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Higher susceptibility to central crowding in glaucoma

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Abtract

Clinical relevance: Crowding limits many daily life activities, such as reading and the visual search for objects in cluttered environments. Excessive sensitivity to crowding, especially in central vision, may amplify the difficulties of patients with ocular pathologies. It is thus important to investigate what limits visual activities and how to improve it.

Background: Numerous studies have reported reduced contrast sensitivity in central vision in patients with glaucoma. However, deficits have also been observed for letter recognition at high contrast, suggesting that contrast alone cannot completely account for impaired central perception.

Method: Seventeen patients and fifteen age-matched controls were randomly presented with letters in central or parafoveal vision at 5° eccentricity for 200 ms. They were asked to decide whether the central T was upright or inverted. The T was either presented in isolation (uncrowded) or flanked by two Hs (crowded) at various spacings. Contrast was manipulated: 60% and 5%.

Results: Compared to controls, patients exhibited a significant effect of crowding in central vision, with higher accuracy for the isolated T than for HTH only at low contrast. In parafoveal vision, an effect of crowding was also observed only in patients. The spacing to escape crowding varied as a function of contrast. Larger spacing was required at low contrast than at high contrast. Susceptibility to crowding was related to central visual field defect for central presentations and to contrast sensitivity for parafoveal presentations, only at low contrast. Controls were at ceiling level both for central and parafoveal presentations.

Conclusion: Crowding limits visual perception, impeding reading and object recognition in cluttered environments. We demonstrate that visual field defect and lower contrast sensitivity in glaucoma can increase susceptibility to central and parafoveal crowding, the deleterious effect of which can be improved by manipulating contrast and spacing between elements.

Key words: glaucoma, crowding, contrast, central vision, parafoveal vision.

Introduction

Glaucoma is a chronic ocular pathology characterized by degeneration of optic nerve fibers and apoptosis of retinal ganglion cells. This results in scotoma starting in the peripheral visual field and progressing towards the central field. Glaucoma was long believed to spare central vision until an advanced stage, but evidence is growing that patients experience difficulties or deficits in activities reliant on central vision, such as reading,[1-3] visual search[4-5] and face recognition.[6-8] The mechanisms underlying impairments in central vision are not yet completely understood. Several psychophysical studies have shown evidence of abnormal foveal contrast sensitivity in glaucoma.[9-11] Reduced contrast sensitivity in central vision affects reading. Increasing contrast from 10% to 50% has been found to be associated with significant improvement in reading speed in patients with glaucoma at various stages of the disease, whilst font size and line spacing had no effect on reading speed in that study.[12] This result indicates that reduced contrast sensitivity is a critical factor for slower reading in glaucoma. However, contrast alone cannot completely account for abnormalities in central vision. Indeed, with random strings of three letters presented centrally for 200 ms with a contrast of 99%, Kwon et al.[3] found lower accuracy in the identification of centrally displayed letters in glaucomatous patients than in normally sighted participants. This result was interpreted as a shrinkage of the visual span in glaucoma. Stievenard et al.[13] investigated foveal face perception in patients with glaucoma. Performance was compared for the categorization of a facial feature: closed mouth vs. open mouth, presented in isolation vs. in the context of a face. Normally sighted participants exhibited a "face superiority effect" with a better performance in the "mouth within a face" condition than in the "isolated mouth" condition. However, patients with glaucoma exhibited a better performance in the "isolated mouth" condition than in the "mouth within a face" condition. This was interpreted as a higher susceptibility to crowding in central vision in glaucoma. Results also showed that increasing the angular size of the face, and therefore the spacing between facial features, reversed performance in patients who, like controls, exhibited a better performance in the "mouth within a face" condition than in the "isolated mouth" condition for larger faces. These two behavioral studies indicate that crowding may also be a critical factor of perceptual deficit in foveal vision in glaucoma despite good visual acuity.

The present study explores how contrast and spacing together limit discriminability of a letter among neighboring letters (flankers) in central vision. Patients with glaucoma and age-matched controls were presented with letters displayed for 200 ms in fovea and parafovea.

Crowding was manipulated by the spacing between a central letter and its flankers (crowded condition) and compared to an isolated letter (uncrowded condition). Performance was measured at two levels of contrast (5% and 60%). In normally sighted people crowding is usually observed in peripheral vision where spatial sensitivity is reduced whilst little crowding exists in normal central/parafoveal vision.[14-15] Based on previous studies suggesting a higher susceptibility to crowding in foveal vision in glaucoma,[3, 13] and a recent study showing that crowding is exacerbated in parafoveal vision (2° and 4° eccentricity)[16] in glaucoma, crowding was expected to be more pronounced in patients than in controls. Moreover, since previous studies had demonstrated altered contrast sensitivity in central vision in glaucoma, a modulation of the effect of crowding by contrast was expected.

