

2022-04-21

Disruption of Positional Encoding at Small Separations in the Amblyopic Periphery

Hussain, Zahra

<https://pearl.plymouth.ac.uk/handle/10026.1/20879>

10.1167/iavs.63.4.15

Investigative Ophthalmology & Visual Science

Association for Research in Vision and Ophthalmology (ARVO)

All content in PEARL is protected by copyright law. Author manuscripts are made available in accordance with publisher policies. Please cite only the published version using the details provided on the item record or document. In the absence of an open licence (e.g. Creative Commons), permissions for further reuse of content should be sought from the publisher or author.

Disruption of Positional Encoding at Small Separations in the Amblyopic Periphery

Zahra Hussain¹ and Paul V. McGraw²

¹Department of Psychology, American University of Beirut, Lebanon

²School of Psychology, University of Nottingham, United Kingdom

Correspondence: Zahra Hussain,
Department of Psychology,
American University of Beirut, Riad
El-Solh, Beirut 1107 2020, Lebanon;
zahra.hussain@aub.edu.lb.

Received: December 17, 2021

Accepted: March 14, 2022

Published: April 21, 2022

Citation: Hussain Z, McGraw PV.
Disruption of positional encoding at
small separations in the amblyopic
periphery. *Invest Ophthalmol Vis
Sci.* 2022;63(4):15.
<https://doi.org/10.1167/iovs.63.4.15>

PURPOSE. Positional judgments in amblyopia are impaired more at the center of the visual field than in the periphery. However, the effects of visual field position frequently are confounded with stimulus separation. The purpose of this experiment was to parse the effects of stimulus separation and eccentricity on the positional deficit in amblyopia.

METHODS. Subjects adjusted the positions of stimuli of varying separations on isoecentric arcs. The task was simultaneous bisection and alignment of broadband, high-contrast, uncrowded targets with reference to central fixation. Ten strabismic amblyopes and five normally sighted controls performed the task dichoptically; a subset of amblyopes performed the task monocularly with the amblyopic eye. Spread (inverse of precision) and bias were measured at multiple visual field locations comprising two to three separation \times four eccentricity conditions in each visual field quadrant.

RESULTS. In normal controls, both spread and bias increased with eccentricity, and spread (but not bias) increased linearly with separation until 7° eccentricity. Strabismic amblyopes showed a different profile: spread and bias were higher at small separations at all eccentricities, such that performance showed a quadratic trend against separation. Thus, at each eccentricity, the difference in performance between groups was largest at the smallest separation.

CONCLUSIONS. These results are consistent with disruptions in Weber mechanisms of positional encoding in strabismic amblyopia, and indicate that binocular stimulation by proximal targets produces a loss of spatial precision well beyond the fovea.

Keywords: amblyopia, precision, bias, bisection, alignment, suppression, fusion, diplopia, eccentricity

In strabismic amblyopia, the ability to judge object position is impaired such that perceived position is distorted or biased away from true position, and positional thresholds are elevated where normal judgments are highly precise.¹⁻¹¹ As with other amblyopic visual deficits, the positional deficit is larger in the foveal region than in the periphery.^{3,5,8,10,12} The difference in performance between the amblyopic and fellow eye, or between amblyopic and normally sighted control eyes, typically is greater at the fovea and decreases at eccentric locations, with some evidence for nasotemporal asymmetries that depend on strabismus direction and other factors.^{8,11,13,14} The gradient of the positional impairment against eccentricity is consistent, potentially, with anomalous cortical scaling of visual input (⁴ but see ¹⁵), but does not rule out anomalies in other mechanisms of positional encoding. Here, we decouple stimulus eccentricity from interstimulus separation in a positional adjustment task to demonstrate a separation-dependent positional impairment in strabismic amblyopia that is not confined to the foveal region.

In normal vision, positional thresholds are proportional to stimulus separation at small separations, and to eccentricity at large separations.¹⁶⁻¹⁸ Thus, Weber's law for position holds at separations where performance depends purely

on the output of first- and second-stage spatial filters, but at large separations, performance depends on cortical scaling.¹⁷⁻¹⁹ To parse the effects of separation from eccentricity, separation is varied for stimuli placed on isoecentric arcs.^{17,18} Although this approach has proven useful for characterizing normal positional encoding, it has not frequently been used to study the amblyopic deficit. Separation-related foveal deficits in amblyopia have been reported under the rubric of contour interactions²⁰⁻²³ or crowding^{1,3,24,25} for a number of visual judgments, typically performed monocularly. In these studies, resolution, contrast detection, and other visual judgments are impaired in the amblyopic fovea by proximal stimuli that either facilitate^{22,23} or have little effect on performance of normally sighted observers.

There is some evidence in amblyopia for an exaggerated positional deficit at small stimulus separations outside the fovea.^{8,26} Levi et al.²⁶ found that sensitivity to two-dimensional Gaussian positional jitter in arrangements of Gabor patches was disproportionately poorer at small than large stimulus separations for strabismic amblyopes (i.e., the normal Weber relationship was perturbed). In their study, stimuli comprised either horizontal arrays of equally spaced patches (string experiments), or patches arranged in a circle (ring experiments), and subjects reported which of the two

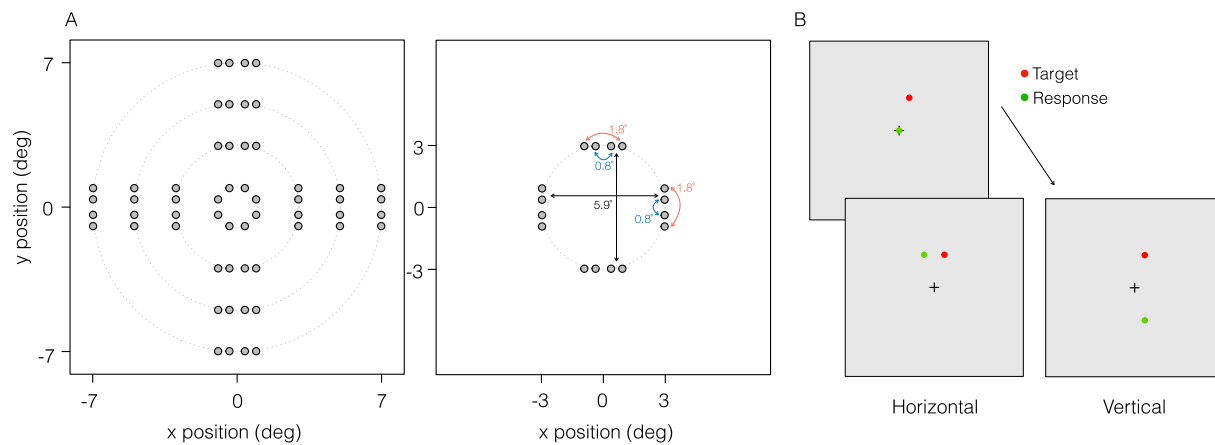


FIGURE 1. Target positions and schematic of task. (A) Fifty-six locations were tested: four eccentricities \times three separations in the upper and lower visual fields, except at 1° where only two separations were tested. The largest separation at each eccentricity was sampled twice. The center panel shows the three separations tested at 3° eccentricity, in the horizontal and vertical directions (0.8° , 1.8° , 5.9°). (B) Schematic of task. The target appeared with a response probe positioned on the fixation cross. In the horizontal condition, the response dot was placed horizontally across the target, equidistant from the vertical meridian. In the vertical condition, the response dot was placed vertically across the target, equidistant from the horizontal meridian.

