaucoma. We also obtained the central visual field sensitivity from HFA 10-2 to evaluate glaucomatous damage in the central vision. To obtain the central visual field sensitivity data, we first constructed the binocular visual field sensitivity map (Shamsi, Chen, Liu, Pergher, & Kwon, 2021) by setting the binocular sensitivity value as the monocular total deviation value of the more sensitive eye at each testing locations in HFA 10-2 test. We then computed the mean of total deviation values within 2 degrees retinal eccentricities (i.e. the central 4 degrees visual field) and the resulting average value was considered as the central visual field sensitivity.

Results

We first examined the difference in foveal crowding zone (threshold horizontal spacing) between patients with glaucoma and age-matched healthy controls. Figure 2A(i) plots foveal crowding zone for glaucoma (orange circles) and healthy control (green circles) subjects. The two-sample *t*-test showed no significant difference in foveal crowding zone between patients with glaucoma (0.061 degrees ± 0.021 degrees) and healthy controls (0.056 degrees ± 0.014 degrees); $t\ (46) = 0.90$, $p = 0.375$. Notably, these values (e.g. a mean value of approximately 0.06 degrees) are well in line with the range of foveal crowding zone observed in young normally sighted adults (Coates et al., 2018; Danilova & Bondarko, 2007; Flom et al., 1963; Levi et al., 2002; Marten-Ellis & Bedell, 2021; Pelli et al., 2016; Siderov et al., 2013; Toet & Levi, 1992; Wolford & Chambers, 1984; see Figure 2A(i)).

Next, in order to put our foveal crowding results into perspective, we visualized both age-related and glaucoma-related changes in crowding zone at different eccentricities, including foveal vision using the data obtained from both the current study and previously published studies (Liu et al., 2017; Ogata et al., 2019; Pelli et al., 2016; Shamsi, Liu, & Kwon, 2022). Figure 2A(ii) shows a plot of crowding zone as a function of eccentricity for glaucoma (orange triangles, mean age = 65.21 years old), old healthy control (green squares, mean age = 60.08 years old), and young healthy control groups (gray circles, mean age = 22.6 years old). The average crowding zone for the three groups was compared at the foveal (<0.25 degrees eccentricity), parafoveal (2 degrees and 4 degrees eccentricities), and peripheral (8 degrees and 10 degrees eccentricity) retinal locations. Values of crowding zone for glaucoma and old healthy subjects were reported in studies by Shamsi et al. (Shamsi, Liu, & Kwon, 2022; 2 degrees and 4 degrees eccentricity) and Ogata et al. (Ogata et al., 2019; 10 degrees eccentricity). For old versus young normally sighted subjects, the crowding zone data were obtained from a study by Liu et al. (Liu et al., 2017; 2 degrees, 4 degrees, and 8 degrees eccentricities). Foveal crowding for young healthy control subjects was reported by Pelli et al. (Pelli et al., 2016). (Note that the exact age information for the data from Pelli et al., 2016 is not given.) Ogata et al. measured crowding zone using a 2-AFC identification task (i.e. to report whether the target "T" is upward or downward) and its critical spacing corresponded to a criterion recognition accuracy of 75%. For this reason, their crowding zones appears to be much smaller (see filled symbols in Figure 2A(ii)) for a given retinal eccentricity. On the other hand, other studies shown in Figure 2A(ii) measured the crowding zone using 10-AFC (2 degrees, 4 degrees, and 8 degrees eccentricities) and 9-AFC (fovea) tasks and criterion recognition accuracy of 79% (2 degrees, 4 degrees, and 8 degrees eccentricities) and 70% (fovea). Although absolute values of crowding zones differ across studies, the pattern of the results remains consistent: significantly increased parafoveal and peripheral crowding for glaucoma compared with age-matched normal vision.

As demonstrated in Figure 2A(ii), there seems to be a lack of evidence for age-related or glaucoma-related changes in the extent of foveal crowding. On the other hand, in parafoveal and peripheral vision, the crowding zone is significantly larger in glaucoma versus old healthy control groups (Shamsi, Liu, & Kwon, 2022) and in old versus young normally sighted subjects (Liu et al., 2017; all p values < 0.01). These results further confirmed the presence of both age-related and glaucoma-related changes in parafoveal and peripheral crowding despite some obvious methodological differences among studies.

Next, we investigated the relation between the extent of foveal crowding and either Pelli's foveal acuity (threshold horizontal size or width), Pelli-Robson contrast sensitivity, or the severity of glaucoma indicated by MD values of HFA 24-2 test and the central visual field sensitivity obtained from HFA 10-2 test (see the Methods section). As shown in Figure 2B(i) to (iii), we first compared Pelli's foveal acuity (i.e. threshold horizontal size or width), Pelli-Robson contrast sensitivity, and the central visual field sensitivity of patients with glaucoma (orange circles) with those of age-matched healthy controls (green circles). No significant difference in the foveal acuity was found between the two groups (0.02 degrees ± 0.02 degrees for glaucoma versus 0.02 degrees ± 0.01 degrees for healthy controls); $t\ (46) = 1.13$, $p = 0.263$. On the other hand, there was a significant difference for both Pelli-Robson contrast sensitivity (1.72 ± 0.15 log units for glaucoma versus 1.92 ± 0.12 log units for healthy controls, $t\ (46) = -5.13$, $p < 0.001$) and the central visual field sensitivity (0.10 ± 2.42 dB for glaucoma versus 1.56 ± 1.22 log units for healthy controls, $t\ (38) = -2.32$, $p < 0.05$). However, as shown in Figure 2C, we did not find any significant correlation between foveal crowding and the aforementioned visual functions, including foveal acuity, contrast sensitivity, and the severity of glaucoma (all p values > 0.05).