Method

Participants

Seventeen patients (11 females) with a visual field (VF) defect due to primary open-angle glaucoma participated. They ranged from 47 to 74 years of age (mean: 65.5 years SD: 8.6). Each patient underwent a complete ophthalmological examination including a visual field evaluation just before the experiment. Visual field sensitivity (expressed as the mean deviation: MD) was measured with a central 10-2 strategy on the Humphrey Field Analyzer SITA Standard (HFA II, Carl Zeiss Medical, CA, USA). We included patients with different deviations at the 10-2 visual field to assess whether sensitivity to central crowding occurs even at early stages of glaucoma. Visual acuity and contrast sensitivity were measured using the Freiburg Vision Test (FrACT).

Fifteen age-matched controls (9 females) ranging from 53 to 78 years in age (mean: 61.9 years SD: 7.1) were recruited among the patients' relatives and staff of the ophthalmology department. Inclusion criteria for both patients and controls were the following: no history of neurological and/or psychiatric disease, no ocular disease other than glaucoma for patients, and no family history of glaucoma for controls. Cataract was an exclusion criterion. The characteristics of the two populations are summarized in Table 1.

Patients and controls were tested monocularly. Controls were tested on their preferred eye. For patients with bilateral glaucoma, the tested eye was the one that met the inclusion criteria: a deviation on the 10-2 visual field test and an acuity equal to or better than 8/10 (0.1

LogMAR). If both eyes were impaired at the 10-2, the better eye was chosen. The 10-2 visual fields of the tested eyes are displayed in Figure 1.

For both groups, a binocular acuity lower than 8/10 (0.1 LogMar) was an exclusion criterion. All participants were asked to attend with their usual optical correction. Older patients and age-matched controls wore progressive spectacles for close and distant vision. Patients and age-matched controls did not differ significantly in age (t(30) = 1.28, p = 0.20). They differed marginally in acuity (t(30) = 2.01, p<.053) and contrast sensitivity was significantly lower in patients than in controls (1.9 vs 1.63 t(30) = 3.84, p<.001). The study was approved by the ethics committee for behavioral sciences of the University of Lille. In accordance with the tenets of the Declaration of Helsinki, written informed consent was obtained from all participants.

[Table1 about here]

Stimuli and apparatus

The stimuli were uppercase letters H and T, in Arial font, presented on a 15-inch DELL computer screen. The target was the letter T, either oriented upright or inverted. The flankers were the letter H positioned left and right of the target. The angular size of the letters was 0.4° vertically and 0.3° horizontally at a viewing distance of 57 cm with a chin rest. Two grey levels of luminance were selected for the stimuli (76 cd/m^2 and 103 cd/m^2). Presented on a light gray background (luminance: 113 cd/m2) the levels of contrast (Michelson) of the stimuli were 60% and 5%.

Procedure

Each trial started with a central black fixation cross (0.5°) displayed for 500 ms. After a 500-ms blank gap, the stimulus appeared randomly at three possible spatial locations (0° central, 5° left, 5° right of fixation cross). The spatial locations -5 to +5° corresponds to the size of the central visual span in Kwon et al.[3] The paradigm is illustrated in Figure 2. A pilot experiment conducted on five other patients (not included in the present experiment), with stimuli displayed for 150 ms, showed that they were at chance on most trials. In the experimental session, the duration of the stimuli was set at 200 ms. There was no control of fixation as the fixation cross disappeared for 500 ms before the presentation of the stimulus to avoid it masking a central stimulus. The fixation cross also disappeared for 500 ms before the presentation of parafoveal stimuli to avoid the fixation marker serving as a cue that the stimulus would appear in the parafoveal field.

Crowding was assessed (1) by manipulating the spacing between target and flankers and (2) by comparing performance between the crowded conditions (target and flankers) and a baseline uncrowded condition (isolated T). In the crowded conditionsthere were three spacings between target and flankers at 5° eccentricity. According to Bouma's law,[17] the critical spacing for identification of small letters is roughly half the eccentricity. The three chosen spacings were 2.5° (half of 5°), 2° (below critical spacing) and 3° (above critical spacing) edge-to-edge. For central stimuli, the spacings between target and flankers were 0 (no spacing) and 0.3° (corresponding to the width of a capital letter).

Target letter T, either isolated or flanked, was randomly presented upright in 50% of the trials and inverted in the other 50%. Participants were asked to decide whether the letter T was upright or inverted regardless of the presence of flankers. The response was given using the arrow keys of the computer keyboard (pointing top for upright and bottom for inverted). The inter-trial interval was set at 1500 ms after response.

