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Central Perimetric Sensitivity Estimates are Directly Influenced by the Fixation Target

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1 **Central perimetric sensitivity estimates are directly influenced by the**
2 **fixation target**

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27
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33 **Keywords:** perimetry, microperimetry, visual fields, central vision loss

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1 **Abstract**

2
3 **Purpose**

4 Perimetry is increasingly being used to measure sensitivity at central visual field locations.
5 For many tasks, the central (0°, 0°) location is functionally the most important, however
6 threshold estimates at this location may be affected by masking by the nearby spatial
7 structure of the fixation target. We investigated this effect.

8
9 **Methods**

10 First we retrospectively analysed microperimetry (MAIA-2, CenterVue, Padova, Italy) data
11 from 60 healthy subjects, tested on a custom grid with 1° central spacing. We compared
12 sensitivity at (0°, 0°) to the mean sensitivity at the 8 adjacent locations. We then prospectively
13 tested 15 further healthy subjects on the same instrument using a cross-shaped test pattern
14 with 1° spacing. Testing was carried out with and without the central fixation target, and
15 sensitivity estimates at (0°, 0°) were compared. We also compared sensitivity at (0°, 0°) to the
16 mean of the adjacent 4 locations in each condition. Three subjects undertook 10 repeated
17 tests with the fixation target in place to assess within-subject variability of the effect.

18
19 **Results**

20 In the retrospective analysis, central sensitivity was median 2.8dB lower (95% range 0.1 to
21 8.8dB lower, $p < 0.0001$) than the mean of the adjacent locations. In the prospective study,
22 central sensitivity was median 2.0dB lower with the fixation target vs. without (95% range 0.4
23 to 4.7dB lower, $p = 0.0011$). With the fixation target in place central sensitivity was median
24 2.5dB lower than mean sensitivity of adjacent locations (95% range 0.8 to 4.2dB lower,
25 $p = 0.0007$), whilst without the fixation target there was no difference (mean 0.4dB lower, SD
26 0.9dB, $p = 0.15$). These differences could not be explained by reduced fixation stability. Mean
27 within subject standard deviation in the difference between central and adjacent locations'
28 sensitivity was 1.84dB for the repeated tests.

29
30 **Conclusions**

31 Perimetric sensitivity estimates from the central (0°, 0°) location are, on-average, reduced by
32 2 to 3dB, corresponding to a 60-100% increase in stimulus luminance at threshold. This effect
33 can be explained by masking by the nearby fixation target. The considerable within- and
34 between-subject variability in magnitude, and the unknown effects of disease may hamper
35 attempts to compensate threshold estimates for this effect. Clinicians should interpret central
36 perimetric sensitivity estimates with caution, especially in patients with reduced sensitivity
37 due to disease.

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39

40

1 Introduction

2
3 Though perimetry is commonly associated with non-central vision, perimetric tests of foveal
4 and parafoveal vision have been in common use for some time. With the recently increased
5 interest in measurement of central vision in both retinal disease and glaucoma (for reviews
6 see Hood et al¹ and Rohrschneider et al²), central perimetric tests like the 10-2 program of the
7 Humphrey Field Analyzers (Carl Zeiss Meditec, Jena, Germany, <http://www.zeiss.com>) and
8 those performed by microperimeters such as the MAIA-2 (CenterVue, Padova, Italy,
9 <http://www.centervue.com>) and MP-1 and MP-3 (Nidek, Japan, <http://www.nidek-intl.com>)
10 are seeing increasing clinical use.

11
12 Many central perimetric tests (e.g. 10-2) do not include a test location at the central location
13 ($0^\circ, 0^\circ$), in part due to the use of a fixation target that occupies this location. The more recent
14 MAIA-2 microperimeter uses a central annulus fixation target that enables testing of the
15 central location within the annulus. Indeed, the common “Expert” and “Fast” test patterns,
16 used in the MAIA-2 include a measurement of central sensitivity. This would seem
17 advantageous for assessment of the highest resolution region of central vision, important for
18 tasks such as reading, face-recognition and watching television.