intervals contained the jittered stimuli. Viewing distance and patch separation were varied for both configurations, such that eccentricity varied simultaneously; however, separation and not eccentricity was identified as the limiting factor for rings. Four normally sighted observers and seven strabismic amblyopes were tested monocularly in all conditions. Across all manipulations, amblyopes' thresholds were elevated at small separations/eccentricities, interpreted as a type of 'Weber noise' in amblyopic positional encoding. Demanins and Hess⁸ had previously used a three-element alignment task to point out the role of element separation in the scale invariance of threshold deficits in strabismic amblyopia, but the precise effects of separation were idiosyncratic across subjects and were not examined independent of eccentricity.

Here, we examined the effects of stimulus separation on positional precision and accuracy in the extrafoveal visual field of strabismic amblyopes, using spatially broadband, uncrowded, high-contrast stimuli in a dichoptic free localization task. The task combines spatial interval with alignment judgments on each trial (Figure 1). We have used this task previously to show a larger central than peripheral positional impairment in amblyopia, and to infer properties of binocular correspondence and cortical spatial coding across the amblyopic visual field.^{10,11} The dichoptic judgment provides a measure of the positional mismatch between the eyes and is useful in evaluating interocular effects on perceived position in habitual (binocular) viewing conditions (e.g.,²⁷). In our previous work, stimulus eccentricity and separation were coupled, leaving unclear the effects of separation on the measured positional distortions. Here, stimulus separation was varied at each of four eccentricities at multiple locations in the visual field to disambiguate these effects. As in our previous work, we compared performance between strabismic amblyopes and normally sighted subjects and between dichoptic and monocular viewing conditions for a subset of amblyopes. Unlike the studies cited earlier showing separation effects on monocular positional judgments, the approach used here distinguishes monocular from interocular effects on positional encoding.

MATERIALS AND METHODS

Subjects

Ten strabismic amblyopic subjects and five normally sighted subjects were tested. The strabismic subjects and three normally sighted subjects were tested at the University of Nottingham, UK. Two additional normally sighted subjects were tested at the American University of Beirut, Lebanon. Three strabismic subjects participated in a subset of the dichoptic stimulus conditions (i.e., in some separation \times eccentricity \times judgment direction combinations and not others) and three strabismic subjects performed the task in both dichoptic and monocular (amblyopic eye) viewing conditions. Table 1 provides clinical details for the strabismic subjects. All subjects were informed of the purpose and procedure of the study. Strabismic subjects provided a detailed ophthalmic history and were examined by a registered optometrist prior to testing. Ocular alignment for distance and near were measured using the prism cover test.^{28,29} LogMAR acuity was measured using the Early Treatment Diabetic Retinopathy Study chart.³⁰ Ocular deviation ranged from 2 to 18 prism diopters. None of the subjects had alternating strabismus. All subjects were amblyopic (0.20 logMAR or more difference in acuity between the eyes). Best optical correction was determined by subjective refraction for all strabismic subjects.

Apparatus and Stimuli

The experiment was performed on an Apple G5 iMac computer with a Trinitron Dell P1130 monitor with a screen width of 40 cm and resolution of 1280×1024 pixels (Nottingham) and on an Intel Skull Canyon NUC computer with a ViewPixx monitor with a screen width of 57 cm and resolution of 1920×1200 pixels (American University of Beirut). Mean background luminance was $\approx 41 \text{ cdm}^{-2}$. Both experiments were performed using PsychoPy.³¹ The viewing distance was 114 cm.

The fixation mark was a black cross subtending 0.38° of visual angle, and the target and response stimuli were dots of uniform luminance subtending 0.28° of visual angle. To

TABLE 1. Strabismic Subject Clinical Details

ID	Age, Sex	Eye, Alignment (Prism Diopters)	Patching, Operation	Refractive Error	LogMAR
BM	35 F	R Micro 2	No, No	OD +0.75/−0.50 × 105 OS −4.00/−0.50 × 120	0.50 0.06
JH*	21 F	RSOT 2	Yes, Yes	OD +2.75/−0.50 × 140 OS +1.75DS	0.62 −0.06
JO**	21 M	LXOT 12	Yes, No	OD −2.50/−0.50 × 30 OS plano/−3.5 × 160	0.06 1.04
JP**	35 M	RSOT 2	Yes, No	OD +2.50/−0.50 × 130 OS plano	0.32 0.02
LS	48 F	LSOT 18	No, No	OD +0.75/−0.50 × 15 OS +1.75/−2.00 × 150	0.02 1.12
MP**	24 M	LXOT 16	Yes, No	OD −1.50DS OS +4.00/−1.50 × 180	−0.10 1.00
PB	67 M	LSOT 6	Yes, No	OD +6.75/−1.75 × 85 OS +6.75/−1.75 × 80	0.08 0.38
RB*	28 F	RXOT 6	No, No	OD +3.50/−5.50 × 10 OS +0.50DS	0.34 −0.20
SM*	34 M	RSOT 8	Yes, No	OD −0.50DS OS −0.50/−0.50 × 160	1.02 0.00
SS	33 M	RSOT 2	Yes, No	OD −0.75/−0.75 × 103 OS −1.25DS	0.98 −0.10

SOT, esotropia; XOT, exotropia; L vs. R, left or right eye.

* Performed the task in dichoptic and monocular conditions.

** Performed a subset of dichoptic conditions.

counteract interocular suppression, the dots flickered at 8 Hz. Target position was calculated assuming a gaze-normal display (i.e., $1^\circ = 2$ cm at 114 cm viewing distance for both eyes). Target-response separation in the horizontal and vertical directions was varied at each of four eccentricities (1° , 3° , 5° , 7°) in the four quadrants of the visual field. Two fixed separations (0.8° and 1.8°) were used at each eccentricity, and a third, larger separation proportional to eccentricity was used at 3° , 5° and 7° . This produced 56 target locations corresponding to the configuration shown in Figure 1, with stimuli positioned exactly on isoeccentric arcs except at the second separation (1.8°), where the target was offset slightly from the arc so as to maintain the same absolute separation at each eccentricity. The same locations were used for localization in the horizontal and vertical directions (i.e., across the vertical and horizontal meridians), resulting in the largest separations being sampled more often than the smaller separations. Targets at the two smaller separations in the horizontal direction provided the largest separation for localization in the vertical direction (see Figure 1, center).

