

# Interocular suppression patterns in binocularly abnormal observers using luminance- and contrast-modulated noise stimuli

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In binocular viewing, images presented to the amblyopic eye are suppressed in the cortex to prevent confusion or diplopia. The present study measures depth and extent of interocular suppression across the central circular 24° visual field in observers with strabismus and microstrabismus. Visual stimuli were concentric rings of alternating polarity, each divided into sectors. Rings were defined by luminance (L), luminance-modulated noise (LM), or contrast-modulated noise (CM). They were viewed binocularly except for the tested ring, which was viewed dichoptically, so that the modulation of one sector presented to the weaker or amblyopic eye was adjusted to perceptually match the surrounding ring presented to the preferred eye. A two alternative forced-choice paradigm combined with a staircase procedure allowed for measurement of the point of subjective equality, or perceptual match. Depth of suppression was calculated as the difference between physical modulations presented to the two eyes at this point. Strabismic participants showed suppression deeper centrally than peripherally, and in one hemifield of the visual field more than the other. Suppression was deeper for L than LM, and CM than LM stimuli. Microstrabismic suppression was weaker than that of strabisms, central for L and LM stimuli, with suppression of CM stimuli being broader, deeper and more in one hemifield. Suppression depth was positively correlated with interocular visual acuity difference and stereoacuity reduction. Clinically, LM stimuli could be used for assessment of deeper amblyopes to assess suppression patterns, while more sensitive detection of mild suppression would be possible using CM stimuli.

## Introduction

Interocular suppression occurs when binocularity is disrupted such as in strabismus, anisometropia, or pathology affecting one eye's input more than the other. If images presented to each eye cannot be fused into a single clear percept, one image is cortically suppressed (Sengpiel, Blakemore, Kind, & Harrad, 1994; Harrad, Sengpiel, & Blakemore, 1996; Sengpiel & Blakemore, 1996; Sengpiel, Jirmann, Vorobyov, & Eysel, 2006; Farivar, Thompson, Mansouri, & Hess, 2011), such that visual sensitivity of the suppressed eye is reduced during binocular, compared to monocular viewing (Mehdorn, 1989). Interocular suppression is also associated with amblyopia, and long-term suppression might be a factor in amblyopia development (Sireteanu & Fronius, 1981). The present study employs dichoptic stimuli to measure suppression across the visual field (Chima, Formankiewicz, & Waugh, 2015) in participants with abnormal binocular vision.

A positive correlation between suppression depth and degree of amblyopia (as measured by magnitude of interocular acuity difference) has been reported for both adult and child observers (Sireteanu & Fronius, 1981; Agrawal, Conner, Odom, Schwartz, & Mendola, 2006; Li et al., 2011; Narasimhan, Harrison, & Giaschi, 2012; Li et al., 2013). In amblyopic monkeys, single-cell recordings from cortical V1 and V2 neurones revealed that the proportion of neurones with suppressive actions (i.e., lower binocular than monocular peak amplitude response) was proportionally higher in stronger amblyopes (Bi et al., 2011). However, in one

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previous study (Holopigian, Blake, & Greenwald, 1988) a negative correlation between suppression and interocular acuity difference was found. In that study, four of nine participants were not amblyopic, in that they had little difference in interocular visual acuities and alternating strabismus such that they could fixate equally well with either eye, but never both together.

The present study is concerned with measuring suppression in participants who have binocularly disrupted visual systems due to ocular misalignment (i.e., participants with strabismus or microstrabismus). Strabismus and microstrabismus are thought to be separate clinical entities, whereby microstrabisms have a smaller ocular misalignment that is not always apparent with routine clinical testing (Helveston & von Noorden, 1967; Lang, 1969; Parks, 1969), and a smaller interocular acuity difference (Irvine, 1948). Mehdorn (1989) suggested that suppression in microstrabisms (<6 prism diopters ocular deviation) is an artefact of measurement and that the development of harmonious anomalous retinal correspondence (hARC), in which the visual direction associated with the fovea of the preferred eye corresponds to that of an extrafoveal point in the other eye under binocular conditions (Bagolini, 1967), relieves the need for it. Other studies using different measurement methods to Mehdorn disagree, and have indeed measured suppression in microstrabismus (e.g., Bagolini & Campos, 1983; Babu, Clavagnier, Bobier, Thompson, & Hess, 2013). In order to measure interocular suppression, dichoptic presentation is required, so that the image to the stronger eye can be weakened (or to the weaker eye, strengthened) to “break” suppression. Artificial conditions are therefore required to present different images to each eye for measurement of suppression, which can disrupt natural viewing conditions, not allowing for measurement of habitual interocular suppression.