19
20 In static automated perimetry, sensitivity is typically measured for stimuli presented on a
21 uniform, fixed luminance background. However, when measuring the central location with an
22 annulus fixation target, the annulus introduces a change in the background near to the
23 stimulus. Stimulus detection is commonly affected by the presence of surrounding structure
24 due to visual masking mechanisms, the nature and strength of which depend on the spatial
25 properties of the stimulus/surround³, their location in visual space⁴ and the psychophysical
26 task being performed^{5, 6}. Masking of foveal Gabor targets by surrounding flankers, for example,
27 influences contrast detection thresholds when the flankers are separated from the target
28 Gabor by up to approximately 2° ⁷; considerably further than the distance between the fixation
29 annulus and the central test location in the MAIA-2 microperimeter.

30
31 Masking of perimetric stimuli by surrounding texture spatially similar to the fixation annulus
32 used in the MAIA-2 has not been previously investigated to our knowledge. Here we
33 investigate the hypothesis that masking by the fixation annulus affects central sensitivity
34 estimates made by the MAIA-2 microperimeter.

36 Methods

37
38 We conducted two investigations using the MAIA-2 microperimeter. First, data from 60
39 healthy observers collected for another study on a custom spatially dense grid was
40 retrospectively reviewed, and sensitivity estimates at the central location were compared to
41 estimates from surrounding locations. Based on previous studies of the hill of vision⁸⁻¹⁰, we
42 expected that the central location would have higher sensitivity than surrounding locations.
43 Lower sensitivity could indicate an effect of the fixation annulus. Second, we prospectively
44 tested 15 healthy observers on another custom grid, both with and without the central
45 annulus fixation target. This second study was designed to directly test the hypothesis that
46 central sensitivity is reduced by the presence of the fixation annulus. As an adjunct to this
47 study we also assessed within-subject variation in central sensitivity reduction.

48
49 All studies had common inclusion criteria of visual acuity 0.2 logMAR or better in the tested
50 eye, spherical refractive error within the range that can be compensated for by the MAIA-2 (-

1 15.00D to +10.00D), cylindrical refractive error less than 4.00D, age over 18 years and no
2 known current or previous ocular disease. One eye was tested per participant, chosen
3 randomly if both eyes met the inclusion criteria. All participants gave written informed
4 consent to take part and for their anonymised data to be used in future studies. Both studies
5 were approved by a local research ethics committee. All participants undertook at least one
6 practice test using the “4-2 Expert” strategy of the MAIA-2 before experimental data were
7 collected. Sensitivity thresholds were estimated using the MAIA-2’s standard 4-2 staircase
8 algorithm and Goldmann III (0.43° diameter) stimuli. Any tests with fixation not classified as
9 “stable” by the MAIA-2 software were discarded and repeated.

11 Retrospective study

12
13 Data collected for another study were retrospectively reviewed. Healthy participants (n=60,
14 age 19-50, median 23 years, 59 naïve to the original study purpose) undertook MAIA-2
15 microperimetry using 237 custom test locations placed on a square grid with 1° spacing up to
16 5° eccentricity and 2° spacing from 5 to 13° eccentricity (Figure 1). Participants were
17 instructed to fixate the standard 0.76° diameter fixation annulus (Figure 1). Testing was
18 broken into four randomly-ordered blocks in each of which an evenly-spaced subset of test
19 locations was tested. Testing was completed over one or two study sessions lasting up to one
20 hour, incorporating rests between tests as needed.