All subjects performed the task dichoptically, with the display viewed through monochromatic red–green filters that were matched to the spectral profile of the stimuli such that the target and response dots were viewed separately by each eye. Kodak Wratten filters (numbers 58 and 29) were used. The red filter (no. 29) transmits only wavelengths above 600 nm, and green filter (no. 58) transmission is between 470 and 610 nm. The 10 nm overlap between filters was insufficient to perform the task monocularly, particularly in darkness, where human scotopic luminous efficiency is low for wavelengths of greater than 600 nm. Additionally, the background was calibrated to eliminate any crosstalk between filters. The fixation cross, in black, passed through both filters, and therefore was seen by both eyes. The stimuli and screen appeared grey when viewed through the filters, and the background appeared uniform to each eye in the region where the other eye was stimulated (i.e., only one dot and the fixation cross was visible to each eye). Multiple

observers confirmed that the task could not be performed monocularly.

The fixation cross, in black, was not perceived diplopically because it was not dissociated between the eyes. (Diplopia is induced in strabismic subjects for stimuli in the same visual direction that are dissociated between the eyes.) We confirmed that subjects saw only one cross (i.e., the diplopic image of the cross was either suppressed, or in anomalous correspondence with the fixing eye under these viewing conditions). None of the subjects reported diplopia of the fixation cross in dichoptic viewing.

Procedure

All subjects were fitted with best optical correction using trial lenses. No contact lenses were used. Subjects were then seated in a darkened room in front of the display, with viewing stabilized by a chin rest. Several practice trials were given before the session began.

Each trial comprised a fixation cross in the center of the screen, the target dot positioned randomly at 1 of the 56 locations, and the response dot positioned on the fixation cross. The subject was instructed to use the mouse to position the response dot to a symmetric position across the target in the opposite hemifield. In the horizontal condition, they positioned the response across the vertical meridian in the left or right visual field (i.e., horizontal bisection, vertical alignment). In the vertical condition, they positioned the response dot across the horizontal meridian in the upper or lower visual field (i.e., vertical bisection, horizontal alignment). Thus, in both conditions, the task involved a dual bisection and alignment judgment, with the fixation cross serving as the midpoint. Subjects were instructed to maintain fixation throughout the trial. Response time was unlimited and the response was registered by keypress. Each location was sampled seven times (i.e., subjects responded seven times per location) for a total of 420 trials per localization direction.

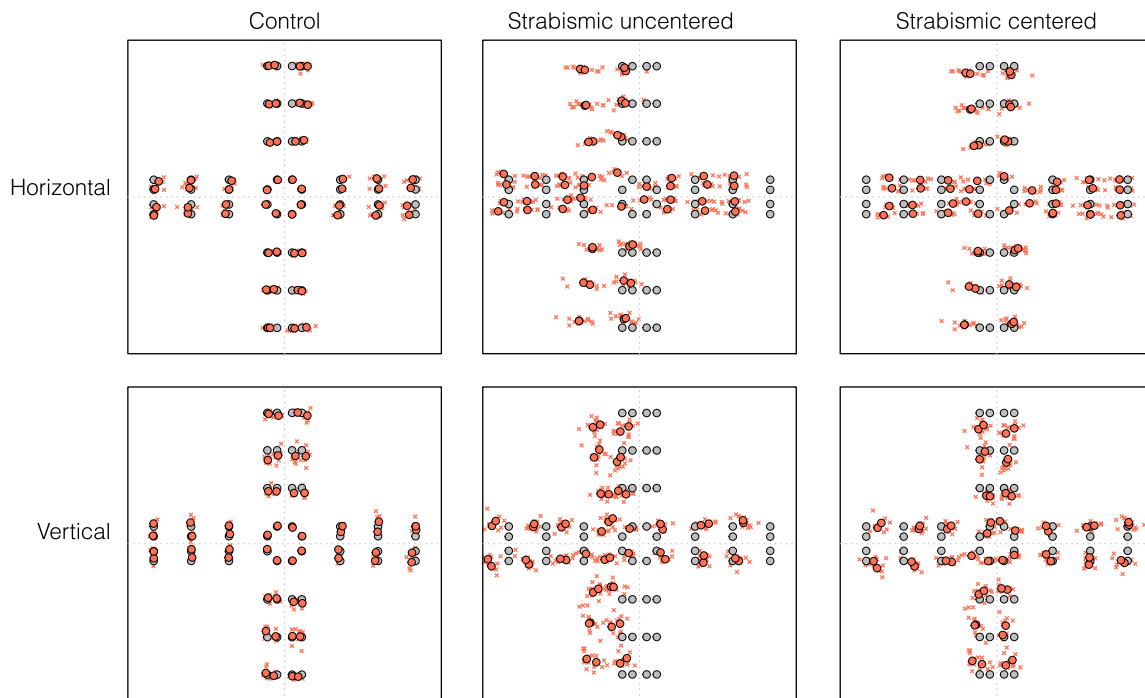


FIGURE 2. Representative performance of a normally sighted control subject and a strabismic subject on the positional judgment task, in the horizontal and vertical conditions. Uncentered and centered data shown for the strabismic subject. Grey symbols: veridical/target locations; orange crosses: subject's individual responses for the given target; orange circles: mean response location for that target.

In dichoptic conditions, the target was always green, and for the strabismic group, always viewed by the fixing eye; the response dot was always red and viewed by the deviating eye. Target and response dots were randomized between the eyes of normal subjects. Three strabismic subjects performed the task monocularly with the amblyopic eye, with both dots passing through a single filter, and the entire display viewed through one eye, with the fellow eye patched.

Figure 2 shows representative performance of a normally sighted control observer and a strabismic subject in all stimulus conditions for the horizontal and vertical judgment directions. The veridical locations are shown in grey, and the subject's mean response locations for those locations are shown in orange. Individual responses for each location are shown as small orange crosses. Thus, each panel is a map of all target and response locations for the particular judgment direction for that subject. Control subjects were highly precise, with variability increasing toward the periphery. Strabismic subjects were much less precise, and showed a displacement in all responses commensurate with their strabismus direction (center panel, uncentered responses; see¹¹ for retinal geometry of this task in strabismus vs. normal controls). The effect of ocular deviation was removed for each subject by subtracting the mean x-offset of the entire set of responses from each response. This produced a centered map (right panel, Figure 2), better representing accuracy at each location for each subject. Mean-centering was performed for all strabismic and control subjects before the analyses that follow, although normal mean displacement was negligible.

