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Rapid fine-scale sensorimotor plasticity in human foveal vision

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The foveola is the most important region of the human retina, yet little is known about how the visuomotor system responds to subtle visual disruptions in this region. Using an Adaptive Optics Scanning Light Ophthalmoscope (AOSLO) for high-resolution retinal imaging and retinal-contingent stimulation, we show that even a minute foveolar scotoma (≈0.03 degrees^2) produces measurable perceptual deficits and triggers fine-scale reorganization of fixation behavior. Observers, without explicit reports of awareness of the loss, rapidly adopt new preferred retinal loci shifted by ≈5 arcmin to bring stimuli into a visible region. These loci fall in regions of lower cone density than neighboring regions, suggesting that fixation control is not solely determined by sampling efficiency and involves trade-offs between sensory and motor factors. These findings uncover a fine scale visuomotor plasticity and suggest oculomotor biomarkers for detecting early retinal disease before symptoms emerge.

Visual resolution peaks within the foveola, a small central retinal region characterized by the highest cone density and supporting high-acuity vision[1,2]. Loss of foveal vision, such as in age-related macular degeneration (AMD), severely impairs visual functions and leads patients to adopt an eccentric preferred retinal locus (PRL) near the scotoma border, with saccades re-referenced to this location[3–5]. Similar visuomotor adaptations have been observed in healthy observers using simulated foveal scotomas[6–8]. However, prior work has focused on large scotomas generally covering a few degrees of visual angle, and it remains unknown whether tiny localized losses of vision within the foveola, spanning only a few arcminutes, produce measurable perceptual deficits or alter fixation behavior.

If a small foveolar scotoma disrupts central sampling at the PRL, increased fixational instability may represent a simple coping strategy, increasing the probability of the stimulus falling outside the small scotoma. However, a stable alternative PRL could develop. This latter scenario would require a finely orchestrated coordination between high-acuity vision and fixation behavior leading to minute shifts of the line of sight. Further, cone density varies across the foveola, and the PRL is typically offset from both the point of peak cone density and the cone density centroid[9,10], leading to asymmetries in cone density around the PRL and prompting the question of whether, following fine-scale vision loss, the visuomotor system preferentially selects regions of higher cone density.

To address this question, we examined the impact of a foveolar scotoma on visual performance and fixation behavior using an AOSLO to render a simulated 10-arcmin-wide scotoma while subjects (n = 7) performed a four-alternative forced choice visual acuity discrimination task (see Figure S1A published in Supplemental information with this article online for participant demographic and ocular characteristics). Stimuli consisted of optotypes whose size (5 arcmin in width) was considerably above the acuity threshold as they were viewed under diffraction-limited conditions. Stimuli were presented for 500 ms at a fixed location. The task was either performed in the presence or absence of the scotoma (Figures 1B and S1B). In the scotoma condition, a 10-arcmin-wide simulated scotoma, perceptually seamless with no visible edges, was stabilized at each subject's PRL. To achieve threshold performance in both conditions (paired t-test comparing scotoma vs. no-scotoma conditions: $t(6) = 2.42$, $p = 0.052$, Cohen's $D = 0.98$, $BF10 = 1.93$), contrast was increased by more than a factor of three on average (3.3 ± 0.3, paired t-test comparing scotoma vs. no-scotoma conditions: $t(6) = -9.25$, $p < 0.0001$, Cohen's $D = 3.09$, $BF10 = 284.63$). These results show that scotoma at the center of gaze, with a width of only 10 arcmin, produces a measurable visual deficit (Figure S1C).

We then analyzed the distribution of stimulus position on the retina in the two conditions. The visuomotor system responded to the scotoma by shifting the stimulus distribution away from the control PRL by approximately half the width of the scotoma, bringing the stimulus into a region of partial visibility near the scotoma border (Figure 1C, left column; the mean offset magnitude between the control PRL and the alternative PRL was 5.5 ± 2.9 arcmin). In a control experiment in which a smaller (7-arcmin-wide) scotoma was used, no alternative PRL was established, as shown in Figure 1C (right column). The smaller scotoma, covering only 49 arcmin^2, occluded a retinal area that was smaller than the average 68% contour area of 64 ± 19 arcmin^2 covered by fixational instability. Consistent with this, subjects performed above chance in both conditions of the 7-arcmin experiment (control: 79 ± 5% correct; scotoma: 66 ± 9% correct). Therefore, normal fixational instability in this condition was sufficient to bring the stimulus into the visible region for a duration long enough to perform the task significantly above chance level. In the 7-arcmin condition, the mean PRL offset amplitude was 2.0 ± 0.7 arcmin (n = 4). In contrast, PRL offsets were systematically larger in the 10-arcmin scotoma condition (linear mixed-effects model using all available data, Amplitude ~ Scotoma size + (1|Subject), Δ = 2.4 arcmin, 95% CI [1.04, 3.75], $p = 0.003$; marginal test: $F(1,9) = 15.95$, $p = 0.003$). These results suggest that there may exist a minimum occlusion size before substantial changes in fixation behavior are observed.