21
22 For the present study, we compared sensitivity at the central (0°, 0°) location to mean
23 sensitivity at the eight immediately adjacent test locations (Figure 1).
24

25 Prospective study

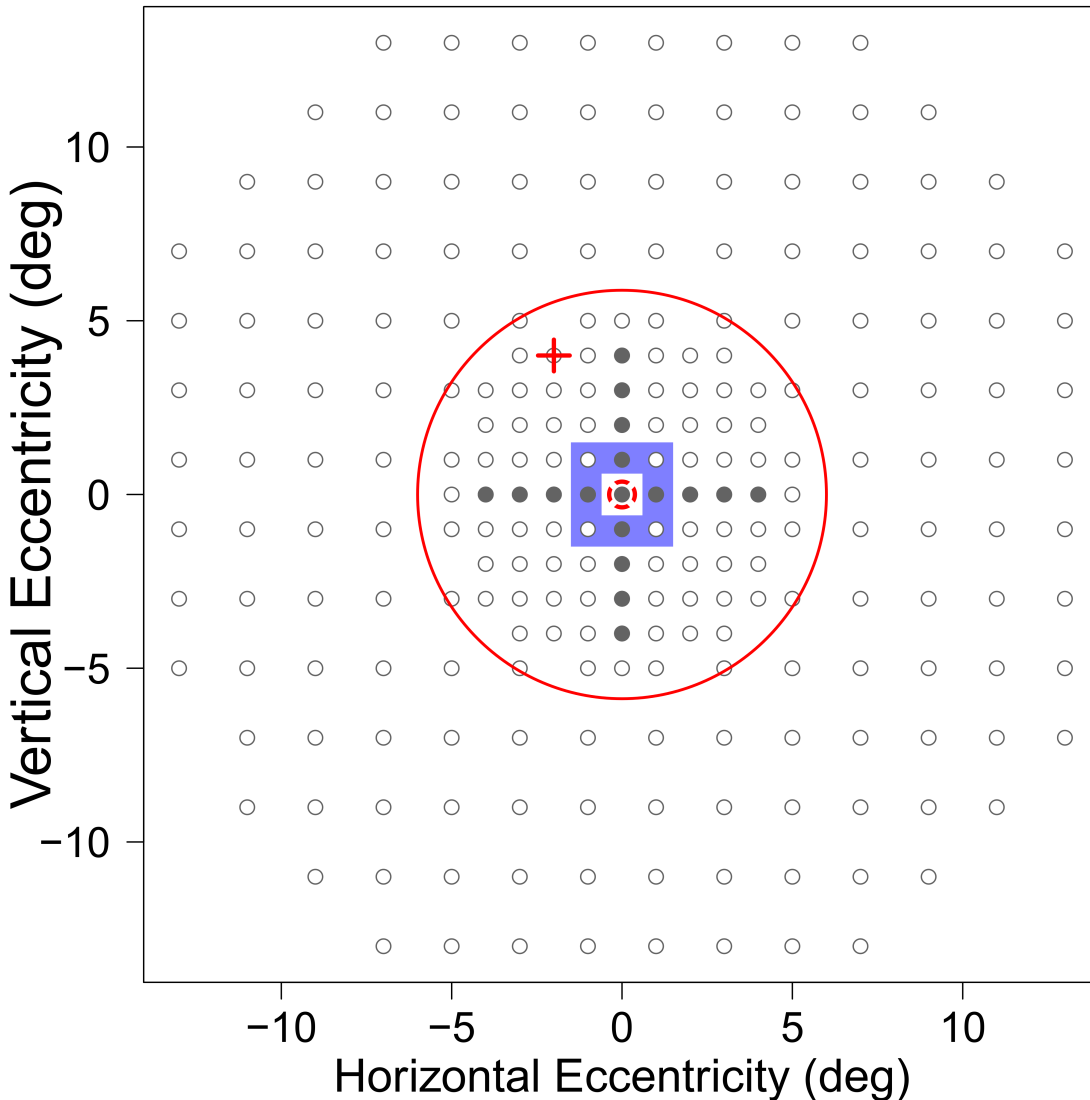
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27 Healthy participants (n=15, age 21-51, median 26 years) undertook MAIA-2 microperimetry
28 using a custom grid with 17 locations arranged in a cross pattern centred on (0°, 0°) with 1°
29 spacing up to a maximum of 4° eccentricity (Figure 1). This pattern was chosen to allow short
30 test duration but with spatial uncertainty approaching that of the 4-2 “Expert” test commonly
31 used on the MAIA-2. Both authors participated; the remaining participants were naïve to the
32 purpose of the study.