Dependent Measures

For each localization response, x- and y-errors were calculated as the difference between the coordinates of the objec-

tively accurate response location (i.e., the mirror symmetric location across the target in the horizontal or vertical direction, see Figures 1 and 2) and coordinates of the subject's response location:

$$x_{\text{err}} = x_{\text{response}} - x_{\text{correct}} \quad (1)$$

$$y_{\text{err}} = y_{\text{response}} - y_{\text{correct}} \quad (2)$$

The inverse of precision (i.e., spread), and bias were calculated over the seven responses per location as:

$$\text{spread} = \sqrt{s_{x_{\text{err}}}^2 + s_{y_{\text{err}}}^2} \quad (3)$$

$$\text{bias} = \sqrt{\bar{x}_{x_{\text{err}}}^2 + \bar{y}_{y_{\text{err}}}^2} \quad (4)$$

Thus, *spread*, or the inverse of precision, is the root mean squared variance of response locations along x and y coordinates, in degrees of visual angle. *bias* is the root mean squared distance of the average response location from the target.

The data were analyzed using R 4.1.2,³² using linear mixed-effects models (packages lme4 v1.1-27.1 and lmerTest v3.1-3),^{33,34} which are appropriate for designs that use a combination of continuous and categorical variables. This approach also is well-suited to dealing with unbalanced data, as in the present case where some subjects participated in a subset of experimental conditions, and separation was not fully crossed with eccentricity, that is, the smaller separations were the same at all eccentricities (0.8° and 1.8°), and the largest separation was unique at each eccentricity (≈6°, 10°, 14°). R^2 for the models was computed using r.squaredGLMM from the MuMIn v1.43.17 package, which gives R^2 for the fixed effects (marginal R^2) and for the entire model including random effects (conditional R^2).³⁵ The fixed effects in

the model were group (strabismic vs. normal), eccentricity (1° – 7°), the logarithm of separation (0.8° – 14°), task (horizontal vs. vertical), visual field (factor 1: left vs. right; factor 2: upper vs. lower), with eccentricity and separation treated as continuous variables. Subject was included as a random effect. The model evaluated all main effects and interactions involving the fixed factors, analogous to a mixed factorial (repeated measures) ANOVA.

RESULTS

Figure 3 shows the spread and bias of responses across eccentricity and interstimulus separation for the two groups, averaged over task and visual field quadrant. For the normally sighted group, spread but not bias increased linearly with separation at each eccentricity, and both spread and bias increased with eccentricity overall. The strabismic group was less precise and more biased than normal in all conditions, with both spread and bias larger at the smallest separation than at the intermediate level, and increasing thereafter. Therefore, performance showed a quadratic and not linear relationship with separation. Thus, the groups differed more at the smallest separation than at larger separations in most conditions. As expected, the group difference averaged over separation was largest at 1° compared with the other eccentricities, that is, there was a disproportionate central visual field loss, consistent with previous work.

Spread

A linear mixed-effects model of the fixed and random effects on log spread showed significant main effects of group, $F(1, 13.07) = 26.25, p = 0.00019$; eccentricity, $F(1, 13.75) = 53.51, p < 0.0001$; and log separation, $F(1, 48.01) = 49.71, p < 0.0001$; and significant interactions

between group and eccentricity, $F(1, 13.75) = 8.23, p = 0.012$; group and log separation, $F(1, 48.01) = 15.20, p = 0.0003$; eccentricity and log separation, $F(1, 1113.56) = 33.04, p < 0.0001$; and group, eccentricity and log separation, $F(1, 1113.56) = 7.32, p = 0.0069$. No other main effects or interactions were significant ($F < 3.5, p > 0.05$). Marginal R^2 and conditional R^2 were 0.51 and 0.83. The significant main effects of group, eccentricity and separation confirm the overall greater precision of the normal group, and that precision of both groups depended on both stimulus variables. The significant interaction of group with eccentricity confirms that the groups differed more in the central visual field than in the periphery, seen clearly in Figure 2. The significant interaction of group with separation confirms that the groups differed more at certain separations, or that the trend of performance against separation differed between groups. The group \times eccentricity \times separation interaction suggests that the group difference in trend against separation was not the same at all eccentricities. Subsequent analyses showed that the group \times separation interaction was significant at each eccentricity ($p < 0.05$); therefore, the linear and quadratic trends of spread against separation were compared between groups at each eccentricity.

Table 2 gives the linear and quadratic slopes of log spread against log separation for each group at each eccentricity. The linear slopes of the normal group were significantly positive at all eccentricities except at 7° , and the quadratic slopes were not significantly different from zero throughout. A different pattern was found for the strabismic group: the quadratic trend was significant throughout, and the linear slopes did not differ significantly from zero except at 7° where there was a negative linear trend. This pattern of results confirms the observations made earlier. To further evaluate whether the slopes differed between groups, the linear and quadratic slopes of log spread against log

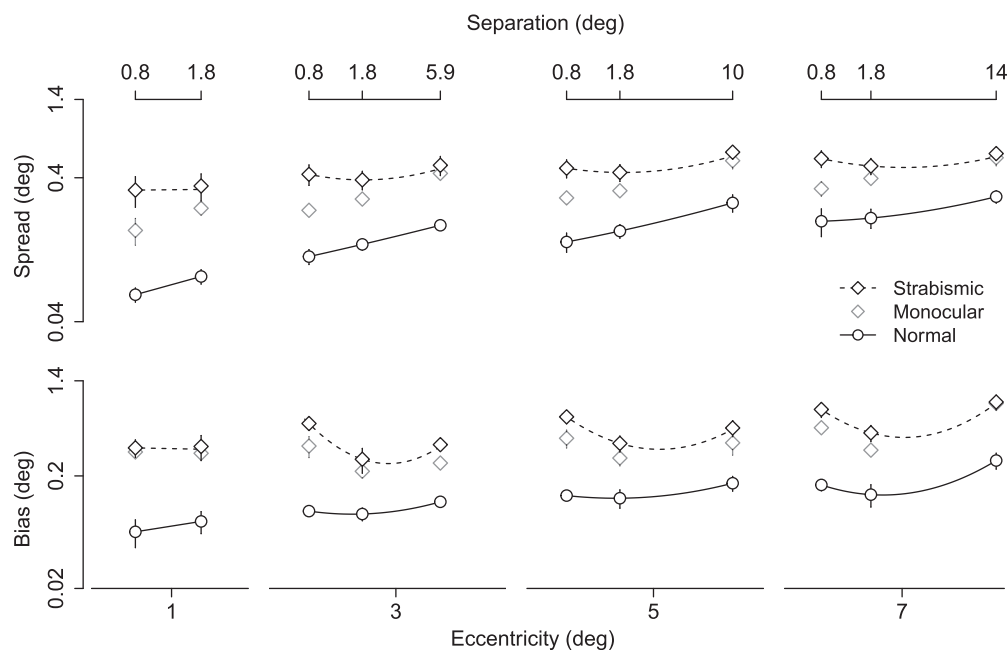


FIGURE 3. Spread and bias of strabismic ($n = 10$) and normally sighted subjects ($n = 5$) as a function of stimulus eccentricity and interstimulus separation, in degrees of visual angle. Monocular data are shown from the amblyopic eye of three subjects (lighter symbols). Performance is averaged over task. Error bars show standard error of the mean.