Methods of presenting different images to each eye in studies of amblyopic suppression include placing a red lens in front of one eye (von Graefe, 1856; Travers, 1938; Campos, 1982), use of red–green anaglyph filters before the two eyes (Harms, 1937; Sireteanu & Fronius, 1981; Campos, 1982; Gottlob, Charlier, & Reinecke, 1992), use of increasing monocular vertical and horizontal prisms (Irvine, 1948; Jampolsky, 1955; Hallden, 1982; Pratt-Johnson & Tillson, 1983; Mehdorn, 1989), mirror haploscope dissociation (Travers, 1938; Herzau, 1980; Campos, 1982; Joesse et al., 1997), use of polarizing filters (Sireteanu, Fronius, & Singer, 1981), phase-difference haploscopy (Mehdorn, 1989), and more recently, head-mounted virtual reality displays (Babu et al., 2013). The more dissimilar the images presented to each eye, the smaller the scotoma measured (Herzau, 1980; Campos, 1982; Mehdorn, 1989). The most highly cited of these studies was carried out by Campos (1982), in which participation

or exclusion perimetry was performed. In participation perimetry, while fixating a target, a white test stimulus is moved across the binocular visual field of strabismic participants wearing red–green anaglyph lenses. The patient reports the color of the stimulus. In exclusion perimetry, a red test stimulus is used and presence or absence of the stimulus reported. Participation perimetry involves a less dissociative technique, more similar to habitual viewing, than exclusion perimetry for which the red light would not be visible through the green lens. In 10 of 13 esotropic amblyopes (inward deviation of one eye relative to the midline by  $3.4^{\circ}$ – $9.1^{\circ}$ , or six to 16 prism diopters), participation perimetry revealed suppression regions (or scotomata), but exclusion perimetry either did not, or revealed smaller ones. Thus, if more similar images are presented to each eye, like in habitual viewing conditions, larger suppression scotomata might be measured, more accurately reflecting suppression in everyday life.

One criticism of Campos’s study is that the view from each eye through different color filters is still far removed from habitual viewing conditions. Recently, a novel method was developed by Babu et al. (2013), who used head-mounted displays with independent stimulus screens placed close to the eyes. This method combines complete dissociation with a comfortable virtual viewing distance. They mapped interocular suppression zones in amblyopes by presenting binocularly viewed rings, one viewed dichoptically, within a  $20^{\circ}$  circular visual field. The contrast of an adjustable sector within the dichoptically viewed ring presented to the preferred eye was reduced using a method of adjustment, until it perceptually matched the surrounding ring seen by the amblyopic eye. Deeper central than peripheral suppression was found for four microstrabismic, six strabismic, and four anisometropic amblyopes. Although in this study, preferred eye advantage—rather than amblyopic suppression per se—may have been measured (Huang, Zhou, Lu, & Zhou, 2011; Ding, Klein, & Levi, 2013), the interocular matching task did provide estimates of suppression using suprathreshold stimuli similar to real-world viewing, unlike the studies mentioned above, or those in which detection thresholds for each eye obtained under dichoptic conditions are compared (Joesse, Simonsz, van Minderhout, Mulder, & de Jong, 1999).

In some studies, suppression in strabismus has been found to occur at the center of the visual field of the deviating eye and also in that part of the visual field corresponding to the nondeviating eye’s fovea (Travers, 1938; Irvine, 1948; Jampolsky, 1955; Herzau, 1980; Sireteanu et al., 1981). In other studies, suppression of one hemifield (Pratt-Johnson & Tillson, 1984), the full field (Joesse et al., 1999), or only central regions (Campos, 1982; Hallden, 1982; Mehdorn, 1989; Joesse et al., 1997; Babu et al., 2013) have been found. Further

disagreement can be seen for suppression estimates in microstrabismics. Generally, discrete central suppression is measured (Sireteanu et al., 1981; Hallden, 1982; Mehdorn, 1989; Babu et al., 2013), although different techniques in the same participants measured differently sized scotomata (Herzau, 1980; Bagolini, 1982; Campos, 1982).