33
34 Testing was carried out under two conditions, one with the central annulus fixation target,
35 and one without. In the “without” condition, the large annulus target (12° diameter, Figure 1)
36 was displayed, centred on (0°, 0°). Since it is not possible for the MAIA-2 to display only the
37 large circle, an additional small cross was displayed at (-2°, 4°). This is the furthest available
38 location from the centre and does not impinge on any tested locations. In the “without”
39 condition the observers were instructed to ignore the cross and fixate as steadily as possible
40 in the centre of the large circle. In the “with” condition observers fixated in the centre of the
41 standard 0.76° diameter annulus as normal. Each condition was repeated twice in random
42 order, and the results of the two repeats were averaged. Testing was completed within a
43 single session of up to 30 minutes, incorporating rests as needed. All participants gave
44 informed consent to take part.

45
46 To test the hypothesis that the fixation annulus alters central sensitivity estimates, we made
47 within-subject comparisons of:

- 48 (i) Central sensitivity with vs. without the fixation annulus.
- 49 (ii) Central sensitivity vs. the mean of the four immediately adjacent locations (Figure
50 1) with the fixation annulus (similar to the retrospective study).

1 (iii) Identical to (ii) except without the fixation annulus.
 2 We also compared sensitivity at the four immediately adjacent locations with vs. without the
 3 fixation annulus within subjects. To assess within-subject variation in central sensitivity
 4 difference from surrounding locations, three participants (ages 30-35, including both authors)
 5 undertook a further eight tests under the “with” condition (total n=10 repeats). In-between
 6 these repeated tests the participants moved away from the instrument, and the instrument
 7 was adjusted to a completely different position before re-positioning for the participant in
 8 order to simulate separate clinic visits.
 9



10
 11 **Figure 1:** Test locations used, locations compared to the central ($0^\circ, 0^\circ$) location, and the
 12 positions of the two fixation annuli. The unfilled grey circles represent the test locations used in
 13 the retrospective study. The filled grey circles represent test locations used in both studies. The
 14 smaller red annulus represents the standard fixation annulus, the larger red annulus represents
 15 the annulus used only in the “without” condition in the prospective study. The red cross at (-2,4)
 16 was present only for the “without” condition in the prospective study. Test locations shown on
 17 the shaded blue background were included in the comparisons to the central location. Stimuli
 18 and annuli are drawn to scale.