The crowded and uncrowded conditions, the contrast of the stimuli (60%, 5%), the spatial locations of the stimuli (left/right) and the orientation of the T were randomly presented. The experimental session was composed of 440 trials determined by 120 central trials (isolated T and two spacing conditions X two contrast conditions X 20 repetitions) and 320 parafoveal trials (isolated T and three spacing conditions X two contrast conditions X two spatial locations X 20 repetitions). The 20 repetitions were 10 upright Ts and 10 inverted Ts. A pause was proposed after 110, 220 and 330 trials. Participants resumed the experiment by pressing the space bar of the keyboard. Following a training session of 20 trials, the experimental session lasted 20-25 minutes depending on the response time of participants.

[Figure 1 about here]

Statistical analysis

As the number of spacing conditions was different for parafoveal and central presentations, separate ANOVAs were carried out. As the percentage of correct responses is not linear accuracy was converted to a Z-score for each group. Analyses were conducted on the Z-scores using Systat 8 software (Systat Software, Inc. San Jose, California). Though the upright T was detected more accurately than the inverted T the orientation of the T was not included as factor in the analysis since the advantage of the upright T was observed for both groups (patients F(1, 16) = 18.9, p<.001, controls F(1, 14) = 17.7, p<.001), for the two levels of contrast, for foveal and parafoveal presentations and for crowded and isolated stimuli. The analyses were therefore based on 20 measures/condition. Owing to significant inter-individual variability, we did not analyze response times as some patients were fast (around 500 ms) while others were very slow (above 3 sec). The group (patients/age-matched controls) was the between-subject factor. The spatial location of the stimuli (left/right), contrast (60% and 5%) and spacing between target and flankers were the within-subject factors. The relations between clinical data (acuity, contrast sensitivity, visual field defect: MD), age and amplitude of crowding were assessed using a Spearman correlation analysis.

[Figure 2 about here]

Results

Central presentations

The results are presented in Figure 3. Accuracy was higher for controls than for patients (F(1, 30) = 10.8, p<.003). Performance was better in the high than in the low contrast condition for both groups (F(1, 30) = 12.5, p<.001). A significant main effect of spacing was observed (F(2, 60) = 4.62, p<.014). Although the interaction between group and spacing was not significant (F(2, 60) = 1.08, p = 0.35), Figure 3 shows that the effect of spacing resulted mainly from the patients' group (F(2, 32) = 3.6, p<.039) and not from the control group (F(2, 28) = 2.3, p = 0.11). A significant effect of crowding was observed for patients in the low contrast condition, with a better performance for the isolated T than for the crowded condition with no spacing (T vs. HTH: t(16) = 3.63, p<.002), but not between the isolated T and the crowded condition with a larger spacing (T vs; H T H: t(16) = 1.7, p = 0.11). No significant effect of crowding was found in the high contrast condition for patients. Age-matched controls exhibited no statistically significant effect of crowding for central presentations even for low contrast (T vs THT: t(14) = 1.38, p = 0.18). Individual data are presented in Figure 4 for patients at low contrast. The results show that 12 out of the 17 patients exhibited a better performance for the isolated T than for the crowded condition with no spacing, four patients had the same performance for both T and HTH, and patient 4 with the higher central field defect was at chance for the isolated T and perceived the trigram of letters better.

[Figures 3 and 4 about here]

Parafoveal presentations

The results are presented in Figure 5. Accuracy was significantly higher in controls than in patients (F(1, 30) = 23.6, p<.001). Performance was better for high than for low contrast (F(1, 30) = 26.9, p<.001). There was no main effect of spatial location of the stimuli (temporal: 80.1% vs. nasal: 79.3%, F(1, 30) = 0.10, p = 0.74), although it interacted significantly with group (F(1, 30) = 8.7, p<.006). This interaction resulted from the patients who exhibited a higher accuracy in the temporal than in the nasal field (by 8.3%, F(1, 16) = 4.42, p<.05). Examination of individual data showed that the higher accuracy in the temporal field resulted from the five patients (P1, P4, P5, P9 and P12) with the greater alteration of the visual field (Figure 1): temporal field 83.5% vs nasal field 62%. Performance was equivalent in the temporal and the nasal fields (67.9% vs 66.5%) for the 12 other patients with a smaller alteration of the visual field. On average, the spacing between target and flankers did not affect accuracy (F(3, 90) = 0.8, p = 0.49), while it interacted significantly with group (F(3, 90) = 4.13, p<.009) and contrast in a three-way interaction (F(3, 90) = 3.33, p<.023). The interaction resulted from the patients' group. At high contrast their performance was significantly better for the isolated T than for the T with flankers in the smaller spacing condition (t(16) = 2.53, p<.022). At low contrast, accuracy was significantly higher with the large spacing than with the medium spacing (t(16) = 2.18, p<.045). The comparison between spacing conditions for controls revealed no statistically significant effect of spacing.