Differences in results found could be related to different stimuli and methods employed to measure strabismic and microstrabismic interocular suppression. To best measure suppression, we suggest that similar stimuli should be presented dichoptically to corresponding retinal points of the two eyes and compared using a suprathreshold interocular perceptual matching task. Carrying out perceptual matching in different areas of the visual field can then provide measures of both depth and extent of suppression.

Previously mentioned studies of amblyopic suppression have used first-order spatial targets (e.g., those defined by luminance). More recent studies have used a dichoptic global motion coherence paradigm to measure suppression depth, but not extent, for large ( $5^{\circ}$ – $22^{\circ}$ ) stimulus areas in amblyopes (Mansouri, Thompson, & Hess, 2008; Black, Thompson, Maehara, & Hess, 2011; Li et al., 2011; Narasimhan et al., 2012). Here, the interocular luminance contrast ratio is adjusted until observers are able to correctly identify a coherent direction of motion of signal dots within random direction noise dots, presented dichoptically. The interocular contrast ratio providing a similar coherence threshold, irrespective of signal presentation to the amblyopic or nonamblyopic eye, gives a measure of depth of suppression. This measure was found to correlate with degree of amblyopia (Li et al., 2011; Li et al., 2013). Furthermore, making repeated measures forms part of a treatment regime (Hess, Mansouri, & Thompson, 2010).

In addition to luminance and motion stimuli, the visual system is also sensitive to second-order spatial characteristics, such as modulations of contrast (contrast-modulated or CM stimuli) or texture, without a change in mean luminance. These second-order targets require extra stages of processing to be extracted by the visual system above that required for first-order luminance targets, which may occur in cortical units receiving predominantly binocular input (Wong, Levi, & McGraw, 2001, 2005; Hairol & Waugh, 2010; Chima et al., 2015; Skerswetat, Formankiewicz, & Waugh, 2016). In amblyopia and strabismus, reduced sensitivity to CM stimuli above that found in normal eyes may be expected due to binocular disruption. Indeed sensitivity to CM, compared to luminance-modulated (LM) stimuli in both amblyopic and preferred eyes is reduced when compared to normal eyes (Wong et al., 2001, 2005; Simmers, Ledgeway, Hess, & McGraw, 2003; Mansouri, Allen, & Hess, 2005, but see Gao et

al., 2015). Potentially then, use of CM spatial targets for interocular suppression assessment in early amblyopia may provide a spatially localized, more sensitive clinical tool than standard luminance and motion stimuli.

In this study we measure depth and extent of interocular suppression for luminance (L), LM, and CM stimuli in participants with naturally occurring, developmental binocular disruption associated with strabismus and microstrabismus. To create LM and CM stimuli, we use dynamic binary noise. Noise is known to reduce stimulus detectability (Nordmann, Freeman, & Casanova, 1992; Rovamo & Kukkonen, 1996; Schofield & Georgeson, 1999, 2003) and discriminability (Legge, Kersten, & Burgess, 1987), so deeper suppression for LM, than L stimuli, may be expected. However, clinically it is thought that temporal transients (such as blinking, or those created by dynamic noise) break suppression (e.g., Scheiman & Wick, 2008). The effect of adding dynamic noise on suppression depth measures in abnormal binocular visual systems, however, has not been previously reported.

## Methods

### Participants

A qualified optometrist performed eye examinations on all participants prior to inclusion in this study. Clinical details of the nine binocularly abnormal participants are provided in Table 1. Four participants were classified as strabismic, with ocular misalignments greater than 6 prism diopters and/or previous surgery for large angle strabismus. Five participants were classified as having primary microstrabismus, with deviations of 6 prism diopters or less, and no previous strabismus surgery (e.g., Mehdorn, 1989; Kilwinger, Spekrijse, & Simonsz, 2002; Millodot, 2014). Microstrabismus in adults is a condition associated with a repeatable interocular visual acuity difference and either central or nonabsolute eccentric fixation, or absolute eccentric fixation with harmonious abnormal retinal correspondence (hARC; Helveston & von Noorden, 1967), so-called microtropia “with identity” (Lang, 1969; Rowe, 2012).