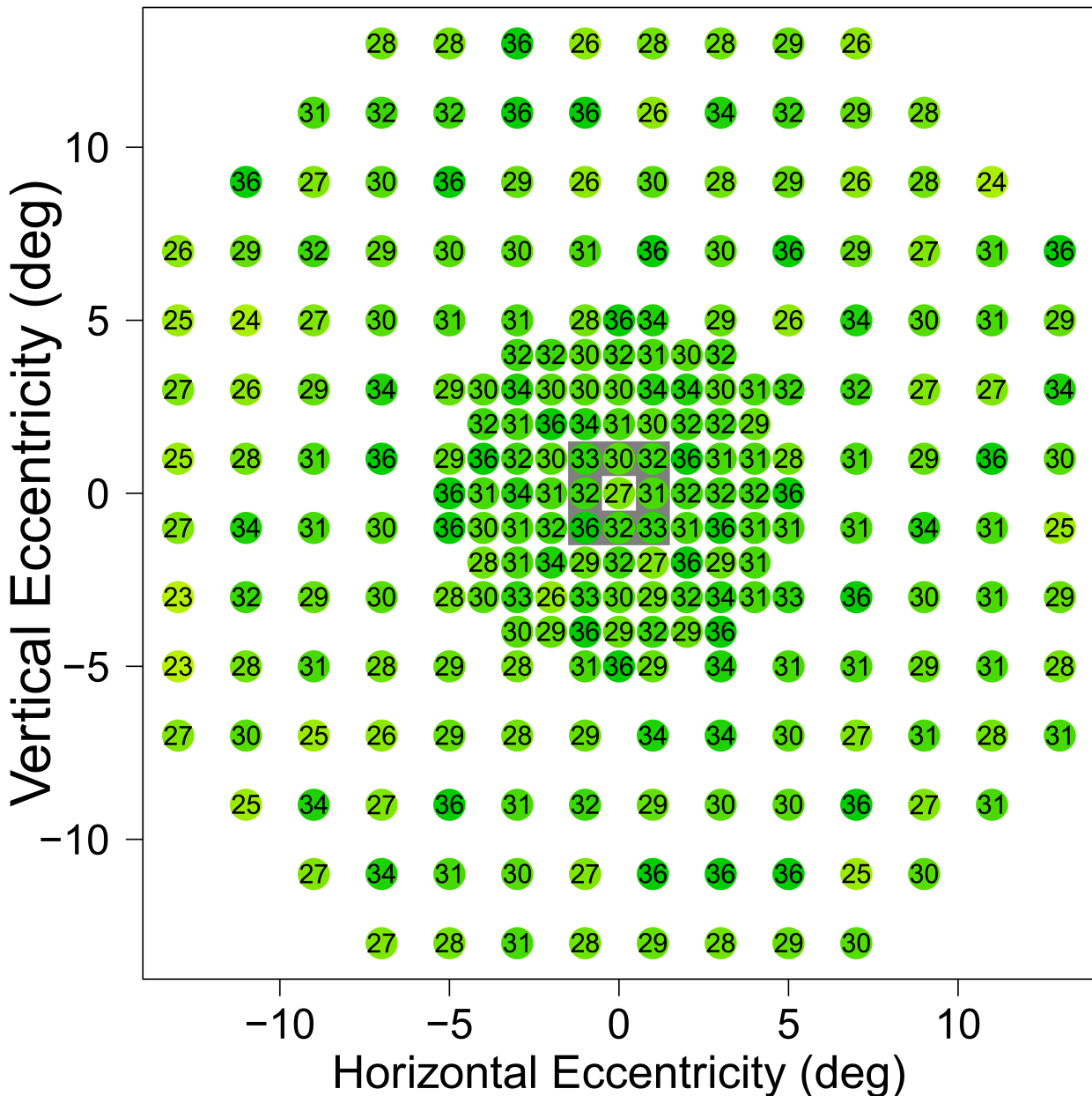
19
 20
 21 All statistical analyses for both studies were carried out in the open-source environment, R^{11}
 22 (version 2.15.0, <https://www.r-project.org/>). Comparisons were made on a within-subject
 23 basis using paired t-tests when data were normally distributed or Wilcoxon signed-rank tests

1 when they were not. Normality of data was assessed by Kolmogorov-Smirnov tests and visual
 2 comparison of data quantiles to normal quantiles. Statistical significance was assumed at
 3 $p < 0.05$. Since we made a relatively small number of planned comparisons we did not use a
 4 correction for multiple comparisons.¹²
 5

6 Results

7 Retrospective study

8 Figure 2 shows example data from one participant, including the custom pattern of test
 9 locations and those included in the comparison with the centre location.
 10