Discussion

Visual crowding is a perceptual phenomenon that impairs the recognition of targets when surrounded by flankers (Balas, Nakano, & Rosenholtz, 2009; Bouma, 1970; Greenwood, Szinte, Sayim, & Cavanagh, 2017; Harrison & Bex, 2015; He, Cavanagh, & Intriligator,

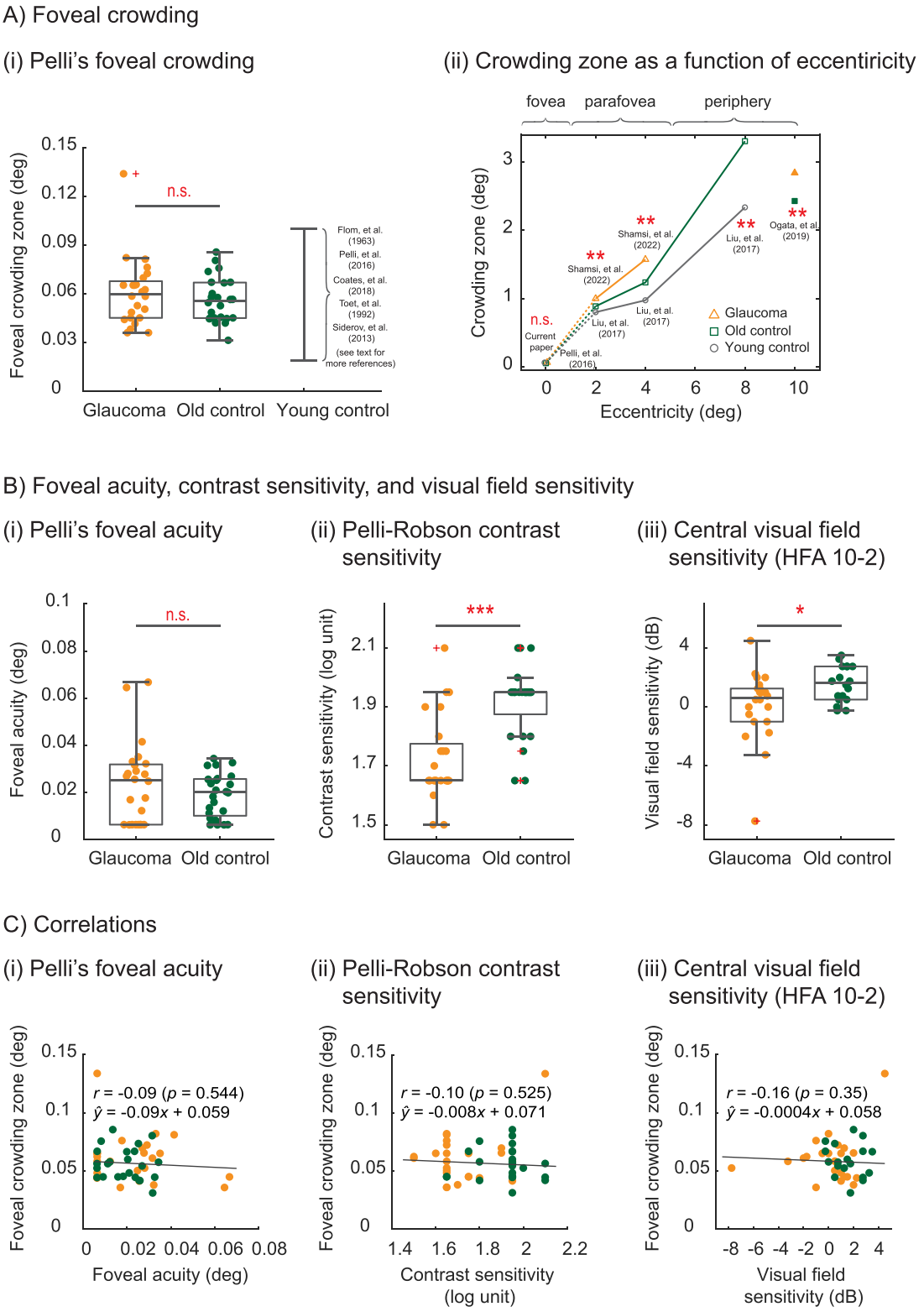

Figure 2. (**A**) Foveal crowding. (i) Foveal crowding zone for patients with glaucoma, old healthy control (age-matched) group, and the range of foveal crowing zone for young normally sighted individuals from previous studies (Coates et al., 2018; Danilova & Bondarko, 2007; Flom et al., 1963; Marten-Ellis & Bedell, 2021; Pelli et al., 2016; Siderov et al., 2013; Toet & Levi, 1992; Wolford & Chambers, 1984). (ii) The average crowding zone as a function of different eccentricities including the foveal, parafoveal, and peripheral retinal locations. Data for the glaucoma, old control, and young control groups are shown using triangles, squares, and circles, respectively. Filled shapes are used for the data from Ogata et al. (Ogata et al., 2019) to denote the methodological differences between theirs and the rest of the studies cited in Figure 2A(ii), that may explain unusually smaller crowding zones observed in Ogata et al. (Ogata et al., 2019). Dotted lines show the interpolated lines between crowding values at the fovea and 2 degrees of eccentricity (parafoveal