TABLE 2. Linear (L) and Quadratic (Q) Slopes of Spread and Bias Against Separation for Each Group

	1°		3°		5°		7°	
	L	Q	L	Q	L	Q	L	Q
Spread								
Normal	0.36*	—	0.24*	0.01	0.21*	0.02	0.05	0.04
Strabismic	0.07	—	-0.14	0.13*	-0.13	0.10*	-0.19*	0.09*
Monocular	0.40*	—	0.25*	0.04	0.18	0.03	0.29*	-0.04
Bias								
Normal	0.26	—	-0.12	0.14	-0.10	0.09	-0.32	0.20*
Strabismic	0.01	—	-0.98*	0.48*	-0.78*	0.33*	-0.70*	0.32*
Monocular	-0.03	—	-0.79*	0.40*	-0.59	0.28*	-0.74*	0.38

*Slope differs significantly from zero, $p < 0.05$.

separation were computed for each subject at each eccentricity, and the slopes were compared using independent-samples t tests. The linear slopes differed significantly between groups at 3° and 5°; the quadratic slopes did not differ significantly at any eccentricity. Thus, the effect of separation on spread differed most clearly between groups at 3° and 5°.

Bias

Bias was analyzed using the same procedure as for spread. A mixed-effects model evaluating the effects of group, eccentricity, log separation, and the other stimulus variables on log bias found significant main effects of group, $F(1, 13.33) = 26.54, p = 0.00017$; and eccentricity, $F(1, 15.21) = 29.42, p < 0.0001$; and significant interactions between group and log separation, $F(1, 69.71) = 9.10, p = 0.0035$, eccentricity and log separation $F(1, 1115.47) = 10.99, p = 0.0009$ and group, eccentricity and log separation $F(1, 1115.47) = 4.67, p = 0.03$. In addition, there were significant main effects of visual field, upper vs. lower; $F(1, 1108.85) = 11.42, p = 0.0007$; and significant interactions between group and visual field, $F(1, 1108.85) = 4.69, p = 0.03$, eccentricity and visual field $F(1, 1108.84) = 9.10, p = 0.002$, group and task $F(1, 1113.68) = 5.61, p = 0.018$; and group, eccentricity and visual field left vs. right; $F(1, 1108.84) = 4.68, p = 0.03$. The visual field and task effects were not of central interest, and did not interact simultaneously with separation and group, and are not considered further. Marginal R^2 and conditional R^2 for the model were 0.46 and 0.63.

The group \times eccentricity \times separation interaction was decomposed as before by examining the group \times separation interaction at each eccentricity separately, and by comparing the linear and quadratic slopes between groups. The two-way interaction was significant at 3° and 5° ($p < 0.05$), but not at 1° and 7°, suggesting that separation affected the groups differently at 3° and 5°, but not at 1° and 7°. The linear and quadratic slopes of log bias against log separation are shown in Table 2. At 1°, bias was constant across separation for both groups. At the remaining eccentricities, the normal group's bias did not vary with separation except at 7°, where there was a significant quadratic trend, whereas for the strabismic group there were significant negative linear- and positive quadratic trends throughout. The linear and quadratic slopes of log bias against log separation were computed for each subject at each eccentricity, and the slopes were compared between groups using independent-samples t tests. The linear slopes differed significantly

between groups at 3° and 5°, but not at 1° and 7°. Quadratic slopes did not differ between groups at any eccentricity. Thus, the effect of separation on bias differed most clearly between groups at 3° and 5°.

Monocular Condition

Figure 3 shows monocular performance (amblyopic eye) of a subset of three strabismic subjects who performed the task in both viewing conditions. Monocular performance was worse than normal at all eccentricities and separations, and this group difference was larger at 1° than at other eccentricities consistent with the dichoptic results. However, spread increased linearly with separation, such that performance resembled a scaled version of the normal group. In contrast, bias showed the same quadratic trend observed in dichoptic viewing, with the differences against the normal group more pronounced at small separations.

The above observations were confirmed using an identical set of analyses as that used above, but with the monocular condition compared against the dichoptic condition for the strabismic group only ($N = 3$ monocular vs. 10 dichoptic). Table 2 shows the linear and quadratic slopes for the monocular group. Spread follows the pattern of the normal group, whereas bias follows the pattern of the strabismic group. Thus, in monocular viewing, the positional deficit at small separations was reflected only in bias and not precision of responses.

Supplementary Figure S1 and Supplementary Table S1 show dichoptic performance of the three strabismic subjects who did the task in both viewing conditions (i.e., excluding subjects who performed the task in the dichoptic condition only; normal and monocular data are the same as in Figure 3). Performance of this subset of subjects did not differ from that of the full sample, confirming that individual differences did not produce the difference between viewing conditions.

DISCUSSION

Interocular positional judgments were less precise- and more biased than normal at small stimulus separations than at larger separations in the extrafoveal visual field of strabismic subjects. For normally sighted subjects, spread increased linearly with separation, and bias was generally unaffected by separation at all eccentricities. In contrast, for strabismic subjects, spread was roughly equal at the smallest and intermediate separations, and bias was largest at the smallest separation at all eccentricities. Thus, the largest group differences in spread and bias were at the smallest separations at all eccentricities. These results indicate a separation-specific disruption of positional encoding in strabismic amblyopia, in addition to the well-known eccentricity-dependent impairment also shown here. Thus, the amblyopic deficit is larger in the central visual field than in the periphery, and it is exaggerated at small stimulus separations at multiple visual field locations. This result is consistent with, but distinct from, a previous report of abnormally high Weber fractions at small separations for amblyopes in a monocular jitter detection task. Those results were interpreted as a type of Weber noise produced by anomalous spatial sampling.²⁶ The effect at small separations shown here in dichoptic conditions likely arises from additional factors, such as binocular interference from competing ocular inputs outside fixation.