11 **Figure 2:** Example of one participant's central visual field from the retrospective study. The
 12 custom test pattern included locations spaced on a 1° square grid up to an eccentricity of 5°,
 13 then spaced on a 2° square grid from 5 to 13° eccentricity. Sensitivity at the central location (0°,
 14 0°) was compared to the mean of the surrounding eight locations, shown here on a gray shaded
 15 background. Sensitivity (dB) at each location is indicated. Note the reduced sensitivity at the
 16 central location.
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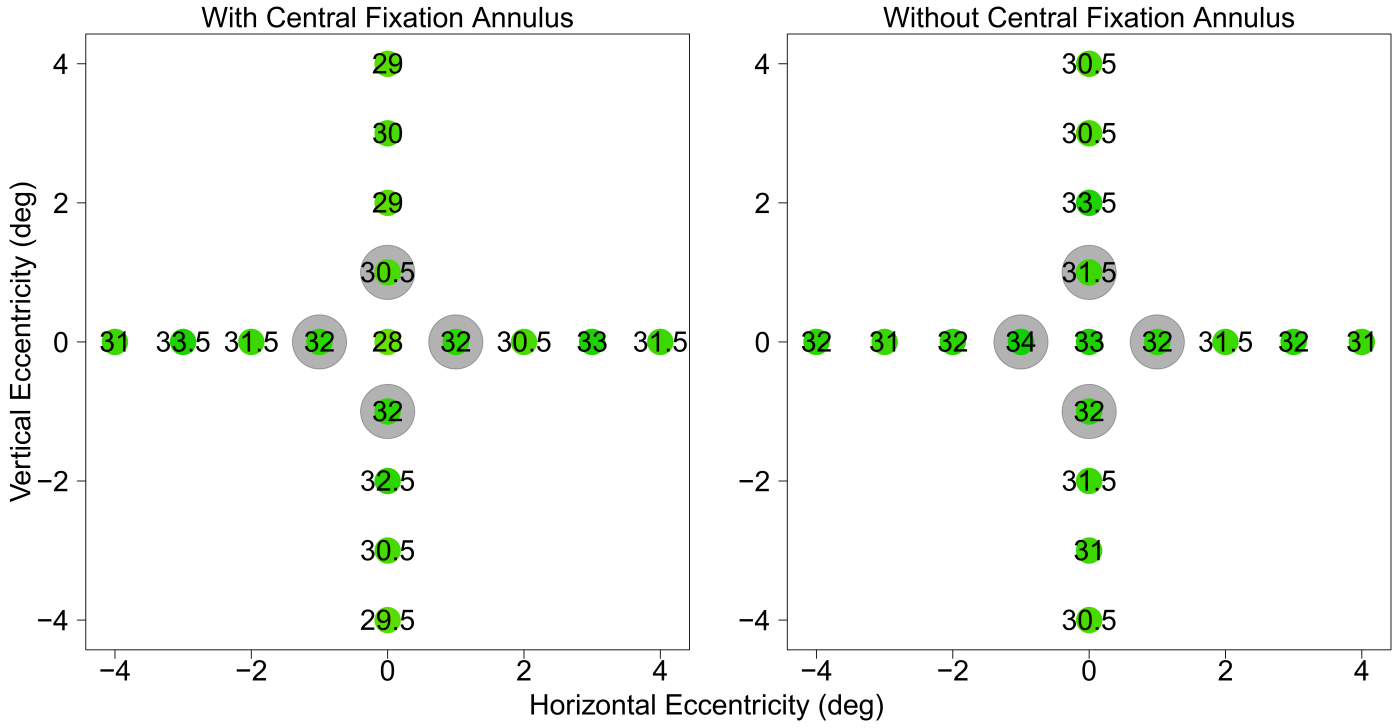
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Contrary to what would be physiologically predicted in the absence of confounding factors, threshold sensitivity at the central location was median 2.8dB (95% range -8.8 to -0.1dB) lower than the mean of the surrounding eight locations ($p < 0.0001$, Wilcoxon signed-rank test). Central sensitivity was at least 1dB lower than the mean of the surrounding locations for 54 of 60 participants (90%).

We additionally compared sensitivity at the central location to the mean sensitivity at the four closest cardinal points (shaded points within the blue box in Figure 1) and to the mean sensitivity at the four closest ordinal points ($(\pm 1^\circ, \pm 1^\circ)$ unshaded points within the blue box in Figure 1) since the latter are 0.41° further away from the fixation annulus. Mean sensitivity at the cardinal points was mean 0.6dB (SD 1.0dB) lower than mean sensitivity at the ordinal points (paired t-test, $t(59) = 4.34$, $p < 0.0001$). Sensitivity at the central location was median 3.3dB (95% range -8.4 to -0.5dB) lower than mean sensitivity at the ordinal points ($p < 0.0001$, Wilcoxon signed-rank test) and was median 2.5dB (95% range -9.3 to 1.1dB) lower than mean sensitivity at the cardinal points ($p < 0.0001$, Wilcoxon signed-rank test).