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vision). Solid lines denote the interpolated lines between crowding values at parafovea and periphery (2 degrees, 4 degrees, and 8 degrees eccentricities) for the data obtained from identical paradigms. (**B**) Foveal acuity, contrast sensitivity, and visual field sensitivity. (i) Pelli's foveal acuity, (ii) Pelli-Robson contrast sensitivity, and (iii) central visual field sensitivity (i.e. a value averaged across the central 4 degrees visual field based on the HFA 10-2 test) for glaucoma and old control subjects. (**C**) Correlations between foveal crowding zone and (i) Pelli's foveal acuity, (ii) Pelli-Robson contrast sensitivity, and (iii) central visual field sensitivity (i.e. a value averaged across the central 4° visual field based on the HFA 10-2 test). Note that orange, green, and gray colors show the data from glaucoma, old control, and young control groups, respectively. "n.s." denotes no statistical significance,
* shows $p < 0.05$, ** indicates $p < 0.01$, and *** stands for $p < 0.001$.

1996; Kwon & Liu, 2019; Parkes, Lund, Angelucci, Solomon, & Morgan, 2001; Pelli, & Tillman, 2008; Pelli et al., 2004; Toet & Levi, 1992; Wallis & Bex, 2011; Whitney & Levi, 2011). Although crowding is typically associated with the peripheral vision, emerging evidence has pointed to the presence of measurable crowding in the foveal vision (Coates et al., 2018; Coates et al., 2022; Danilova & Bondarko, 2007; Flom et al., 1963; Lev et al., 2014; Pelli et al., 2016; Siderov et al., 2013; Strasburger et al., 1991; Toet & Levi, 1992). Studies have used a variety of tasks, targets (different types and sizes), and flankers (different numbers and types of flankers), under limited or unlimited stimulus durations to measure the spatial extent of foveal crowding and reported a range of approximately 0.0125 degrees to 0.1 degrees for the extent of foveal crowding for normal healthy vision (Coates et al., 2018; Danilova & Bondarko, 2007; Flom et al., 1963; Marten-Ellis & Bedell, 2021; Pelli et al., 2016; Siderov et al., 2013; Toet & Levi, 1992; Wolford & Chambers, 1984) as summarized in Figure 2A(i). Particularly, more pronounced foveal crowding has been observed in visually impaired individuals, such as amblyopia (Bonneh et al., 2007; Flom et al., 1963; Hariharan et al., 2005). Importantly, the increased foveal crowding has been closely related to slower reading speed in amblyopia (Levi, Song, & Pelli, 2007), underscoring the detrimental impact of foveal crowding on everyday visual activities.

Here, we aimed to investigate the impact of glaucomatous damage on foveal crowding.

As glaucoma has been traditionally considered as peripheral vision loss, relatively little attention has been paid to central vision deficits in glaucoma. However, accumulating evidence has shown substantial structural damage (i.e. degeneration of ganglion cell bodies and their axonal and dendritic structures) and functional deficits in the central vision of patients with glaucoma (Anctil & Anderson, 1984; Elze et al., 2015; Glen et al., 2012; Hood, 2017; Hood et al., 2012; Hood et al., 2013; Hood et al., 2014; Kwon et al., 2017; Medeiros et al., 2013; Ramulu et al., 2013; Roux-Sibilon et al., 2018; Shamsi, Liu, Owsley, et al., 2022; Stievenard et al., 2021; D. L. Wang et al., 2015; Min Wang et al., 2009; Mengyu Wang, Tichelaar, Pasquale, Shen, Boland, Wellik, De Moraes, Myers, Ramulu, Kwon, Saeedi, Wang, Baniasadi, Li, Bex, & Elze, 2020). More relevantly, increased parafoveal and peripheral crowding have been observed even in relatively mild and moderate glaucoma (Ogata et al., 2019; Shamsi, Liu, & Kwon, 2022). Furthermore, a recent study done by Kwon and Liu (Kwon & Liu, 2019) demonstrated a close linkage between the spatial extent of crowding and RGC density/counts. Considering the fact that glaucoma involves the death and/or dysfunction of RGCs, these findings collectively suggest that foveal crowding is likely to be implicated in glaucoma.

Thus, we asked whether there is any increased foveal crowding following glaucomatous damage. The spatial extent of foveal crowding was measured in glaucoma ($n = 24$) and age-matched normal vision ($n = 24$) using the novel method proposed by Pelli et al. (Pelli et al., 2016). As shown in Figure 2A(i), we found that the average crowding zone was 0.061 degrees for glaucoma and 0.056 degrees for age-matched normal vision, respectively. These values fall into the range of crowding zones observed in young adults with normal vision. We, however, did not find any evidence supporting significantly increased foveal crowding in glaucoma compared to age-matched normal vision ($p > 0.05$). As somewhat expected, the extent of foveal crowding was not significantly correlated with either Pelli's foveal acuity, Pelli-Robson contrast sensitivity, or the severity of glaucoma indicated by either the MD value of HFA 24-2 test or the central visual field sensitivity obtained from the HFA 10-2 test.

