Spatial Alignment over Retinal Scotomas

Michael D. Crossland1,2 and Peter J. Bex1,5

PURPOSE. Perceptual completion can mask the presence of physiological and pathologic retinal scotomas. This psychophysical study used a spatial alignment task to examine the processes underlying this perceptual completion. Similarities between the completion of pathologic and physiological scotomas would be consistent with large-scale reorganization of the visual system in eye disease.

METHODS. In five control subjects with no eye disease, Vernier alignment thresholds were measured over the physiological blind spot at the optic nerve head and over equally eccentric temporal retina. For nine subjects with retinal scotomas, alignment thresholds were measured over the maximum vertical extent of the larger scotoma in one eye and at an equal separation and eccentricity in the eye with a smaller or no scotoma.

RESULTS. In control subjects, alignment thresholds were better over the physiological blind spot than over equally eccentric temporal retina (P < 0.05). Alignment thresholds were no better over pathologic retinal scotomas than more intact, equally eccentric retina (P = 0.9).

CONCLUSIONS. These quantitative differences implicate different mechanisms for perceptual completion over pathologic and physiological retinal scotomas. Filling in across pathologic scotomas appears to involve higher level image processing-based mechanisms that operate even when their input is interrupted. Filling-in at the optic nerve head involves additional low-level processes that may be hard wired, in which receptive fields span the blind spot and support fine orientation discriminations. These results argue against low-level reorganization of the visual system in people with retinal disease.

Retinal scotomas caused by macular disease are the leading cause of visual impairment in North America and Europe.1 People with macular disease are frequently unaware of their scotoma; less than 60% are able to discern their scotoma on an Amsler grid chart.2,3 A principal cause of this is thought to be the phenomenon of “perceptual completion” or “filling-in” whereby the absence of visual input is not perceived.4 Filling-in of the physiological blind spot at the optic nerve head has been known for many years,5 but this phenomenon can also be observed over pathologic retinal scotomas,6,7 in scotomas caused by cortical lesions,8,9 over simulated scotomas,10 and over featureless areas in the peripheral visual field.11

Filling-in of retinal scotomas is important for two reasons. First, there is considerable debate in the literature as to whether retinal scotomas lead to remapping of the primary visual cortex in humans.12-13 If the mechanism of filling-in an adult-onset retinal scotoma is similar to that supporting filling-in of the physiological blind spot, this would provide evidence for reorganization of the visual cortex. The presence of cortical reorganization has important implications for the visual rehabilitation of people with retinal disease, particularly for the development and use of visual training programs based on the principles of perceptual learning. Second, a full understanding of how retinal scotomas fill in may lead to the development of new clinical screening tests for macular disease that are not confounded by filling-in.14

In principle, filling-in could arise from low- or high-level visual processes and probably involves both. At a low level, filling in could arise if the receptive fields of visually responsive neurons were to remap transiently or permanently, after interruption of their retinal inputs by real or artificial scotomas. Such reorganization has not been observed in the lateral geniculate nucleus,15 but there are many reports of receptive field reorganization in primary visual cortex.16-20 Behavioral evidence for such reorganization comes from shifts in the positions of contours at the boundary of an artificial scotoma during filling in.21,22 At higher levels of visual processing, neurons with large receptive fields that are insensitive to image projection or position have been identified in the inferotemporal cortex.25-30 and medial superior temporal sclusus.27-30 The firing rate of many neurons at these higher levels of visual processing does not change with the position, projection, or partial occlusion of the image. The presence of a scotoma in part of the receptive field may therefore produce relatively little response change in these areas and, consequently, an unawareness of the local loss of vision, in the same way that occluded and amodally completed objects do not appear to be fragmented.31

Vernier alignment thresholds increase with the distance between the two elements32 because sensitivity is limited by the orientation of the smallest receptive fields that respond to the bars.33 Therefore, this task can be used to examine visual processing around the scotoma. If filling-in involves (re)organization of small receptive fields across scotomas, this would reduce the effective distance between the lines and performance would improve.