Prospective study

Figure 3 shows example data from one participant, including the custom pattern of test locations and those included in the comparison with the centre location.



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Figure 3: Example of one participant's central visual field from the prospective study when the central fixation annulus was present (left) and absent (right). The custom test pattern included 17 locations spaced 1° apart in a cross pattern as shown. Sensitivity at the central location ($0^\circ, 0^\circ$) was compared to the mean of the surrounding four locations, shown here on a grey shaded background. Sensitivity (dB) at each location is indicated. Note that sensitivity at the central location was reduced when the fixation annulus was present (left), but not when it was absent (right).

1
2 In our participants, fixation stability was acceptable, though reduced when the central
3 annulus was removed. With the central annulus, median 95% bivariate contour ellipse area of
4 fixation was 0.30 deg², whilst without the central annulus this increased to 2.05 deg²
5 (p=0.0011, Wilcoxon signed-rank test). If unstable fixation had affected the results, we would
6 expect the surrounding locations to have greater average sensitivity when the fixation
7 annulus was not present due to fixation wandering to the stimulus locations. There was in fact
8 no significant difference in mean sensitivity at surround locations under the two conditions
9 (mean difference 0.1dB higher without the fixation annulus, standard deviation 0.8dB, paired
10 t-test: t(14)=0.31, p=0.76).

11
12 Central sensitivity was median 2.0dB (95% range -4.7 to -0.4dB) lower when the central
13 fixation annulus was present compared to when it was not (p=0.0011, Wilcoxon signed-rank
14 test).

15
16 Similar to the retrospective study, when the fixation annulus was present, central sensitivity
17 was median 2.5dB (95% range -4.2 to -0.8dB) lower than the mean of the surrounding four
18 locations (p=0.0007, Wilcoxon signed-rank test). When the fixation annulus was not present,
19 however, there was no clinically or statistically significant difference in sensitivity between
20 the central and surrounding four locations (mean difference central location 0.4dB lower,
21 standard deviation 0.9dB, paired t-test: t(14)=1.51, p=0.15).

22
23 For the three subjects who conducted ten repeats with the standard fixation annulus present,
24 within-subject standard deviation in difference between sensitivity estimates at the central
25 location and the four adjacent locations was 1.84dB.

27 Discussion

28
29
30 The presence of the standard central fixation annulus in the MAIA-2 microperimeter reduced
31 estimates of healthy observers' central sensitivity by 2-3dB on average. This effect was not
32 present when testing was conducted without the fixation annulus. This is a large and
33 potentially clinically significant reduction in sensitivity, being equivalent to a 60-100%
34 increase in stimulus luminance at threshold.

35
36 The effect of the fixation annulus on detection thresholds observed in this study can be
37 described as masking by the fixation annulus. Masking effects of nearby or surrounding
38 texture on the detection of stimuli are ubiquitous in human vision, and their nature depends
39 on a variety of factors including location in visual space⁴, relative spatial properties of the
40 stimulus and surround³ and the psychophysical task being performed^{5,6}. Key examples
41 include overlay masking, in which non-target objects overlay the receptive fields involved in
42 detection of the target stimulus, and surround suppression in which surrounding objects
43 stimulate receptive fields not directly involved in detection of the target stimulus yet still
44 impair stimulus detection by lateral inhibitory processes⁴. It is therefore likely that the
45 present observation can be explained by similar mechanisms to those already reported in
46 laboratory psychophysics and animal models, though an in-depth exploration of these
47 possibilities is beyond the scope of this study.