[Figure 5 about here]

Correlations

We used a Spearman measure of correlation between clinical measures (MD, contrast sensitivity and acuity) and crowding. For foveal presentations, the effect of crowding (isolated T minus HTH in the no spacing condition) at low contrast was significantly related to the severity of the central visual field loss MD (r = 0.671, p<.003), but not to contrast sensitivity (r = 0.224, p = 0.387) and acuity (r = 0.132, p = 0.613). For parafoveal presentations, the lower performance for the crowded condition HTH with the medium spacing than with the large spacing at low contrast was correlated with contrast sensitivity (r = 0.506, p<.038), but not with MD (r = 0.122, p = 0.638) and acuity (r = 0.20, p = 0.442). Performance at high contrast in parafoveal vision was not related to clinical variables: MD (r = 0.205, p = 0.430), contrast sensitivity (r = 0.226, p = 0.381) and acuity (r = 0.240, p = 0.352). Contrast sensitivity was significantly related to age in the patients' group (r = 0.536, p<.026).

Discussion

This study sought to investigate the mechanisms underlying impairments in central vision in glaucoma. We were especially interested in testing whether the association of two factors, crowding and contrast sensitivity, is responsible for impaired foveal and parafoveal perception of letters. A significant effect of crowding was observed in central vision in 12 out of the 17 patients at low contrast, but not at higher contrast, although a tendency was present. No crowding was observed in controls who were at ceiling for both foveal and parafoveal presentations. In parafoveal vision, the level of contrast modulated the target-to-flanker distance for patients to perceive the central letter. Indeed, a larger target-to-flanker spacing was required to escape crowding at low contrast (3°) than at higher contrast (2.5°). Accuracy was significantly lower with a medium spacing (2.5°) than with a larger spacing (3°) at low contrast, while the lowest accuracy was observed at a target-to-flanker distance of 2° at high contrast. The issue of contrast dependency of crowding has been examined in several studies; however, the contrast of target and flankers is usually manipulated asymmetrically with a higher or lower contrast for target than for flankers. The results classically show that the strength of crowding is related to the contrast of flankers: crowding is weak when the target is of higher contrast than the flankers and strong when the contrast of flankers is higher than that of the target.[18-20] However, a study in which the contrast was the same for both target and flankers showed that the critical spacing between target and flankers decreased when the contrast was reduced below approximately 24% in foveal vision and below 17% in peripheral vision (at 3 to 10°) in five normally sighted observers.[21] Contrast is also known to affect reading in normally sighted individuals.[22-24]

The greater effect of crowding in parafoveal vision in patients than in controls is consistent with the findings of previous studies who showed that glaucomatous damage was associated with increased crowding in the parafoveal region (2 and 4°) and in peripheral vision (10°).[16, 25]

In the present study, normally sighted age-matched controls did not exhibit the foveal or parafoveal effect of crowding. Moreover, their mean accuracy was only 1% lower in parafoveal than in foveal vision, while accuracy was 8.4% lower in parafoveal than in foveal vision in patients. This result indicates that the task was too easy for controls, likely owing to a too long presentation time (200 ms) and a too large target-to-flanker spacing.

Susceptibility to central crowding in patients was found to be related to central visual field defect but not to contrast sensitivity. Patients' contrast sensitivity was measured in foveal vision using the Freiburg Vision Test (Fract). In this test, contrast is measured at threshold, at a viewing distance of 1m on the orientation of the small aperture in a C letter. In the experimental session, stimuli were displayed above contrast threshold at a shorter viewing distance. These easier viewing conditions may account for the absence of relation between crowding and contrast sensitivity in foveal vision in patients.

Although there is no consensus regarding the mechanisms underlying crowding, there is agreement on its cortical origin.[26-28] Some authors have suggested V1 as the earliest source of crowding with an overlapping of the features of target and flankers within the same receptive field or an inappropriate feature integration.[29] For other authors, it is the representation that is degraded with a combination of the target's features and those of the flankers modifying the appearance of the target.[30-31] These accounts are not mutually exclusive as crowding is not a unitary process. Impaired processing in V1 can propagate to later stages of visual processing in higher cortical areas, such as V4, where receptive fields are larger and may integrate the features of target and flankers. Neuroimaging studies have been carried out in normally sighted individuals to investigate the neural origin of crowding with a measure of BOLD signals resulting from crowded and non-crowded peripheral stimuli in various cortical areas. Millin et al.[32] found that crowding was associated with suppressed fMRI signals as early as V1. Anderson et al.[33] found that crowding influences neural responses throughout the visual cortex and increases in strength from V1 to V4, suggesting a multistage process. Although there is growing evidence from MRI studies in humans that glaucomatous damage propagates from the optic nerve to the cortex, resulting in structural and functional cortical changes,[34-35] we cannot speculate on a cortical origin of the higher susceptibility to central crowding in glaucoma in the present psychophysical study. The significant crowding effects were not found to be related to the central visual field defect in all patients. Patient 15, with a mild central field defect, exhibited a better performance for the isolated T than for the target with flankers, while Patient 4, with a severe central field defect, performed better in the crowded than in the uncrowded condition, suggesting inter-individual variability in susceptibility to crowding. Inter-observer variability on central crowding has been reported previously in another ocular pathology: strabismic amblyopia.[36-37]