Our microstrabismic participants lacked the bifoveation required to obtain 60 arcsec or better on a random-dot stereotest (Tomas & Altay, 2000), achieving stereoacuties of 120 to  $>480$  arcsec. This level of stereopsis combined with the presence of eccentric or unsteady fixation and an interocular acuity difference (of 0.1 logMAR or more) were used to classify our participants as microstrabismic (see Table 1). Although

| Participant | Age/Sex | Type                                     | Refraction                             | Acuity         | Cover test                                                   | Monocular fixation                      | Stereo-acuity | Clinical suppression                        | History                                     |
|-------------|---------|------------------------------------------|----------------------------------------|----------------|--------------------------------------------------------------|-----------------------------------------|---------------|---------------------------------------------|---------------------------------------------|
| AH          | 18/F    | Strab. (Int.), aniso.                    | R −3.25 DS<br>L −1.50 DS               | 0.25<br>−0.04  | 20 <sup>Δ</sup> (variable) R<br>XOT, 2 <sup>Δ</sup> R<br>HYP | R 1.83° sup.<br>L central unsteady      | >480"         | Sbisa: (variable) L sup. 1<br>W4d: variable | Surgery at 7 years<br>Patching from 5 years |
| CMa         | 32/F    | Strab.                                   | R +3.00/−2.25×11<br>L +2.25/−2.00×65   | −0.08<br>0.4   | 26 <sup>Δ</sup> L SOT                                        | R steady central<br>L 0.52° nasal       | >480"         | Sbisa: 11 (R)<br>W4d: L sup.                | Patching from 3 years                       |
| CMc         | 30/F    | Strab.                                   | R +5.50/−1.00×102<br>L +6.00/−1.00×100 | −0.06<br>0.54  | 7 <sup>Δ</sup> L XOT                                         | R steady central                        | 480"          | Sbisa: 15 (R)<br>W4d: L sup.                | Surgery at 4 years<br>Patching from 4 years |
| JB          | 59/F    | (Surgery corrected)<br>Strab., Aniso.    | R +4.25/−0.50×80<br>L +1.00/−1.00×100  | 0.4<br>−0.04   | NMD                                                          | R sup. nasal 0.86°<br>L central steady  | >480"         | Sbisa: 12 (L)<br>W4d: R sup.                | Patching at 5 years<br>Surgery at 5 years   |
| AW          | 20/F    | Microstrab.                              | R +6.50/−2.75×164<br>L +6.25/−3.25×3   | −0.16<br>−0.06 | 6 <sup>Δ</sup> L SOT                                         | R central steady<br>L 0.30° nasal       | >480"         | Sbisa: 11 (R)<br>W4d: normal                | Patching when child (patient unsure when)   |
| AR          | 20/F    | Microstrab., aniso.                      | R +2.25/−0.50×5<br>L +5.00/−0.75×22    | −0.08<br>0.02  | NMD                                                          | R central, steady<br>L temp., steady    | 120"          | Sbisa: 13 (R)<br>W4d: normal                | None                                        |
| DM          | 19/F    | Microstrab.                              | R +2.25/−1.75×162<br>L +3.00/−2.25×7   | −0.16<br>0.02  | NMD                                                          | R central, steady<br>L inf. temp. 0.58° | 120"          | Sbisa: 8 (R)<br>W4d: normal                 | Patching at 4 years                         |
| IR          | 20/F    | Microstrab., aniso.                      | R −3.25/−2.00×35<br>L −0.75/−0.50×175  | 0.1<br>0.0     | NMD                                                          | R 0.58° sup. temp.<br>L central steady  | 120"          | Sbisa: 2 (L)<br>W4d: normal                 | Refractive correction since childhood       |
| NS          | 19/F    | Microstrab. (with refractive correction) | R +8.50/−2.25×5<br>L +8.25/−2.50×3     | 0.12<br>−0.20  | NMD (20 <sup>Δ</sup> R<br>SOT s. Rx)                         | R inf. nasal<br>L central steady        | 240"          | Sbisa: 6 (L)<br>W4d: normal                 | Refractive correction since 4 years         |

Table 1. Clinical attributes of participants. Notes: F = female; strab. = strabismus; Int. = intermittent; aniso. = anisometropia; R = right eye; DS = diopter sphere; XOT = exotropia; HYP = hypertropia; sup. = superior; L = left eye; Sbisa = red filter bar; W4d = Worth 4-Dot test; SOT = esotropia; nas. = nasal; NMD = no movement detected; micro. = microstrabismus; temp. = temporal; inf. = inferior; s. Rx = without refractive correction. All deviations are reported in prism dioptres (<sup>Δ</sup>). Monocular fixation was measured with the Haidinger Brush where magnitude of deviation is given. Measurements with location only were performed with visuoscopy. All acuities were measured with a logMAR chart (five letters per line). Stereoacuity was measured with the Toegepast Natuurwetenschappelijk Onderzoek (TNO) Stereotest. Suppression was detected with the Worth 4-Dot test, and quantified with a Sbisa red filter bar.

we do not measure retinal correspondence, we did assess the presence and the position of eccentric fixation, using a Haidinger Brush (Macular Integrity Tester; Bernell, Mishawaka, IN) and visuoscopy (Professional Direct Ophthalmoscope reticule filter, Keeler, Windsor, UK).