Previous work examining a similar two-dot alignment task34 found that Vernier alignment thresholds were approximately the same across the physiological blind spot as across the corresponding visual field location in the opposite eye not containing the optic disc. Similarly, Maertens and Pollmann35 examined completion of the induced contours of a Kanizsa square using a modified orientation discrimination task.36 These authors also found that sensitivity to the curvature of illusory contours that passed over the physiological blind spot was worse than to contours at equivalent, sighted retinal locations. These studies argue against the presence of specialized low-level receptive field organization around the optic disc. However, the stimuli used in these studies did not directly abut the boundary of the blind spot, and it is possible that the small region of the background between the edge of the scotoma

From the 1University College London Institute of Ophthalmology, London, United Kingdom; 2Moorfields Eye Hospital NHS Foundation Trust, London, United Kingdom; and 3Scheffens Eye Research Institute, Harvard Medical School, Boston, Massachusetts.

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Corresponding author: Michael D. Crossland, University College London Institute of Ophthalmology, 11-43 Bath Street, London EC1V 9EL, UK; m.crossland@ucl.ac.uk.


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A thresholding strategy was used. The contralateral eye was occluded from the screen. The initial stimulus intensity was set to 0 dB, and the “fast” means of a button press when a Goldman III size stimulus appeared on the test screen.

Subjects and Methods

Ethical Approval

The study was approved by the Moorfields and Whittington Research Ethics Committee and conformed to the tenets of the Declaration of Helsinki. All participants gave their written informed consent before data collection.

Subjects

Both authors and three of their colleagues acted as control subjects in this experiment. All control subjects had corrected visual acuity of 0.0 logMAR (20/20) or better, no history of any eye disease, and less than 4 D of ametropia in the studied eye. The age range of the control subjects was 20 to 41 years.

Eight subjects with retinal scotomas were recruited from the optometry clinics at Moorfields Eye Hospital NHS Foundation Trust, and one was a colleague. Subjects with scotomas had a diagnosis, confirmed by an ophthalmologist, of age-related macular disease, Stargardt disease, Best disease, toxoplasmosis, or choriotetinal scar and no concomitant eye disease (see Table 1 for subject characteristics). All patients had at least a 5-year history of visual loss. The presence of filling-in was assessed by asking subjects to report the appearance of an Amsler grid presented in the tested eye (with an eccentric fixation target for subjects with noncentral scotomas). No subjects reported the absence of any structure on this test. All participants were older than 18 years and were in good general health.

Retinal Microperimetry

For participants with eye disease, scotoma size and position were determined with a microperimeter (Nidek MP1; Nidek Technologies, Padova, Italy). A modified 10–2 strategy was used. Patients were asked to observe a central fixation cross of height 1° while reporting by means of a button press when a Goldman III size stimulus appeared on the screen. The initial stimulus intensity was set to 0 dB, and the “fast” thresholding strategy was used. The contralateral eye was occluded throughout. The area of dense scotoma was measured by drawing the smallest possible polygon to encompass all regions that failed to detect the target at 0-dB attenuation.

Alignment Threshold

Stimuli were produced by software written in Matlab (Mathworks, Natick, MA) using elements of the Psychophysics Toolbox37,38 and were displayed on a CRT monitor of mean luminance 50 cd/m² and a refresh rate of 60 Hz. Subjects viewed the monitor monocularly from a distance of 50 cm. Participants were asked to fixate a central fixation point of 0.05° radius (0.25° radius for those with central scotomas). Alignment thresholds were determined by presenting pairs of vertically oriented black bars, presented for 150 ms, with abrupt onset and offset against a white background.