Limitations: In contrast to the literature no crowding effect was observed in normally sighted controls. The experimental conditions: an exposure duration long enough to trigger a saccade and a large edge-to-edge spacing might be responsible for the lack of crowding effect and a performance at ceiling in this group. Nevertheless, a crowding effect was observed both in foveal and lateral presentations in patients with the same experimental conditions.

Conclusion

The present study demonstrates that susceptibility to foveal crowding reported in a previous study with faces as stimuli [13] extends to letters. A higher effect of crowding was also observed in parafoveal vision in patients, but the crowding distance was modulated by contrast. Susceptibility to crowding was related to central visual field defect but not to contrast sensitivity in central vision, probably because the stimuli were displayed above contrast threshold. A higher effect of crowding was not observed in all patients. The patients were not questioned about their reading frequency and general interest in the practice. In normally sighted observers, Chung[38] showed that crowding in peripheral vision could be reduced through training.

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Figure and table captions

Table1: Clinical and demographic data for patients and controls. Acuity is expressed in LogMar. CS = contrast sensitivity, R = Right eye L = Left eye.

Fig.1. 10-2 visual field of the tested eye of the 17 patients. RE = right eye, LE = left eye.

Fig.2. Schematic illustration of the experimental paradigm for foveal and parafoveal presentations.

Fig.3. Z-scores as a function of spacing conditions and levels of contrast in foveal presentations for patients with glaucoma G and healthy controls H. ** : $p<.002$.

Fig.4. Individual data in terms of Z-scores as a function of the visual field defect (MD) in foveal presentations for the isolated T and the crowded condition without spacing (THT).

Fig.5. Z-scores as a function of spacing conditions and levels of contrast for patients with glaucoma G and healthy controls H in the parafoveal visual field. * : $p<.05$.

Table1: Clinical and demographic data for patients and controls. Acuity is expressed in LogMar. CS = contrast sensitivity, R = Right eye L = Left eye.

Patients	LogCS	MD	Acuity	Age	Tested eye	Gender
1	1.9	-12,19	0.0	60	RE	F
2	1.39	-2,75	0.0	69	RE	M
3	1.73	-7,1	0.1	73	LE	F
4	1.2	-24,26	0.1	74	RE	M
5	2.06	-18,53	0.0	54	LE	F
6	1.58	-4,04	0.0	69	RE	M
7	1.74	-7,27	0.1	63	LE	F
8	1.56	-5,46	0.1	71	LE	M
9	1.32	-11,38	0.0	71	LE	F
10	1.5	-1,17	0.0	60	RE	M
11	1.24	-8,88	0.1	70	RE	F
12	1.9	-11,34	0.0	47	LE	F
13	1.72	-3,24	0.0	49	RE	F
14	1.43	-1,55	0.0	74	RE	F
15	1.67	-4,85	0.1	71	LE	F
16	1.96	-2,15	0.0	66	RE	M
17	1.9	-9,03	0.0	73	LE	F

Controls	LogCS		Acuity	Age	Tested eye	Gender
1	1.76		0.1	78	RE	M
2	1.83		0.0	64	RE	F
3	1.98		0.0	58	RE	F
4	1.93		0.0	61	LE	F
5	1.94		0.0	60	RE	F
6	1.9		0.0	53	LE	M
7	1.86		0.0	65	RE	F
8	1.99		0.0	60	LE	M
9	1.86		0.0	59	LE	M
10	1.94		0.0	53	RE	M
11	2.14		0.0	60	RE	F
12	1.92		0.0	58	LE	F
13	1.78		0.0	77	RE	M
14	1.93		0.0	62	RE	F
15	1.88		0.0	61	RE	F

Fig.1.