Two standard clinical tests of suppression were conducted on all participants. The Worth 4-Dot test (Lunea Ophthalmologie, Prunay Le Gillon, France) is designed to detect the presence or absence of suppression in the central visual field. Four colored dots of light (one red, two green, one white) were presented at the standard clinical viewing distance (the four dots subtend  $0.76^\circ$  at 3 m, where the test was performed for the current study). Wearing red–green anaglyph filters before the eyes, the participant reported the number of dots perceived. A red filter Sbisabar (Sbisabar Industrie SPA, Italy) was used to clinically estimate suppression depth (Bagolini, 1982). The participant binocularly viewed (with appropriate prism correction to correct the ocular deviation) a white fixation light. If a low-density filter was placed in front of the nonsuppressing (preferred) eye, the fixation light appeared red. Filter density was increased until the participant reported that the light was perceived as white and the level of filter when this occurred, was recorded as the clinical depth of suppression.

All participants were female. Amblyopia is not male or female specific (Attebo et al., 1998), so it is unlikely that the suppression extent or depth measured in this study is influenced by having only female participants.

Our protocols were approved by the Faculty Research Ethics Panel at Anglia Ruskin University. Participants were staff and students at Anglia Ruskin University. Informed consent was obtained prior to testing. The conduct of the research project complied with the principles expressed in the Declaration of Helsinki.

## Equipment

An Apple MacBook Pro (Apple Computer, Cupertino, CA) running Matlab (The MathWorks, Natick, MA) with Psychophysics Toolbox (Brainard, 1997; Pelli, 1997) was used to generate stimuli, which were then presented on eMagin DualPro head-mounted OLED displays (Dual Pro Z800; eMagin Corp., Hopewell Junction, NY) via Matrox DualHead2Go adapter (Matrox Graphics Inc., Quebec, Canada). One screen positioned close to each eye allowed for dichoptic presentation of stimuli. Each screen had a resolution of  $800 \times 600$  pixels, refresh rate of 60 Hz, and mean luminance  $45 \text{ cd/m}^2$ . The effective viewing distance for the head-mounted displays was 80 cm.

## Stimuli

Examples of L, LM, and CM stimuli are provided in Figure 1A through F, with associated luminance profiles. For L and LM stimuli (Figure 1A through D), there were eight concentric rings, with the central ring having a radius of  $0.75^\circ$ . Each subsequent ring was doubled in area to account for larger peripheral than central summation areas. Figure 2 illustrates how each ring was split into eight sectors (black lines).

CM stimuli (Figure 1E and F) differed in that the central circular  $24^\circ$  of the visual field was split into four, as opposed to eight rings, as spatial summation areas have been found to be larger for CM than LM stimuli out to  $10^\circ$  eccentricity (Sukumar & Waugh, 2007). Rings were doubled in area with increasing eccentricity for all stimulus types, as the rate of spatial summation change is similar for LM and CM stimuli (Smith & Ledgeway, 1998; Sukumar & Waugh, 2007).

Stimuli were constructed using the following equation (Schofield & Georgeson, 1999):

$$I(x, y) = I_0[1 + nN(x, y) + lL(x, y) + mnM(x, y)N(x, y)] \quad (1)$$

where  $I(x, y)$  is the luminance at position  $(x, y)$  and  $I_0$  is mean luminance;  $n$  is noise contrast (set to 0 for L stimuli). Noise was different for LM ( $n = 0.25$ ) and CM ( $n = 0.50$ ) to give the largest adjustable modulation range for each.  $N(x, y)$  is the value of binary noise at position  $(x, y)$ , either  $-1$  (dark) or  $1$  (bright). The binocular elements of the stimulus are rings of fixed modulation, defined by the baseline modulation. Consecutive rings were increments and decrements of modulation. Baseline modulation is  $l$  for L and LM stimuli (Figure 1A and C) and  $m$  for CM stimuli (Figure 1E). When a particular sector was being adjusted, the surrounding ring was dichoptically presented to the preferred eye only (Figure 1, right column), and the adjustable sector to the amblyopic (or weaker) eye only (Figure 1, left column). For the L ring,  $n = 0$ ,  $m = 0$  and for the adjustable sector,  $l$  is adjusted; for LM rings,  $n = 0.25$ ,  $m = 0$  and  $l$  is adjusted; and for CM rings,  $n = 0.50$ ,  $l = 0$  and  $m$  is adjusted.