On the other hand, Stievenard et al. (Stievenard et al., 2021) using face stimuli reported increased foveal crowding in glaucoma compared to age-matched normal vision. In their study, subjects were asked to determine whether a mouth presented within a face (crowded) or in isolation (uncrowded) was open or closed. They found that unlike the control group, which exhibited a higher accuracy when the mouth was presented in a face (i.e. face superiority effect), 10 of 17 glaucoma subjects performed better for the isolated mouth condition and this result was only observed for the small images (angular size of 0.6 degrees × 0.4 degrees). One possible explanation for the apparent discrepancy between their results and our findings might have to do with the severity range of glaucoma in their study (Stievenard et al., 2021). In

Stievenard et al.'s study (Stievenard et al., 2021), the majority of the patients (13 of 17) were at the moderate to severe stages of glaucoma, whereas patients in our study were mostly at the mild to moderate stages of the disease. Other important differences between the two studies include the nature of tasks in demand (e.g. measuring identification accuracy versus crowding zone; discriminating open/closed mouth in a face versus identifying a target letter/digit surrounded by flankers) and the duration of stimulus presentation. In their study (Stievenard et al., 2021), the stimuli were displayed only for 200 ms, whereas in our current study, the stimulus duration was unlimited. In fact, it has been shown that stimulus duration can affect foveal crowding in normal vision (Lev & Polat, 2015; Lev et al., 2014; Wallace, Chiu, Nandy, & Tjan, 2013; Waugh, Formankiewicz, & Hairol, 2014). Specifically, Lev et al. (Lev & Polat, 2015) reported that the critical duration needed to overcome foveal crowding amounts to 300 ms for some subjects.

Recent studies showed that the extent of crowding was significantly greater in both parafoveal and peripheral vision of patients with glaucoma compared to age-matched healthy controls (Ogata et al., 2019; Shamsi, Liu, & Kwon, 2022). For example, Ogata et al. showed that the critical spacing at 10 degrees retinal eccentricity increased by 17% for patients with glaucoma compared to healthy controls (Ogata et al., 2019). Furthermore, our previous work showed that the crowding zone in the parafoveal vision (2 degrees and 4 degrees eccentricities) was also increased in early or moderate stages of glaucoma: about 13% and 27% larger than that of age-matched healthy controls at 2 degrees and 4 degrees retinal eccentricities, respectively (Shamsi, Liu, & Kwon, 2022).

On the other hand, age-related changes in crowding have been reported in a previous study. Liu et al. observed a significant increase in crowding in older adults – enlargement of crowding zone (an increase by 31%) in the parafoveal and peripheral vision (2 degrees, 4 degrees, and 8 degrees eccentricities) compared to young adults (Liu et al., 2017). Given the fact that normal aging is associated with gradual loss of RGCs and their axons (Curcio & Drucker, 1993; Harwerth & Wheat, 2008; Harwerth, Wheat, & Rangaswamy, 2008; Pearson, Schmidt, Ly-Schroeder, & Swanson, 2006), it is possible that age-related loss of ganglion cells exacerbates the crowding effect in older adults. In Figure 2A(ii), the parafoveal and peripheral crowding zone data were pitted against the foveal crowding data obtained from glaucoma, young, and old normal vision. This comparison enabled us to evaluate both glaucoma-related (glaucoma versus age-matched normal vision) and age-related (old normal vision versus young normal vision) changes in crowding as a function of retinal eccentricity. Despite methodological differences among studies, it becomes apparent that there are significant age-related or glaucoma-related increases in both parafoveal and peripheral crowding, whereas there is little impact of normal aging and glaucoma on foveal crowding. Consistent with these empirical findings, our previous computational work demonstrated that the variation in the spatial extent of crowding is closely linked to the RGC density at least for the visual field between 4 degrees and 20 degrees.

Then, what may explain the lack of evidence supporting age-related or glaucoma-related increases in foveal crowding? Although speculative, it is possible that at least for early or moderate stages of glaucoma, the structural damage at the foveal region (<0.25 degrees eccentricity) may not be severe enough to induce any measurable changes in crowding compared to the parafoveal and peripheral region of the retina that may undergo substantial loss of ganglion cells and significant shrinkage of dendritic structures and cell bodies of remaining cells (Buckingham, Inman, Lambert, Oglesby, Calkins, Steele, Vetter, Marsh-Armstron, & Horner, 2008; Morgan, Uchida, & Caprioli, 2000; Schlamp, Li, Dietz, Janssen, & Nickells, 2006; Weber, Kaufman, & Hubbard, 1998; Williams, Howell, Barbay, Braine, Sousa, John, & Morgan, 2013). However, presumably moderate damage at the foveal region may be enough to impair foveal contrast sensitivity, as shown in the current study as well as previous studies (Bambo et al., 2016; Chien et al., 2017; Hawkins et al., 2003; Lahav et al., 2011). It has been shown that functional deficits in the foveal vision are more pronounced with low contrast targets in the early stage of glaucoma (Glen et al., 2012; Lenoble et al., 2016; Roux-Sibilon et al., 2018). As luminance contrast is known to be a primary parameter encoded by contrast sensitive neurons, such as center-surround RGCs, contrast sensitivity might be the first one to be affected following RGC dysfunction. Taken together, contrast sensitivity appears to be a more sensitive measure to detect glaucoma-related or age-related changes in central visual functions compared with visual acuity or crowding measure where stimuli often appear in high contrast.