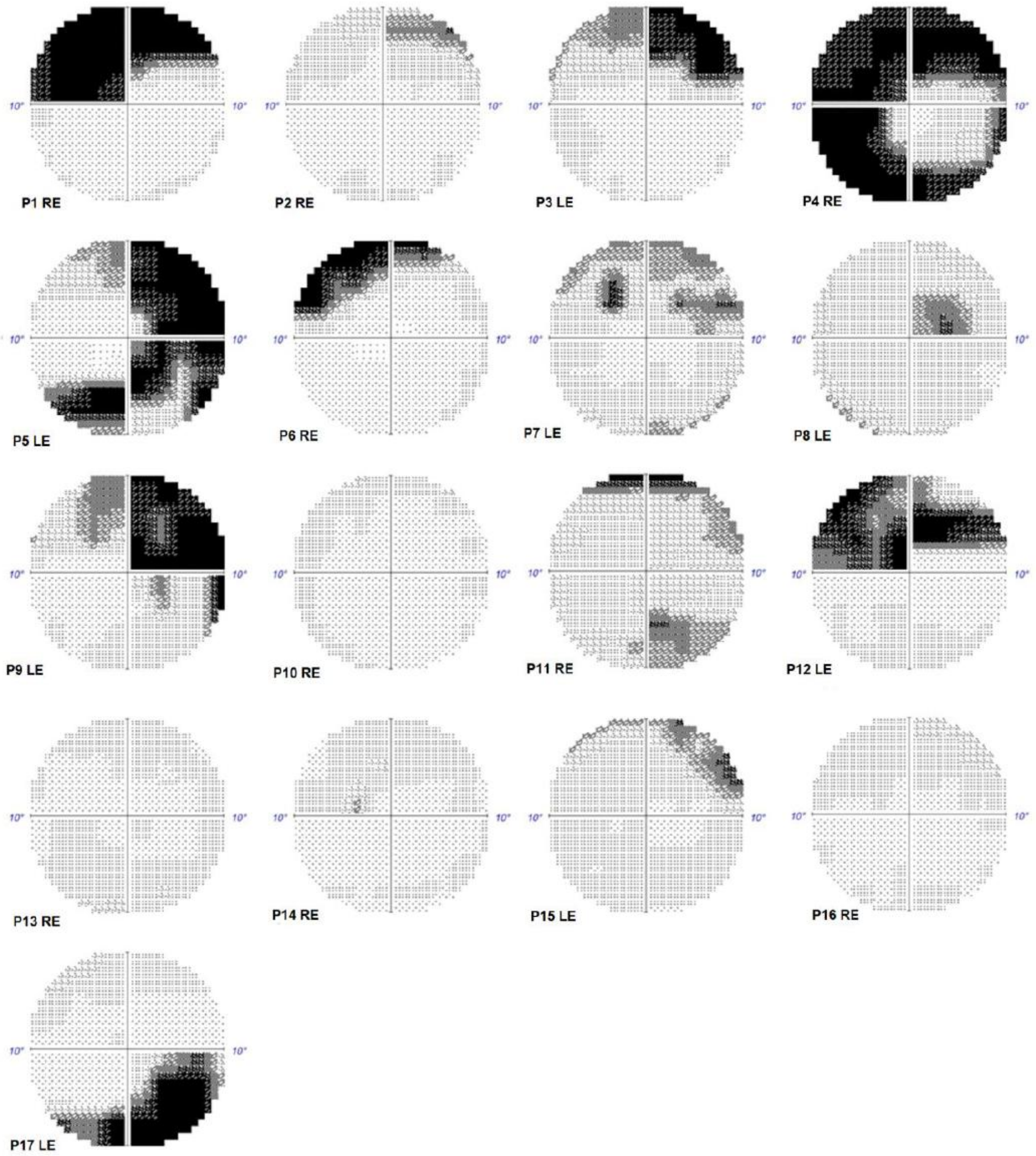

10°
10°
P1 RE
P2 RE
P3 LE
P4 RE
P5 LE
P6 RE
P7 LE
P8 LE
P9 LE
P10 RE
P11 RE
P12 LE
P13 RE
P14 RE
P15 LE
P16 RE
P17 LE

Fig.2.