48
49 It may be tempting to simply employ an empirical correction factor to the central location,
50 such as adding 2-3dB to the estimated sensitivity, for clinical purposes. This may be a useful

1 first pass in reducing bias in central threshold estimates on average and for healthy subjects.
2 However, such a correction must be applied whilst bearing in mind its limitations. First, such
3 a simple correction assumes that the visual system's response to contrast is linear. Whilst this
4 may be approximately true over a narrow range of contrasts, it is demonstrably not true over
5 wider ranges, particularly at low luminance¹³. This may be particularly important for
6 individuals with sensitivity loss due to disease, where this relationship may be less linear and
7 contrast gain may also be altered^{14, 15}. Second, the magnitude of the reduction is empirically
8 highly variable both within- and between-subjects. Some of the masking effects mentioned
9 above change with age¹⁶⁻¹⁸, and vary considerably between individuals¹⁹. This makes a simple
10 correction for the average reduction unlikely to be accurate for any one test. It is also worth
11 emphasising that the effect observed in this study is likely to hamper the monitoring of
12 progressive sensitivity loss at this location, as the effects of the annulus on sensitivity
13 estimates may not be constant or linear with sensitivity loss due to possible concurrent
14 changes in contrast gain and masking mechanisms.

15
16 There are at least three reasons for the high variability in the sensitivity reduction at the
17 central location. Measurement variability and between-individual variability in contrast gain
18 and masking mechanisms (as mentioned above) will surely contribute to this variation, but
19 the third, possibly major, contributor to the variability in our data is parallax displacement of
20 the test stimulus relative to the annulus depending on the precise alignment of the eye
21 relative to the instrument. We note that with the MAIA-2, even small lateral shifts of head
22 position can cause significant parallax displacement, in some cases causing the central
23 stimulus to overlay a portion of the fixation annulus. Clearly, such changes in the distance
24 between the stimulus and the fixation annulus are likely to affect the sensitivity reduction
25 induced by the annulus. To this end, it may be possible to reduce these effects considerably by
26 using an alternative fixation target that does not affect the immediate surround of any
27 stimulus as much. One possibility would be a broken cross target, though this remains to be
28 tested. An alternative might be to have a changing fixation target, depending on the location
29 under test, though this would have the potentially negative affect of providing spatial cueing
30 to the test subject and may also affect fixation stability.

31
32 Though the MAIA-2 and similar microperimeters employ a number of additional technologies
33 (e.g. eye-tracking, fundus imaging) beyond that of conventional perimeters, none of these
34 impact upon our findings. Therefore, although we used a MAIA-2 microperimeter in this study,
35 we expect that our results will generalise to other perimeters or experimental procedures
36 that use a nearby fixation target to enable testing of the central location.

37
38 The comparison of sensitivity at the central location to that of adjacent locations is limited by
39 the assumption that true sensitivity at the central location is at least equal to the adjacent
40 locations. In reality, true central sensitivity is likely to be higher than at adjacent locations⁸⁻¹⁰,
41 so it is likely that the "true" reduction in measured sensitivity is actually slightly greater than
42 reported. Nevertheless, our findings appear robust across a number of participants when
43 tested both prospectively and retrospectively, and the reduction in sensitivity is also apparent
44 when comparing across tests carried out with and without the fixation target in place. When
45 testing without the central fixation target, fixation was worse than with the target in place
46 (though still within acceptable limits). However, this did not affect sensitivity at surrounding
47 locations, and would only be expected to reduce sensitivity at the central location, thereby
48 reducing the difference between the "with" and "without" fixation target conditions.

49
50 The reduction in measured sensitivity at the central (0°, 0°) location is a clinically relevant
51 problem that those using central perimetry should be aware of. Central sensitivity estimates

1 are likely to be significantly reduced by the presence of the annulus. Whilst adjustment of
2 sensitivity estimates by 2-3dB will reduce this bias in healthy subjects, this correction may
3 not be accurate in patients with reduced sensitivity due to disease. In certain perimeters,
4 estimates of central sensitivity may also be highly variable unless great care is taken to align
5 the subject carefully such that the central test location is centred in the annulus, and to
6 maintain this position throughout the test. Central sensitivity estimates should therefore be
7 interpreted with caution when assessing foveal damage or disease progression.

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