Although not likely, we, however, cannot completely rule out the possibility that our study design may have obscured a signal given the variability of the data for the following limitations of our study: First, it is possible that the relatively small number of subjects ($n = 24$ for each subject group) used in the current study might have obscured the power. The number of subjects was determined based on previous studies using 13 or 40 subjects, which found the significant effect of glaucoma on both parafoveal (i.e. 2 degrees and 4 degrees eccentricities) and peripheral (i.e. 10 degrees eccentricities) crowding (Ogata et al., 2019; Shamsi, Liu, & Kwon, 2022). However, it should be noted that the effect size of the current study is small (i.e. Cohen $d = 0.2$). Therefore, in order to detect a signal with

an α level of 0.05 and a power level of 0.8, our power analysis informs us that a sample size of at least 300 is required for each group. This further attests to the negligible change in foveal crowding (if any) compared to a significant increase in parafoveal and peripheral crowding observed in glaucoma. Second, the current study was undertaken to explore whether there is an increased foveal crowding in patients with glaucoma that likely impacts everyday visual activities, such as reading or visual search. Because everyday visual tasks are often performed under binocular viewing, our crowding, acuity, and contrast sensitivity measurements were all done binocularly. However, in our previous study comparing monocular crowding in the parafoveal vision between the worse eyes and the better eyes of patients with glaucoma, we observed that the extent of crowding was significantly larger in the eyes with severer glaucoma (Shamsi, Liu, & Kwon, 2022). We, thus, acknowledge that monocular measurements of foveal crowding and comparison between the two eyes may have helped us to better understand how glaucomatous damage affects foveal crowding in a finer scale. Third, patients with glaucoma used in the current study are at mild to moderate stages of the disease (21 of 24). A wider range of glaucoma severity might have helped us elucidate how the extent of foveal crowding is impacted by various levels of glaucomatous damage. These limitations should be addressed in future studies.

Despite these limitations, our study shows lack of evidence for increased foveal crowding in glaucoma, at least in the early to moderate stages of glaucoma. Furthermore, in the light of previous studies on foveal crowding in healthy young vision, we did not find any evidence supporting age-related changes in foveal crowding. Even if there is any, the effect appears to be inconsequential. Taken together, our findings suggest, unlike parafoveal or peripheral crowding, foveal crowding appears to be less vulnerable to normal aging or moderate glaucomatous damage.

Keywords: crowding, glaucoma, foveal vision, aging, foveal crowding, contrast sensitivity, macular damage, ganglion cells

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References

Anctil, J.-L., & Anderson, D. R. (1984). Early foveal involvement and generalized depression of the visual field in glaucoma. *Archives of Ophthalmology, 102*(3), 363–370.

Balas, B., Nakano, L., & Rosenholtz, R. (2009). A summary-statistic representation in peripheral vision explains visual crowding. *Journal of Vision, 9*(12), 13.

Bambo, M. P., Ferrandez, B., Güerri, N., Fuertes, I., Cameo, B., Polo, V., . . . Garcia-Martin, E. (2016). Evaluation of contrast sensitivity, chromatic vision, and reading ability in patients with primary open angle glaucoma. *Journal of Ophthalmology, 2016*, 7074016.

Bhorade, A. M., Perlmutter, M. S., Wilson, B., Kambarian, J., Chang, S., Pekmezci, M., . . . Gordon, M. (2013). Differences in vision between clinic and home and the effect of lighting in older adults with and without glaucoma. *JAMA Ophthalmology, 131*(12), 1554–1562.

Blumberg, D. M., Liebmann, J. M., Hirji, S. H., & Hood, D. C. (2019). Diffuse macular damage in mild to moderate glaucoma is associated with decreased visual function scores under low luminance conditions. *American Journal of Ophthalmology, 208*, 415–420.

Bonneh, Y. S., Sagi, D., & Polat, U. (2007). Spatial and temporal crowding in amblyopia. *Vision Research, 47*(14), 1950–1962.

Bouma, H. (1970). Interaction effects in parafoveal letter recognition. *Nature, 226*(5241), 177–178.

Brainard, D. H., & Vision, S. (1997). The psychophysics toolbox. *Spatial Vision, 10*(4), 433–436.

Buckingham, B. P., Inman, D. M., Lambert, W., Oglesby, E., Calkins, D. J., Steele, M. R., . . . Horner, P. J. (2008). Progressive ganglion cell degeneration precedes neuronal loss in a mouse model of glaucoma. *Journal of Neuroscience, 28*(11), 2735–2744.

Burton, R., Crabb, D. P., Smith, N. D., Glen, F. C., & Garway-Heath, D. F. (2012). Glaucoma and reading: exploring the effects of contrast lowering of text. *Optometry and Vision Science, 89*(9), 1282–1287.

Chien, L., Liu, R., Girkin, C., & Kwon, M. (2017). Higher contrast requirement for letter recognition and macular RGC+ layer thinning in glaucoma patients and older adults. *Investigative Ophthalmology & Visual Science, 58*(14), 6221–6231.

Coates, D. R., Jiang, X., Levi, D. M., & Sabesan, R. (2022). Cortical distance unifies the extent of

parafoveal contour interactions. *Journal of Vision, 22*(2), 15.

Coates, D. R., Levi, D. M., Touch, P., & Sabesan, R. (2018). Foveal crowding resolved. *Scientific Reports, 8*(1), 1–12.