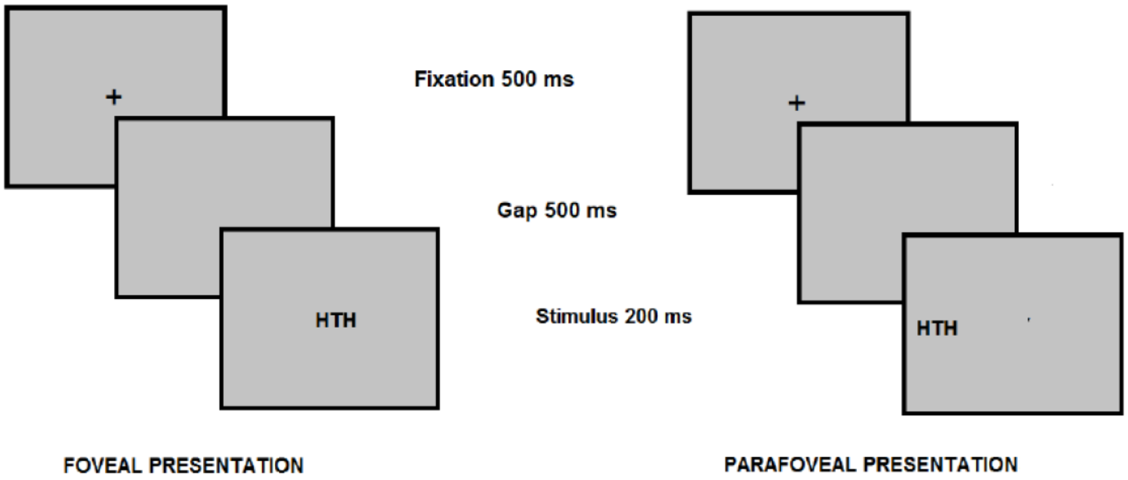

+
Fixation 500 ms
Gap 500 ms
HTH
Stimulus 200 ms
+
HTH
FOVEAL PRESENTATION
PARAFOVEAL PRESENTATION

Fig.3.

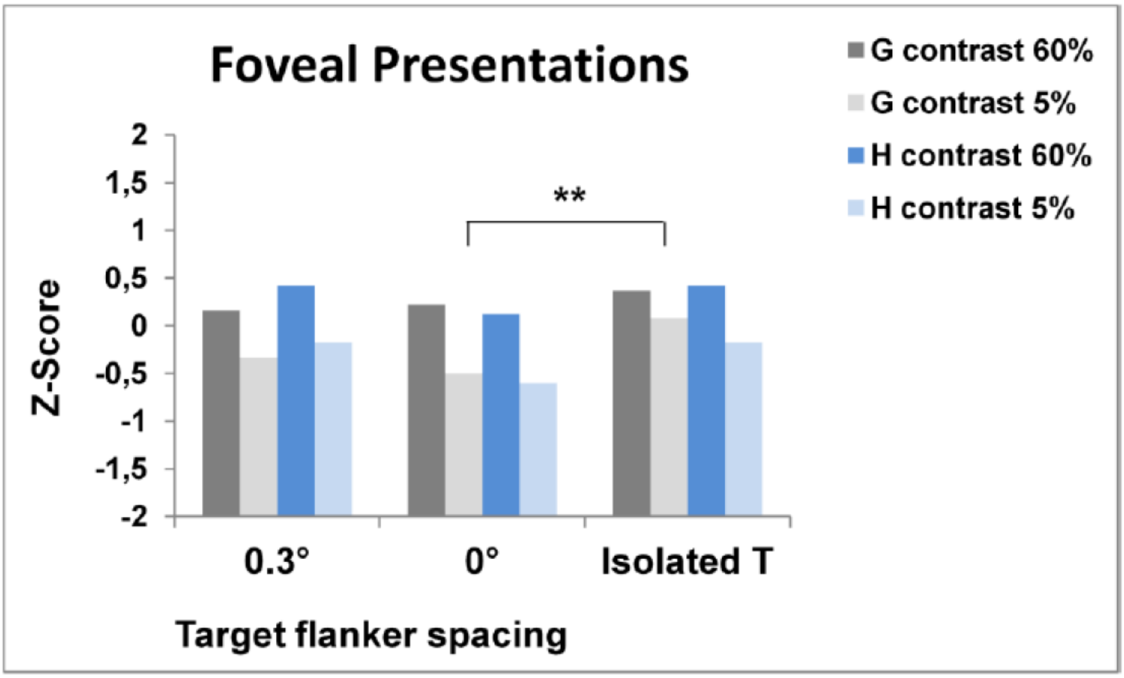

Foveal Presentations
G contrast 60%
G contrast 5%
H contrast 60%
H contrast 5%
Z-Score
2
1,5
1
0,5
0
-0,5
-1
-1,5
-2
**
0.3°
0°
Isolated T
Target flanker spacing

Fig.4.