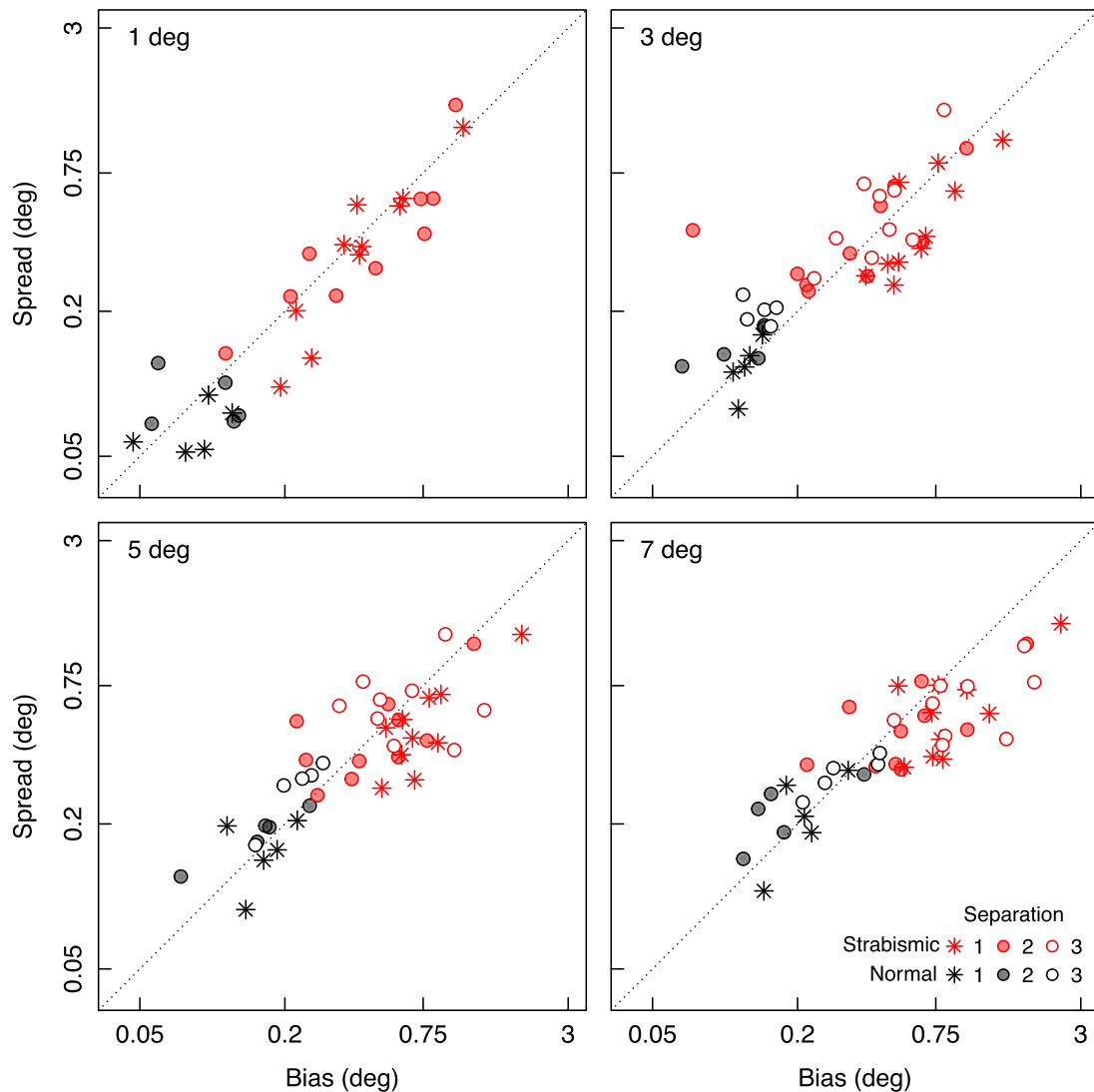


FIGURE 4. Scatterplots of the relationship between spread and bias at each eccentricity and separation. Eccentricities shown in separate panels, separation shown by different symbols. Each symbol represents one subject (black, normally sighted subjects; red, strabismic).

The positional deficit was measured here by the spread (standard deviation) and bias (mean displacement) of response locations in a free localization judgment. The separation effect was evident in both measures dichoptically, and only in bias monocularly. Thus, spread must reflect a purely binocular disruption, but separation effects on threshold (analogous to spread) have been shown by others in monocular conditions.^{8,26} To what extent do spread and bias reflect a common spatial amblyopic impairment? Demanins and Hess⁸ examined this issue by measuring the correlations between threshold and bias (slope and offset of psychometric functions) in a monocular alignment task. They found the two measures uncorrelated with each other and with the amblyopic contrast deficit. The variability across their subjects and absence of normal bias data precluded a clear interpretation of their findings. Here, we find a different result: spread and bias were strongly correlated in strabismic subjects, and the separation effect was associated with strabismus angle.

Figure 4 shows mean spread against bias for each subject in all stimulus conditions (dichoptic viewing). Spread was

significantly correlated with bias for the strabismic group at all eccentricities and separations ($r > 0.75$, $p < 0.05$), except at the largest separations at 5° and 7° ($r < 0.6$, $p > 0.05$). A similar relationship was not evident for the normal group, which was comprised of fewer subjects. Furthermore, the separation-specific effect, calculated as the mean difference in spread and bias between the smallest and intermediate separations outside 1° eccentricity (where only two separations were used), was associated with strabismus angle (Figure 5; spread: $r = 0.73$, $p = 0.015$; bias: $r = 0.63$, $p = 0.048$). Mean spread and bias across all separations in the visual field were not significantly correlated either with strabismus angle or with logMAR acuity of the amblyopic eye; $r < 0.51$, $p > 0.1$. Therefore, spread and bias, particularly at small separations, appear to reflect a common spatial impairment in strabismus that is associated with the amount of ocular misalignment. This outcome is consistent with an association shown previously between strabismus angle and the pattern of spatial biases in a similar localization task.¹¹ Strabismus angle appears to be a more useful predictor of the dichoptic positional deficit than either acuity or contrast

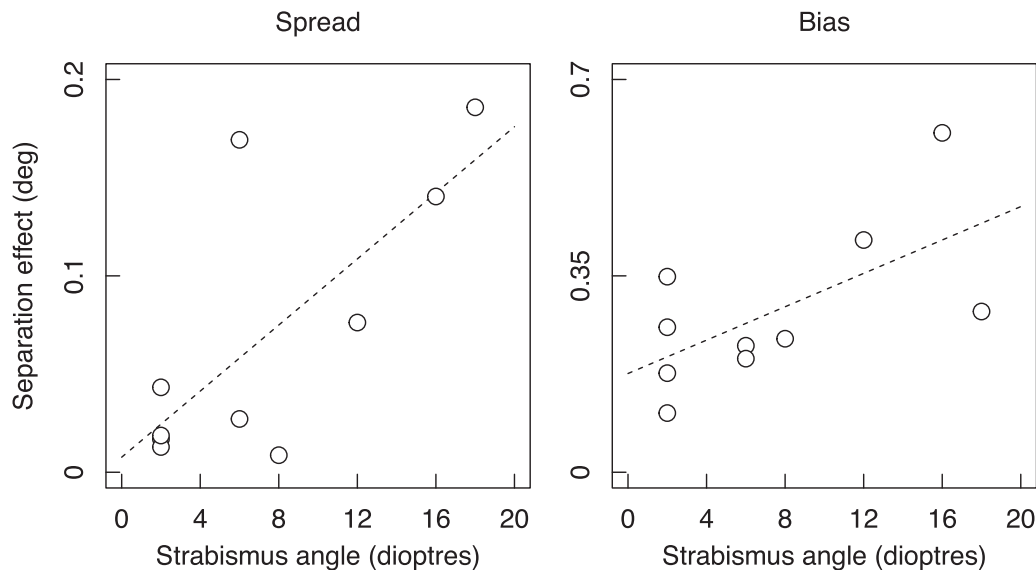


FIGURE 5. Relationship between the separation effect (difference in spread and bias between the smallest and intermediate separations) and strabismus angle. Each symbol represents a single subject. Dashed line shows least-squares fit of separation effect to strabismus angle.

sensitivity, but this remains to be shown for monocular positional judgments.