Crabb, D. P., Smith, N. D., Glen, F. C., Burton, R., & Garway-Heath, D. F. (2013). How does glaucoma look?: patient perception of visual field loss. *Ophthalmology, 120*(6), 1120–1126.

Curcio, C. A., & Drucker, D. N. (1993). Retinal ganglion cells in Alzheimer's disease and aging. *Annals of Neurology, 33*(3), 248–257.

Danilova, M. V., & Bondarko, V. M. (2007). Foveal contour interactions and crowding effects at the resolution limit of the visual system. *Journal of Vision, 7*(2), 25.

Duke-Elder, S. (1969). *Diseases of the lens and vitreous; glaucoma and hypotony (System of Ophthalmology, Vol. XI)*. S. Stewart (Ed.). New York, NY: C. V. Mosby. (pp. 637–640).

Elze, T., Pasquale, L. R., Shen, L. Q., Chen, T. C., Wiggs, J. L., & Bex, P. J. (2015). Patterns of functional vision loss in glaucoma determined with archetypal analysis. *Journal of The Royal Society Interface, 12*(103), 20141118.

Flom, M. C., Weymouth, F. W., & Kahneman, D. (1963). Visual resolution and contour interaction. *JOSA, 53*(9), 1026–1032.

Glen, F. C., Crabb, D. P., Smith, N. D., Burton, R., & Garway-Heath, D. F. (2012). Do patients with glaucoma have difficulty recognizing faces? *Investigative Ophthalmology & Visual Science, 53*(7), 3629–3637.

Greenwood, J. A., Szinte, M., Sayim, B., & Cavanagh, P. (2017). Variations in crowding, saccadic precision, and spatial localization reveal the shared topology of spatial vision. *Proceedings of the National Academy of Sciences, 114*(17), E3573–E3582.

Hariharan, S., Levi, D. M., & Klein, S. A. (2005). Crowding" in normal and amblyopic vision assessed with Gaussian and Gabor C's. *Vision Research, 45*(5), 617–633.

Harrison, W. J., & Bex, P. J. (2015). A unifying model of orientation crowding in peripheral vision. *Current Biology, 25*(24), 3213–3219.

Harwerth, R. S., & Wheat, J. L. (2008). Modeling the effects of aging on retinal ganglion cell density and nerve fiber layer thickness. *Graefe's Archive for Clinical and Experimental Ophthalmology, 246*(2), 305–314.

Harwerth, R. S., Wheat, J. L., & Rangaswamy, N. V. (2008). Age-related losses of retinal ganglion cells and axons. *Investigative Ophthalmology & Visual Science, 49*(10), 4437–4443.

Hawkins, A. S., Szlyk, J. P., Ardickas, Z., Alexander, K. R., & Wilensky, J. T. (2003). Comparison of contrast sensitivity, visual acuity, and Humphrey visual field testing in patients with glaucoma. *Journal of Glaucoma, 12*(2), 134–138.

He, S., Cavanagh, P., & Intriligator, J. (1996). Attentional resolution and the locus of visual awareness. *Nature, 383*(6598), 334–337.

Hodapp, E., Parrish, R. K., & Anderson, D. R. (1993). *Clinical decisions in glaucoma*. New York, NY: Mosby Incorporated.

Hood, D. C. (2017). Improving our understanding, and detection, of glaucomatous damage: an approach based upon optical coherence tomography (OCT). *Progress in Retinal and Eye Research, 57*, 46–75.

Hood, D. C., Raza, A. S., de Moraes, C. G. V., Johnson, C. A., Liebmann, J. M., & Ritch, R. (2012). The nature of macular damage in glaucoma as revealed by averaging optical coherence tomography data. *Translational Vision Science & Technology, 1*(1), 3.

Hood, D. C., Raza, A. S., de Moraes, C. G. V., Liebmann, J. M., & Ritch, R. (2013). Glaucomatous damage of the macula. *Progress in Retinal and Eye Research, 32*, 1–21.

Hood, D. C., Slobodnick, A., Raza, A. S., de Moraes, C. G., Teng, C. C., & Ritch, R. (2014). Early glaucoma involves both deep local, and shallow widespread, retinal nerve fiber damage of the macular region. *Investigative Ophthalmology & Visual Science, 55*(2), 632–649.

Horn, F., Martus, P., & Korth, M. (1995). Comparison of temporal and spatiotemporal contrast-sensitivity tests in normal subjects and glaucoma patients. *German Journal of Ophthalmology, 4*(2), 97–102.

Ichhpujani, P., Thakur, S., & Spaeth, G. L. (2020). Contrast sensitivity and glaucoma. *Journal of Glaucoma, 29*(1), 71–75.

Kwon, M., & Liu, R. (2019). Linkage between retinal ganglion cell density and the nonuniform spatial integration across the visual field. *Proceedings of the National Academy of Sciences, 116*(9), 3827–3836.

Kwon, M., Liu, R., Patel, B. N., & Girkin, C. (2017). Slow reading in glaucoma: is it due to the shrinking visual span in central vision? *Investigative Ophthalmology & Visual Science, 58*(13), 5810–5818.

Lahav, K., Levkovitch-Verbin, H., Belkin, M., Glovinsky, Y., & Polat, U. (2011). Reduced mesopic and photopic foveal contrast sensitivity in glaucoma. *Archives of Ophthalmology, 129*(1), 16–22.