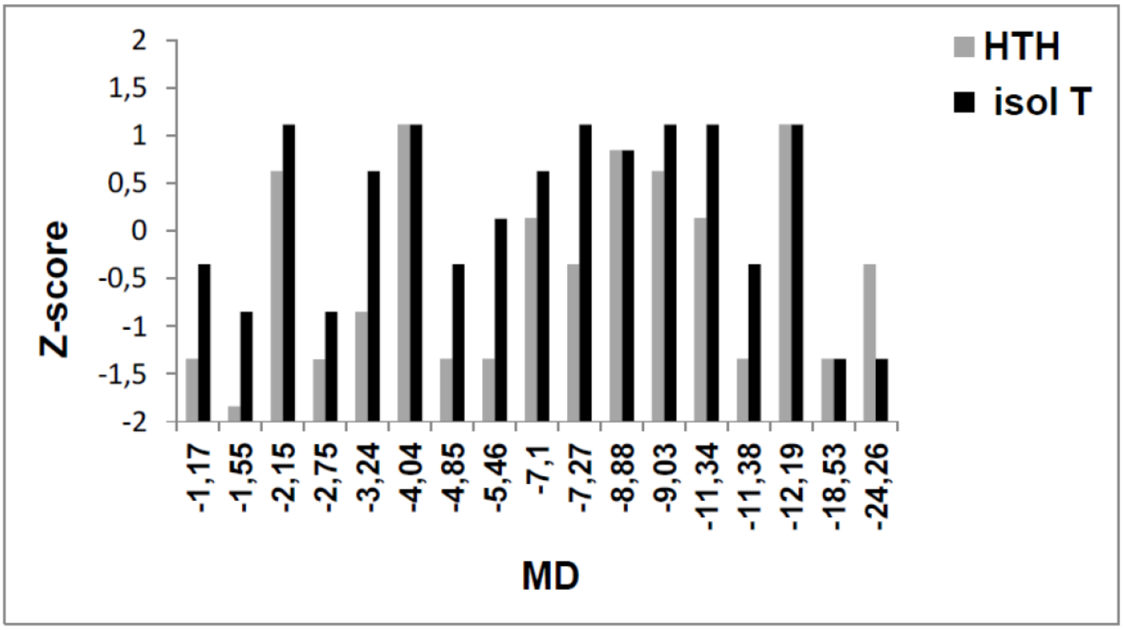
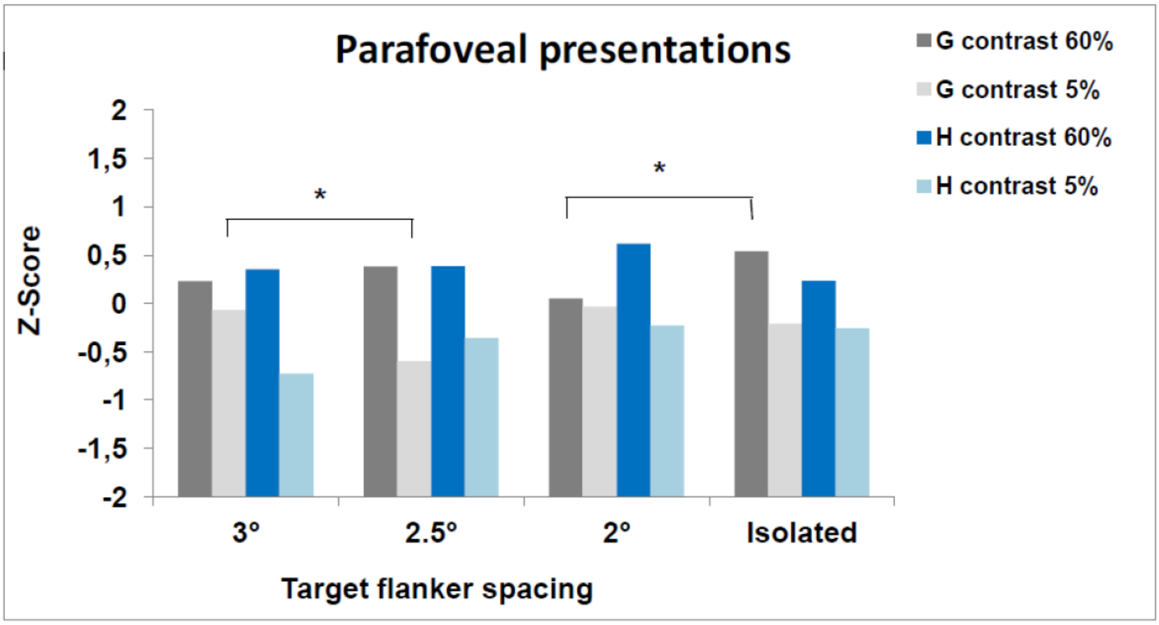

Z-score
2
1,5
1
0,5
0
-0,5
-1
-1,5
-2
-1,17
-1,55
-2,15
-2,75
-3,24
-4,04
-4,85
-5,46
-7,1
-7,27
-8,88
-9,03
-11,34
-11,38
-12,19
-18,53
-24,26
MD
HTH
isol T

Fig.5.


Parafoveal presentations
G contrast 60%
G contrast 5%
H contrast 60%
H contrast 5%
Z-Score
2
1,5
1
0,5
0
-0,5
-1
-1,5
-2
*
*
3°
2.5°
2°
Isolated
Target flanker spacing