The positional deficit at small separations could be mistaken for crowding, but the present task and stimulus properties were outside the typical domain of crowding, which is a failure of recognition or identification of stationary cluttered targets. The stimuli were unflanked flickering dots that required no identity judgment, and were perceived as distinct from each other, unlike the jumbled percept that is typical in crowding. Indeed, the stimulus conditions here are equivalent to uncrowded configurations where crowding has been investigated using positional judgments.³⁶ Furthermore, the data do not follow the expected pattern for crowding: Performance of amblyopes at the smallest separation was slightly better at 1° than at the outer eccentricities (unexpected if abnormally higher central than peripheral crowding constrained amblyopic performance), and was roughly constant at the smallest separation from 3° to 7° (inconsistent with an increase in crowding for stimuli of fixed separation across eccentricity). The normal group also did not show a crowding-like pattern, with performance best at small separations at all eccentricities. The results also are unlikely to have been produced by peripheral characteristics of amblyopia (e.g., fixational instability, aniseikonia), which should produce uniform decrements in performance, and not stimulus- and visual field position-specific effects. For fixational instability to have produced the effect shown here, such instability would have to be disproportionately larger for small than large separations. Furthermore, variation in fixational stability has been shown not to affect the accuracy of spatial and retinotopic mapping methods that require steady fixation (e.g.,^{37–39}, see¹⁰ for further discussion ruling out fixational instability as a contributing factor on this task).

The separation deficit may be better accounted for by monocular or interocular suppressive interactions,^{22,40} or by spatial deficits arising from receptive field properties. Interocular suppression, which has been measured using similar dichoptic matching methods throughout the visual field in strabismus (up to 20°),^{41–44} is strongest near the so-called

zero measure point, that is, the location on the deviating retina corresponding with the fovea of the fixing eye, where diplopia and confusion are likely to be most acute.^{43,45} The dissociative presentation of spatially proximal, high-contrast targets in the periphery mimics stimulus conditions at the zero measure point, and may have unmasked suppressive mechanisms that otherwise are weaker,^{42,46} including disparity-specific mechanisms that normally support fusion but are disrupted here (e.g., fusional suppression, see^{47,48}). These ideas could be tested by examining the regional covariation in the depth of interocular suppression and separation-specific positional distortions such as those shown here.

Interocular suppression cannot account for the separation effects on bias in monocular viewing, which likely reflect anomalies in spatial sampling or other receptive field properties. A positional deficit at small separations independent of eccentricity could be accounted for both by uniformly reduced sampling density throughout the visual field,⁴ and an enlargement of receptive fields serving the finest grain of spatial analysis at each eccentricity.^{49,50} Indeed, Clavagnier et al¹⁵ have shown an enlargement of population receptive fields up to 5° eccentricity in strabismic amblyopes, alongside no change in cortical magnification. Receptive field enlargement in their study was uncorrelated with visual acuity, but may correlate with subtler behavioural measures of the amblyopic deficit. Future work examining the scale dependence of the separation deficit may help to clarify this point.

The amblyopic positional deficit has been characterized using a number of tasks and methods, most frequently 2AFC spatial interval and alignment judgments of monocularly-viewed spatially narrowband targets. It would be worth evaluating whether the effects observed here are borne out in conventional threshold measures, with other target configurations (e.g., alignment within a visual field quadrant, rather than across the vertical or horizontal meridian), and with other spatiotemporal properties that rule out potential masking from interocular temporal delays.^{51,52} The normal spread data in Figure 4 show clear effects of eccentricity and

separation but do not fit the exact profile predicted by Levi et al¹⁶ and others.^{17,18} Levi et al¹⁷ predicted thresholds of approximately 0.03 to 0.05 × separation for elements separated by less than half their eccentricity, and 0.01 to 0.03 × eccentricity for larger separations. With some scaling, this prediction fits the normal data at the intermediate and large separations, but not at the smallest separation (spread is higher than predicted; fits not shown). This divergence is not surprising, given the considerable differences between our task and theirs. The group difference at small separations shown here may indeed be larger in threshold conditions.

CONCLUSION

Two positional encoding mechanisms are impaired in strabismus. The first is an eccentricity-dependent mechanism that underlies the larger foveal disruption of positional judgments. The second, a separation-dependent mechanism associated with greater disruption at small stimulus separations, shows that binocular interference from incompatible visual input extends beyond the foveal region.

Acknowledgments

Funded by The Leverhulme Trust, grant number RPG-2013-216, and by a University Research Board grant from the American University of Beirut.