Although the offset direction of the alternative PRL in the scotoma condition was not systematic across subjects (Figure 1C), we investigated to what extent each subject's offset was related to their unique cone density distribution by quantifying the average cone density surrounding the scotoma and aligning each subject's distribution so that the alternative PRL offset direction was oriented vertically, as shown by the black arrow in Figure 1D (see Figure S2 for cone density binning, PRL angle analysis, and

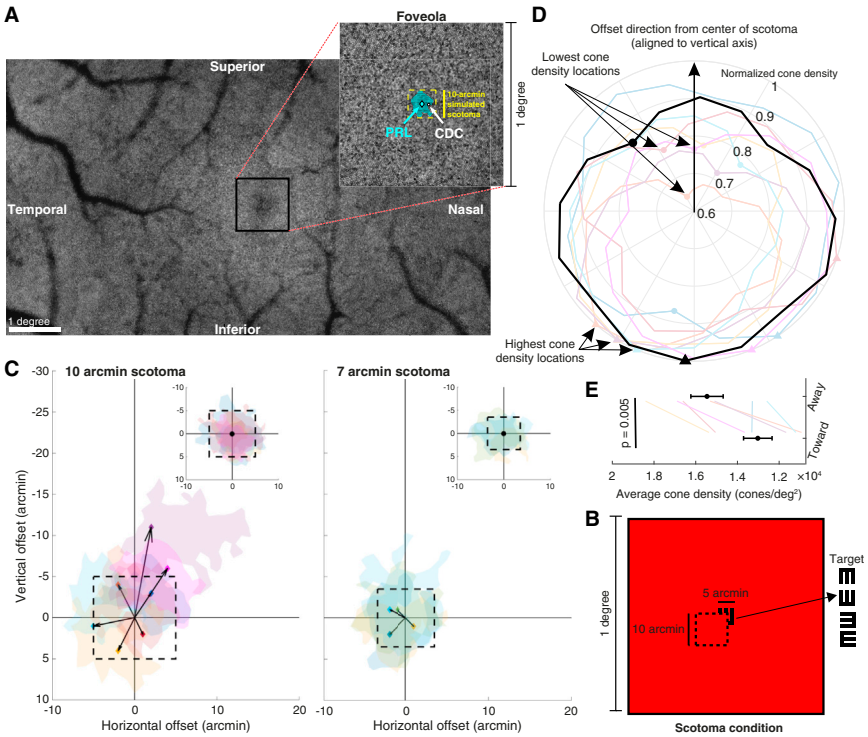

Figure 1. Alternative preferred retinal locus formation in the presence of simulated foveolar scotomas.

(A) Montage of the retina from an example subject showing the foveola, marked at the center. The inset illustrates an example of a simulated foveolar scotoma (10 arcmin width) covering an area comparable with that spanned by normal fixational instability. Simulated scotomas were stabilized at each subject's preferred retinal locus (PRL). (B) Stimulus presentation in the scotoma condition within the 60 arcmin-wide AOSLO imaging field of view. Stimuli consisted of 5 arcmin wide Tumbling Es and were viewed under diffraction limited conditions. The stabilized scotoma is centered at the observer's PRL and, in this example, partially occludes the stimulus. (C) Stimulus position on the retina (68% probability contours; each contour represents a subject), with respect to the PRL location in the control condition in the presence of a scotoma. Arrows indicate the direction and magnitude of alternative PRL shifts relative to the control PRL. Insets in each panel show stimulus distributions in the control condition for reference. (D) Angular distributions of normalized cone density surrounding the scotoma in the 10-arcmin scotoma condition. Individual density profiles were aligned such that the direction of the alternative PRL offset vector pointed vertically upward to enable cross-subject comparison. (E) Average cone density in the direction subjects moved toward when establishing an alternative PRL versus the direction they moved away from (located 180° opposite). Error bars indicate ± s.e.m.

subject-level tests). Surprisingly, across subjects the alternative PRL did not systematically shift toward the highest cone density region available outside the scotoma occlusion. Instead, most observers established their alternative PRL in directions corresponding to lower cone density. The average cone density was 15 ± 10% lower in the direction that subjects moved toward compared to the opposite direction ($t(6) = -4.26$, $p = 0.0053$, Cohen's $D = 1.61$, $BF10 = 10.94$, Figure 1E). This strategy to move away from the highest-density region immediately outside the scotoma suggests that changes in oculomotor behavior in this condition are not driven by sampling maximization. In addition, the direction of the alternative PRL shift tended to follow the same directional bias as the control PRL relative to the cone density centroid, rather than reorienting toward the highest-density region (mean angular difference = 31° ± 32°; Watson-Williams test: $F(1,12) = 0.02$, $p = 0.90$).

These results demonstrate the visuomotor system's ability to compensate for localized losses of visual function within the foveola. It is possible that such changes in fixation behavior occur in early stages of some retinal degenerative diseases before patients observe visual symptoms or changes in retinal morphology are apparent. We therefore highlight the possibility for identifying early visuomotor biomarkers for retinal degenerative diseases.

DECLARATION OF INTERESTS

The authors declare no competing interests.

SUPPLEMENTAL INFORMATION

Supplemental information including two figures, experimental procedures, acknowledgments and author contributions can be found with this article online at https://doi.org/10.1016/j.cub.2026.06.054.

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