Legge, G. E., Cheung, S.-H., Yu, D., Chung, S. T., Lee, H.-W., & Owens, D. P. (2007). The case for

the visual span as a sensory bottleneck in reading. *Journal of Vision, 7*(2), 9.

Lenoble, Q., Lek, J. J., & McKendrick, A. M. (2016). Visual object categorisation in people with glaucoma. *British Journal of Ophthalmology, 100*(11), 1585–1590.

Lev, M., & Polat, U. (2015). Space and time in masking and crowding. *Journal of Vision, 15*(13), 10.

Lev, M., Yehezkel, O., & Polat, U. (2014). Uncovering foveal crowding? *Scientific Reports, 4*(1), 1–6.

Levi, D. M., Klein, S. A., & Hariharan, S. (2002). Suppressive and facilitatory spatial interactions in foveal vision: Foveal crowding is simple contrast masking. *Journal of Vision, 2*(2), 2.

Levi, D. M., Song, S., & Pelli, D. G. (2007). Amblyopic reading is crowded. *Journal of Vision, 7*(2), 21.

Liu, R., Patel, B. N., & Kwon, M. (2017). Age-related changes in crowding and reading speed. *Scientific Reports, 7*(1), 1–10.

Marten-Ellis, S. M., & Bedell, H. E. (2021). A Comparison of Foveal and Peripheral Contour Interaction and Crowding. *Optometry and Vision Science: Official Publication of the American Academy of Optometry, 98*(1), 41.

Mathews, P. M., Rubin, G. S., McCloskey, M., Salek, S., & Ramulu, P. Y. (2015). Severity of vision loss interacts with word-specific features to impact out-loud reading in glaucoma. *Investigative Ophthalmology & Visual Science, 56*(3), 1537–1545.

McKean-Cowdin, R., Wang, Y., Wu, J., Azen, S. P., & Varma, R., & the Los Angeles Latino Eye Study Group. (2008). Impact of visual field loss on health-related quality of life in glaucoma: the Los Angeles Latino Eye Study. *Ophthalmology, 115*(6), 941–948. e941.

Medeiros, F. A., Lisboa, R., Weinreb, R. N., Liebmann, J. M., Girkin, C., & Zangwill, L. M. (2013). Retinal ganglion cell count estimates associated with early development of visual field defects in glaucoma. *Ophthalmology, 120*(4), 736–744.

Morgan, J. E., Uchida, H., & Caprioli, J. (2000). Retinal ganglion cell death in experimental glaucoma. *Br J Ophthalmol, 84*(3), 303–310.

Nelson, P., Aspinall, P., & O'Brien, C. (1999). Patients' perception of visual impairment in glaucoma: a pilot study. *British Journal of Ophthalmology, 83*(5), 546–552.

Ogata, N. G., Boer, E. R., Daga, F. B., Jammal, A. A., Stringham, J. M., & Medeiros, F. A. (2019). Visual crowding in glaucoma. *Investigative Ophthalmology & Visual Science, 60*(2), 538–543.

Parkes, L., Lund, J., Angelucci, A., Solomon, J. A., & Morgan, M. (2001). Compulsory averaging of crowded orientation signals in human vision. *Nature Neuroscience, 4*(7), 739–744.

Pearson, P. M., Schmidt, L. A., Ly-Schroeder, E., & Swanson, W. H. (2006). Ganglion cell loss and age-related visual loss: a cortical pooling analysis. *Optometry and Vision Science: Official Publication of the American Academy of Optometry, 83*(7), 444.

Pelli, D. G. (2008). Crowding: A cortical constraint on object recognition. *Current Opinion in Neurobiology, 18*(4), 445–451.

Pelli, D. G., Palomares, M., & Majaj, N. J. (2004). Crowding is unlike ordinary masking: Distinguishing feature integration from detection. *Journal of Vision, 4*(12), 12.

Pelli, D. G., & Tillman, K. A. (2008). The uncrowded window of object recognition. *Nature Neuroscience, 11*(10), 1129–1135.

Pelli, D. G., & Vision, S. (1997). The VideoToolbox software for visual psychophysics: Transforming numbers into movies. *Spatial Vision, 10*, 437–442.

Pelli, D. G., Waugh, S. J., Martelli, M., Crutch, S. J., Primativo, S., Yong, K. X., … Yiltiz, H. (2016). A clinical test for visual crowding. *F1000Research, 5*, 81.

Ramulu, P. Y., Swenor, B. K., Jefferys, J. L., Friedman, D. S., & Rubin, G. S. (2013). Difficulty with out-loud and silent reading in glaucoma. *Investigative Ophthalmology & Visual Science, 54*(1), 666–672.

Ramulu, P. Y., West, S. K., Munoz, B., Jampel, H. D., & Friedman, D. S. (2009). Glaucoma and reading speed: the Salisbury Eye Evaluation project. *Archives of Ophthalmology, 127*(1), 82–87.

Roux-Sibilon, A., Rutgé, F., Aptel, F., Attye, A., Guyader, N., Boucart, M., … Peyrin, C. (2018). Scene and human face recognition in the central vision of patients with glaucoma. *PLoS One, 13*(2), e0193465.

Sample, P. A., Girkin, C. A., Zangwill, L. M., Jain, S., Racette, L., Becerra, L. M., … Liebmann, J. M. (2009). The African descent and glaucoma evaluation study (ADAGES): Design and baseline data. *Archives of Ophthalmology, 127*(9), 1136–1145.