Disclosure: **Z. Hussain**, None; **P.V. McGraw**, None

References

- Levi DM, Klein SA. Spatial localization in normal and amblyopic vision. *Vision Res.* 1983;23(10):1005–1017.
- Rentschler I, Hilz R. Amblyopic processing of positional information. Part I: Vernier acuity. *Exp Brain Res.* 1985;60(2):270–278.
- Levi DM, Klein SA. Vernier acuity, crowding and amblyopia. *Vision Res.* 1985;25(7):979–991.
- Levi DM, Klein SA, Yap YL. Positional uncertainty in peripheral and amblyopic vision. *Vision Res.* 1987;27(4):581–597.
- Fronius M, Sireteanu R. Monocular geometry is selectively distorted in the central visual field of strabismic amblyopes. *Invest Ophthalmol Vis Sci.* 1989;30(9):2034–2044.
- Hess RF, Holliday IE. The spatial localization deficit in amblyopia. *Vision Res.* 1992;32(7):1319–1339.
- Hess RF, Field DJ. Is the spatial deficit in strabismic amblyopia due to loss of cells or an uncalibrated disarray of cells? *Vision Res.* 1994;34(24):3397–3406.
- Demanins R, Hess RF. Positional loss in strabismic amblyopia: inter-relationship of alignment threshold, bias, spatial scale and eccentricity. *Vision Res.* 1996;36(17):2771–2794.
- Mansouri B, Hansen BC, Hess RF. Disrupted retinotopic maps in amblyopia. *Invest Ophthalmol Vis Sci.* 2009;50(7):3218–3225.
- Hussain Z, Svensson C-M, Besle J, Webb BS, Barrett BT, McGraw PV. Estimation of cortical magnification from positional error in normally sighted and amblyopic subjects. *J Vis.* 2015;15(2):1–16.
- Hussain Z, Astle A, Webb BS, McGraw PV. Position matching between the visual fields in strabismus. *J Vision.* 2018; 18(1):1–23.
- Hess RF, Pointer JS. Differences in the neural basis of human amblyopia: the distribution of the anomaly across the visual field. *Vision Res.* 1985;25(11):1577–1594.
- Sireteanu R, Fronius M. Naso-temporal asymmetries in human amblyopia consequence of long-term interocular suppression. *Vision Res.* 1981;21(7):1055–1063.
- Yu C, Levi DM. Naso-temporal asymmetry of spatial interactions in strabismic amblyopia. *Optom Vis Sci.* 1998;75(6):424–432.
- Clavagnier S, Dumoulin SO, Hess RF. Is the cortical deficit in amblyopia due to reduced cortical magnification, loss of neural resolution, or neural disorganization? *J Neurosci.* 2015;35(44):14740–14755.
- Levi DM, Klein SA, Yap YL. “Weber’s law” for position: unconfounding the role of separation and eccentricity. *Vision Res.* 1988;28(5):597–603.
- Levi DM, Klein SA. The role of separation and eccentricity in encoding position. *Vision Res.* 1990;30(4):557–585.
- Whitaker D, Latham K. Disentangling the role of spatial scale, separation and eccentricity in weber’s law for position. *Vision Res.* 1997;37(5):515–524.
- Wilson HR. Responses of spatial mechanisms can explain hyperacuity. *Vision Res.* 1986;26(3):453–469.
- Flom MC, Weymouth FW, Kahneman D. Visual resolution and contour interaction. *J Opt Soc Am.* 1963;53:1026–1032.
- Hess RF, Jacobs RJ. A preliminary report of acuity and contour interactions across the amblyope’s visual field. *Vision Res.* 1979;19(12):1403–1408.
- Wong EH, Levi DM, McGraw PV. Spatial interactions reveal inhibitory cortical networks in human amblyopia. *Vision Res.* 2005;45(21):2810–2819.
- Polat U, Bonnef Y, Ma-Naim T, Belkin M, Sagi D. Spatial interactions in amblyopia: effects of stimulus parameters and amblyopia type. *Vision Res.* 2005;45(11):1471–1479.
- Levi DM, Hariharan S, Klein SA. Suppressive and facilitatory spatial interactions in amblyopic vision. *Vision Res.* 2002;42(11):1379–1394.
- Hariharan S, Levi DM, Klein SA. “crowding” in normal and amblyopic vision assessed with gaussian and gabor c’s. *Vision Res.* 2005;45(5):617–633.
- Levi DM, Klein SA, Sharma V, Nguyen L. Detecting disorder in spatial vision. *Vision Res.* 2000;40(17):2307–2327.
- McKee SP, Levi DM. Dichoptic hyperacuity: the precision of nonius alignment. *J Opt Soc Am A.* 1987;4(6):1104–1108.
- Fogt N, Baughman BJ, Good G. The effect of experience on the detection of small eye movements. *Optom Vis Sci.* 2000;77(12):670–674.
- Johns HA, Manny RE, Fern K, Hu Y-S. The intraexaminer and interexaminer repeatability of the alternate cover test using different prism neutralization endpoints. *Optom Vis Sci.* 2004;81(12):939–946.
- Ferris FL, Kassoff A, Bresnick GH, Bailey I. New visual acuity charts for clinical research. *Am J Ophthalmol.* 1982;94(1):91–96.
- Peirce JW. Psychopy—psychophysics software in python. *J Neurosci Methods.* 2007;162(1-2):8–13.
- R Core Team. *R: A language and environment for statistical computing.* Vienna, Austria: R Foundation for Statistical Computing; 2020.
- Bates D, Maechler BM, Bolker M, Walker SC. Fitting linear mixed-effects models using lme4. *J Stat Softw.* 2015;67(1):1–48.
- Kuznetsova A, Brockhoff PB, Christensen RHB. lmerTest package: tests in linear mixed effects models. *J Stat Softw.* 2017;82(13):1–26.
- Johnson PC. Extension of nakagawa & schielzeth’s r2glmm to random slopes models. *Methods Ecol Evol.* 2014;5(9):944–946.
- Levi DM, Klein SA, Aitsebaomo AP. Vernier acuity, crowding and cortical magnification. *Vision Res.* 1985;25(7):963–977.

37. Baseler HA, Brewer AA, Sharpe LT, Morland AB, Jägle H, Wandell BA. Reorganization of human cortical maps caused by inherited photoreceptor abnormalities. *Nat Neurosci*. 2002;5(4):364–370.
38. Hoffmann MB, Tolhurst DJ, Moore AT, Morland AB. Organization of the visual cortex in human albinism. *J Neurosci*. 2003;23(26):8921–8930.
39. Crossland MD, Morland AB, Feely MP, Hagen E, Rubin GS. The effect of age and fixation instability on retinotopic mapping of primary visual cortex. *Invest Ophthalmol Vis Sci*. 2008;49(8):3734–3739.
40. Shooner C, Hallum LE, Kumbhani RD, García-Marín V, Kelly JG, Majaj NJ, Anthony Movshon J, Kiorpes L. Asymmetric dichoptic masking in visual cortex of amblyopic macaque monkeys. *J Neurosci*. 2017;37(36):8734–8741.
41. Travers TA. Suppression of vision in squint and its association with retinal correspondence and amblyopia. *Br J Ophthalmol*. 1938;22(10):577–604.
42. Schor C. Zero retinal image disparity: a stimulus for suppression in small angle strabismus. *Doc Ophthalmol*. 1978;46(1):149–160.
43. Babu RJ, Clavagnier SR, Bobier W, Thompson B, Hess RF. The regional extent of suppression: strabismic versus nonstrabismic. *Invest Ophthalmol Vis Sci*. 2013;54(10):6585–6593.
44. Babu RJ, Clavagnier S, Bobier WR, Thompson B, Hess RF. Regional extent of peripheral suppression in amblyopia. *Invest Ophthalmol Vis Sci*. 2017;58(4):2329–2340.
45. Jampolsky A. Characteristics of suppression in strabismus. *AMA Arch Ophthalmol*. 1955;54(5):683–696.
46. Schor CM. Visual stimuli for strabismic suppression. *Perception*. 1977;6(5):583–593.
47. McKee SP, Harrad RA. Fusional suppression in normal and stereanomalous observers. *Vision Res*. 1993;33(12):1645–1658.
48. Harrad R. Psychophysics of suppression. *Eye (Lond)*. 1996;10(Pt 2):270–273.
49. Hess RF, Hayes A. Neural recruitment explains “Weber’s law” of spatial position. *Vision Res*. 1993;33(12):1673–1684.
50. Whitaker D, Bradley A, Barrett BT, McGraw PV. Isolation of stimulus characteristics contributing to weber’s law for position. *Vision Res*. 2002;42(9):1137–1148.
51. Hamasaki DI, Flynn JT. Amblyopic eyes have longer reaction times. *Invest Ophthalmol Vis Sci*. 1981;21(6):846–853.
52. Spang K, Fahle M. Impaired temporal, not just spatial, resolution in amblyopia. *Invest Ophthalmol Vis Sci*. 2009;50(11):5207–5212.