Subjects were asked to determine whether the top line appeared to be to the left or to the right of the bottom line. The bottom line position was fixed, whereas the top line was offset to the left or right of the bottom line. This offset was modulated by a one-up, three-down staircase to find the alignment threshold for performance at the 79.4% correct level. The boundary of the white screen altered with each trial to deter participants from judging the position of the top line in relation to the screen edge. Each experimental run consisted of five reversals or 60 trials at each screen position. A red circle of radius 5° was projected into the physiological blind spot during each trial. Subjects were asked to indicate whether they saw the red target by means of a button press, and these were discarded.

Alignment across the Physiological Blind Spot

For control subjects, the stimulus was a pair of vertical black lines, each of 2° height and 0.1° width. The lines had a center-to-center separation of 7.5° (i.e., a gap of 5.5° existed between the lines), were presented against a white background for 150 ms, and were followed by a mask of isoluminant white noise. All control subjects viewed the target with the left eye occluded (other than S5, who is amblyopic in his right eye and who performed the test with his right eye occluded). Test position (15° to the left or 15° to the right of fixation, either over the physiological blind spot or over the temporal retina) was randomly interleaved across the trial.

Alignment across Pathologic Retinal Scotomas

For patients, the test position was determined on the basis of the characteristics of the eye with the larger scotoma. The line position was selected so that it spanned the maximum vertical extent of the larger scotoma, and the targets were appropriately offset from the fixation position. Center-to-center separation was the same as the vertical size of the scotoma. Line width and height were altered to ensure that both lines were always easily visible to the subjects. Alignment thresholds were measured across the larger scotoma and over the same retinal region in the better eye (Fig. 1). The contralateral eye was occluded in all cases.

Results

Alignment over the Physiological Blind Spot

Mean alignment thresholds were 0.36° for lines projected over the physiological blind spot and 0.63° for those over the intact temporal retina. This difference was statistically significant (matched pairs; P < 0.05; Figure 2).

Alignment over Pathologic Retinal Scotomas

In subjects with age-related macular disease, no significant difference was observed in alignment thresholds in better eyes.

Table 1. Diagnosis and Scotoma Characteristics of Each Participant

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (years)</th>
<th>Diagnosis</th>
<th>Scotoma Size (°)</th>
<th>Poorer Eye</th>
<th>Better Eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>77</td>
<td>AMD</td>
<td>20</td>
<td>5</td>
<td></td>
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<td>A2</td>
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<td>AMD</td>
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<tr>
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<td>AMD</td>
<td>25</td>
<td>10</td>
<td></td>
</tr>
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<td>70</td>
<td>AMD</td>
<td>25</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>A5</td>
<td>88</td>
<td>AMD</td>
<td>22</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>J1</td>
<td>25</td>
<td>Best disease</td>
<td>15</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>J2</td>
<td>53</td>
<td>Stargardt disease</td>
<td>25</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>U1</td>
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<td>Toxoplasmosis</td>
<td>15</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>U2</td>
<td>22</td>
<td>Chorioretinal scar</td>
<td>6.7</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Poorer eye, maximum vertical height of scotoma in poorer eye; better eye, vertical height of scotoma in corresponding retinal location in the better eye.

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Here we used stimuli that could more effectively promote filling-in to reexamine alignment across the physiological blind spot and over the temporal retina. This difference was statistically significant compared across equivalent distances of sighted and unsighted retina in each subject.
and poorer eyes (matched pairs; $P = 0.9$). Two showed lower alignment thresholds in the eye with the larger scotoma, and three showed lower alignment thresholds in the better eye. For the two observers with juvenile macular disease, alignment thresholds were better in the better eye, though this difference did not reach statistical significance ($0.22^\circ$ vs. $0.39^\circ$; matched pairs; $P = 0.33$). Subjects with lifelong scotomas (U1, U2) also had better alignment thresholds in their better eyes. These data can be seen in Figure 3.