Schlamp, C. L., Li, Y., Dietz, J. A., Janssen, K. T., & Nickells, R. W. (2006). Progressive ganglion cell loss and optic nerve degeneration in DBA/2J mice is variable and asymmetric. *BMC Neuroscience, 7*, 66.

Shamsi, F., Chen, V., Liu, R., Pergher, V., & Kwon, M. (2021). Functional Field of View Determined by Crowding, Aging, or Glaucoma Under Divided Attention. *Translational Vision Science & Technology, 10*(14), 14.

Shamsi, F., Liu, R., & Kwon, M. (2022). Binocularly Asymmetric Crowding in Glaucoma and a Lack of

Binocular Summation in Crowding. *Investigative Ophthalmology & Visual Science, 63*(1), 36.

Shamsi, F., Liu, R., Owsley, C., & Kwon, M. (2022). Identifying the Retinal Layers Linked to Human Contrast Sensitivity Via Deep Learning. *Investigative Ophthalmology & Visual Science, 63*(2), 27.

Siderov, J., Waugh, S. J., & Bedell, H. E. (2013). Foveal contour interaction for low contrast acuity targets. *Vision Research, 77*, 10–13.

Smith, N. D., Glen, F. C., Mönter, V. M., & Crabb, D. P. (2014). Using eye tracking to assess reading performance in patients with glaucoma: a within-person study. *Journal of Ophthalmology, 2014*, 120528.

Stievenard, A., Rouland, J. F., Peyrin, C., Warniez, A., & Boucart, M. (2021). Sensitivity to central crowding for faces in patients with glaucoma. *Journal of Glaucoma, 30*(2), 140–147.

Strasburger, H., Harvey, L. O., & Rentschler, I. (1991). Contrast thresholds for identification of numeric characters in direct and eccentric view. *Perception & Psychophysics, 49*(6), 495–508.

Tham, Y.-C., Li, X., Wong, T. Y., Quigley, H. A., Aung, T., & Cheng, C.-Y. (2014). Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology, 121*(11), 2081–2090.

Toet, A., & Levi, D. M. (1992). The two-dimensional shape of spatial interaction zones in the parafovea. *Vision Research, 32*(7), 1349–1357.

Wallace, J. M., Chiu, M. K., Nandy, A. S., & Tjan, B. S. (2013). Crowding during restricted and free viewing. *Vision Research, 84*, 50–59.

Wallis, T. S., & Bex, P. J. (2011). Visual crowding is correlated with awareness. *Current Biology, 21*(3), 254–258.

Wang, D. L., Raza, A. S., de Moraes, C. G., Chen, M., Alhadeff, P., Jarukatsetphorn, R., … Hood, D. C. (2015). Central glaucomatous damage of the macula can be overlooked by conventional OCT retinal nerve fiber layer thickness analyses. *Translational Vision Science & Technology, 4*(6), 4.

Wang, M., Hood, D. C., Cho, J.-S., Ghadiali, Q., De Moraes, G. V., Zhang, X., … Liebmann, J. M. (2009). Measurement of local retinal ganglion cell layer thickness in patients with glaucoma using frequency-domain optical coherence tomography. *Archives of Ophthalmology, 127*(7), 875–881.

Wang, M., Tichelaar, J., Pasquale, L. R., Shen, L. Q., Boland, M. V., Wellik, S. R., … Elze, T. (2020). Characterization of central visual field loss in end-stage glaucoma by unsupervised artificial intelligence. *JAMA Ophthalmology, 138*(2), 190–198.

Watson, A. B., & Pelli, D. G. (1983). QUEST: A Bayesian adaptive psychometric method. *Perception & Psychophysics, 33*(2), 113–120.

Waugh, S. J., Formankiewicz, M. A., & Hairol, M. I. (2014). Effects of stimulus duration on foveal crowding using visual acuity letters. *Journal of Vision, 14*(10), 787.

Weber, A. J., Kaufman, P. L., & Hubbard, W. C. (1998). Morphology of single ganglion cells in the glaucomatous primate retina. *Investigative Ophthalmology & Visual Science, 39*(12), 2304–2320.

Whitney, D., & Levi, D. M. (2011). Visual crowding: A fundamental limit on conscious perception and object recognition. *Trends in Cognitive Sciences, 15*(4), 160–168.

Wilensky, J. T., & Hawkins, A. (2001). Comparison of contrast sensitivity, visual acuity, and Humphrey visual field testing in patients with glaucoma. *Transactions of the American Ophthalmological Society, 99*, 213.

Williams, P. A., Howell, G. R., Barbay, J. M., Braine, C. E., Sousa, G. L., John, S. W., … Morgan, J. E. (2013). Retinal ganglion cell dendritic atrophy in DBA/2J glaucoma. *PLoS One, 8*(8), e72282.

Wolford, G., & Chambers, L. (1984). Contour interaction as a function of retinal eccentricity. *Perception & Psychophysics, 36*(5), 457–460.

Xiong, Y.-Z., Kwon, M., Bittner, A. K., Virgili, G., Giacomelli, G., & Legge, G. E. (2020). Relationship between acuity and contrast sensitivity: differences due to eye disease. *Investigative Ophthalmology & Visual Science, 61*(6), 40.