**DISCUSSION**

**Alignment over the Physiological Blind Spot**

Figure 2 shows that for normally sighted control subjects, alignment thresholds were significantly lower (performance is better) over the physiological blind spot than the same distance over intact retina. These data suggest that filling-in of the physiological blind spot is mediated at least in part by a low-level mechanism limited by the orientation sensitivity of the smallest receptive field in the location of the lines.$^{33}$ The observation that thresholds are lower across the blind spot than the same distance in the sighted temporal visual field suggests that receptive fields in this location span the optic disc and support fine-orientation discrimination.

These results initially appear to conflict with those of two previous studies. Tripathy et al.$^{39}$ found that alignment thresholds were comparable over the physiological blind spot and the corresponding sighted visual field of temporal retina in the other eye. Similarly, Maertens and Pollmann$^{35}$ found that orientation discrimination thresholds were higher for aligned than for misaligned Kanizsa squares that overlapped the blind spot. In contrast, our line stimuli deliberately abutted the edge of the blind spot. Behavioral$^{9}$ and physiological$^{40}$ studies have shown that contour completion requires that line segments abut the boundary of the blind spot; otherwise, the blind spot is (understandably) completed with the background pattern. If the blind spot is completed with the background, it is not surprising that thresholds for the two conditions are the same. Both cover the same perceived visual area. We suggest that our stimuli promote filling-in of the stimulus lines rather than the background, so that our initial hypotheses can be compared.

To examine the role of such background filling-in, we conducted a control experiment with four subjects at an increased line center-to-center separation of $15^\circ$ between the Vernier lines. This generated a gap size of $13^\circ$ between the tips of the lines. In this condition, no significant difference was found between alignment over the optic nerve head and temporal retina (physiological blind spot, $0.64^\circ$; temporal retina, $0.52^\circ$).

![Figure 1](https://jov.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/932958/)

**Figure 1.** An example of the position of test stimuli for a subject with asymmetric retinal scotomas. White polygons describe the minimum possible size of dense scotoma. White cross defines the position of the fixation target (note that fixation is in noncorresponding retinal locations). White bars represent the positions of the test Vernier lines.

![Figure 2](https://jov.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/932958/)

**Figure 2.** Alignment thresholds over intact temporal retina (dark bars) and the physiological blind spot (light bars) for five control subjects. PBS, physiological blind spot. Error bars show 95% confidence intervals.
matched pairs, $P = 0.64$). We also replicated the experiment of Tripathy et al.\textsuperscript{59} and did not find any significant difference in alignment thresholds over the blind spot and over temporal retina, confirming the results of their study.

These control studies highlight the importance of the stimulus at the boundary of the scotoma, because it is this that determines what is filled in across the scotoma and defines the spatial structure that can be integrated around its edges. These results suggest that filling in across the physiological blind spot involves (at least in part) low-level receptive field organization. It is possible (and indeed likely) that filling in across the physiological blind spot also involves higher-level mechanisms; however, the present study does not provide direct evidence for or against this.

**Alignment over Pathologic Retinal Scotomas**

Figure 3 shows that alignment thresholds over pathologic retinal scotomas were not significantly lower than thresholds measured across equally eccentric retina in the more healthy fellow eye. This suggests that the filling-in experienced over pathologic retinal scotomas does not include low-level receptive field reorganization but instead involves higher-level processes of image completion.

Some of our subjects described the Vernier lines as tilted, distorted, or hazy during the experiment, which may indicate metamorphopsia around the scotoma boundary (as described around the boundary of macular holes by Kroyer and colleagues\textsuperscript{40}). Metamorphopsia in these patients could explain their elevated Vernier alignment thresholds.

It is well known that people with macular disease often demonstrate poorer performance on tasks in apparently healthy retina well beyond the boundary of the scotoma observed on funduscopy. For example, reading speed is lower\textsuperscript{42} and temporal processing is slower\textsuperscript{45} than at equivalent locations in normally sighted control subjects. It may be that any advantage in alignment tasks conferred by filling-in is counteracted by preclinical changes in retinal disease beyond the region of measurable scotoma. It is also known that fixation stability is significantly worse in people with macular disease.\textsuperscript{44}

This retinal motion may affect the spatial precision of position encoding in peripheral vision, ameliorating the effects of filling-in. However, in normally sighted subjects, Vernier\textsuperscript{45} and letter acuity\textsuperscript{46} are invariant of very large levels of random positional jitter. Neither of these explanations can account for the higher thresholds of subjects U1 and U2 across their pathologic scotomas, both of whom have normal values of fixation stability, as determined by post hoc examination of fixation data collected on the microperimeter.

An important limitation of our experimental design is that the fundus was not imaged during the alignment task. We have assumed that the retinal location used for fixating the cross target in the alignment task is the same as that used in the microperimeter. Although it is possible that patients used different retinal loci for these two tasks, a red ellipse was presented within the area of the physiological blind spot during all trials. If fixation moved by a significant amount between these conditions, the red disc would have been visible to participants during the experiment and subjects would have reported that they had seen it. This red marker also acts as a simple fixation control: if participants had extremely poor fixation stability, the dot would be visible in many trials. Note that this cannot account for the higher thresholds in subjects U1 and U2 whose scotomas were eccentric and who fixated foveally. A further limitation of our design is that the exact location of the foveal center can be difficult to determine in the eyes with central scotomas, so a small error may exist in the presentation position of the Vernier lines in the healthier eye.

No clear relationship was found between the eccentricity of the Vernier lines and alignment threshold. Although it may be that completion acts differently in the peripheral retina from across the foveal center, our sample size is not large enough to allow a detailed analysis of the effects of retinal position on perceptual completion.

The quantitative difference between Vernier alignment thresholds of the physiological blind spot and pathologic retinal scotomas are likely to reflect structural differences between the areas surrounding the optic nerve head and areas surrounding a pathologic scotoma, either in the retina or later in the visual system. If significant cortical plasticity exists, we would expect alignment thresholds over a pathologic scotoma to be improved in a manner similar to that over a physiological scotoma. Our results argue against large-scale reorganization of visual cortex in people with eye disease.

In functional imaging studies, some of the debate over whether reorganization does\textsuperscript{12} or does not\textsuperscript{13} occur after development of a retinal scotoma is thought to be attributed to the type of task used and whether stimulus viewing is an active or a passive process.\textsuperscript{47} An advantage of a psychophysical paradigm such as ours is that this distinction does not apply.

It is particularly surprising that Vernier alignment thresholds across the lifelong scotoma experienced by subjects U1 and U2 were not as low as those over physiological blind spots. In both subjects, the scotomas were in peripheral visual field locations broadly similar to the physiological blind spot (30° superior retina and approximately 15° in diameter in U1 and 22° inferior retina and approximately 6.7° in diameter in U2). Both subjects were unaware of their scotomas until they were detected during routine eye examinations with an optometrist.

Although there are not thought to be significant structural changes in visual cortex around the physiological blind spot,\textsuperscript{48} some classical and extraclassical receptive fields are known to encompass retina from opposite sides of the optic disc.\textsuperscript{49,50} We suggest that the presence and organization of this class of
receptive field is the basis of the improved alignment performance over the optic disc.

Quantitative differences in filling-in of pathologic and physiological scotomas may guide the future development of tests to identify retinal disease not confounded by the presence of filling-in. For example, the Vernier targets used in this experiment were perceived as filled-in across the physiological blind spot. However, although all our subjects with retinal disease experienced completion of their scotomas on an Amsler chart, not all subjects experienced completion during our Vernier task, possibly because of the tachistoscopic presentation techniques and aperiodic stimuli used here. This type of stimulus presentation could be explored further as a tool to identify the presence of retinal scotomas, perhaps by enabling patients to “see” their own areas of scotoma.

We have shown that although pathologic and physiological scotomas appear filled-in, this perceptual completion confers a presence of retinal scotomas, perhaps by enabling patients to “see” their own areas of scotoma.

References