The surrounding ring was at baseline modulation. To maximize the range of measurable suppression for each participant and each stimulus type, baseline modulation was adjusted; it was  $0.33$ – $0.50$  for L and CM and  $0.25$ – $0.50$  for LM stimuli. A lower baseline allows a deeper level of suppression to be quantified, the ceiling of which is indicated in each individual plot in Figures A1 through A9 in the Appendix). The baseline was reduced for those participants who had deeper suppression, while ensuring that stimuli were detectable. Detection thresholds were not formally measured; however, Chima et al. (2015) showed that for interocularly blurred participants with normal

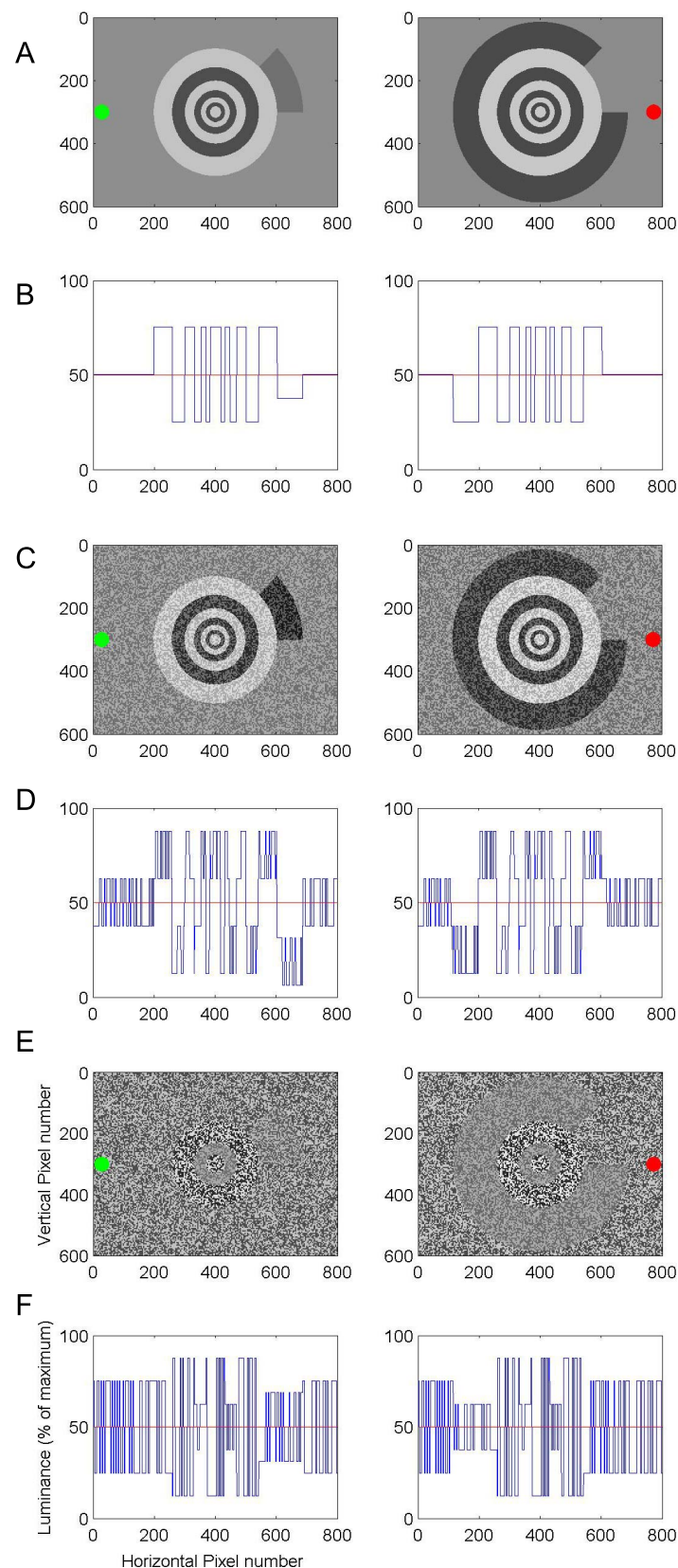


Figure 1. Examples of L stimuli are shown in (A) for amblyopic (left panel) and nonamblyopic (right panel) eyes. (B) shows corresponding luminance profiles taken 1 pixel above the horizontal midline of (A), where the red line is mean luminance. (C) depicts LM stimuli, whilst (D) shows the corresponding luminance profile with noise modulation. (E) shows CM stimuli, with the corresponding luminance profile (F), where the average luminance of the stimuli remains constant about the mean luminance,

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though the contrast of the high and low CM rings and the adjustable sector change. Thus the difference between each ring is the modulation of contrast, rather than modulation of luminance. (A), (C), and (E) also show blind spot markers for right (red) and left (green) eyes. All horizontal axes show horizontal pixel numbers. Ordinate axis vary as in (E) and (F).

binocular vision, baseline adjustment had no significant effect on suppression patterns (see control experiment 3 in Chima et al., 2015).

Dynamic noise was fully correlated between the eyes. For noisy (LM and CM) stimuli, noise check size was  $4 \times 4$  pixels (angular subtense of 10 arcmin per check at the 80-cm effective viewing distance). Our participants all reported being able to resolve these checks. We know from a previous study (Chima et al., 2015) that these checks were resolvable in normal participants. At the greatest eccentricity tested in the present study of  $12^\circ$ , visual acuity has been reported to be equivalent to a check size of 2.5–6.3 arcmin (e.g., Ludvigh, 1941; Millodot, Johnson, Lamont, & Leibowitz, 1975; Rovamo, Virsu, & Näsänen, 1978; Anderson & Thibos, 1999a, 1999b). Sireteanu and Fronius (1981) measured grating acuity across the visual field for nine strabismic and microstrabismic amblyopes. The worst central grating acuity shown (for HF; letter acuity of 6/50) was approximately 4.3 arcmin (7 c/°), which was similar at  $10^\circ$  eccentricity for this amblyope (the worst grating acuity reported at  $10^\circ$  was for a different amblyope, HE, at 5 c/°, or 6 arcmin). Therefore our 10-arcmin noise is likely to have been resolvable by all of our participants (worst central letter acuity of 6/19). Furthermore, in amblyopes (6/18–6/24 acuity), contrast sensitivity functions reveal that at  $10^\circ$  eccentricity a 3 c/° grating of 0.25 contrast is still resolvable (the lowest noise amplitude employed in the present study; Thomas, 1978; Katz, Levi, & Bedell, 1984). Figure 2 shows a schematic of a fused binocular percept of an L stimulus.

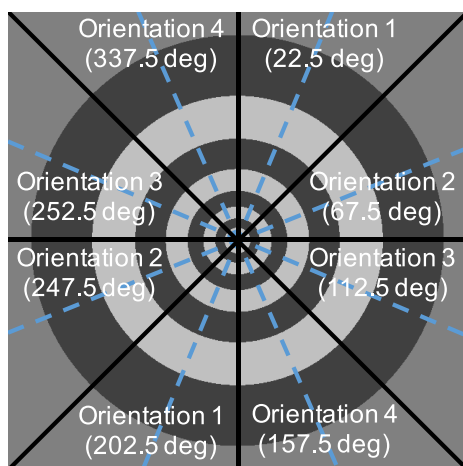


Figure 2. Schematic representation of binocularly fused L stimulus. Black lines delineate sectors. Blue dashed lines show orientations. No lines appear on actual stimulus.

## Procedure

Suppression mapping was carried out four to six times for each participant for each stimulus type: L, LM, and CM. Prior to formal data collection, practice runs were carried out until participants were familiar with the task, and the standard deviation of the final four of six staircase reversals was within 15% of the mean (on average standard deviation for all participants was  $7.7\% \pm 4.3\%$  of the mean).

Stimulus alignment was carried out to ensure that the same images were presented to corresponding points in each eye. Two squares of  $1^\circ$  side length with centers vertically separated by  $1^\circ$  were presented dichoptically (i.e., one square to each eye). If squares appeared to be horizontally offset, participants moved the squares using the keyboard in steps of 1 pixel ( $\sim 2.5$  arcmin) until they were perceived as one directly above the other. Alignment in pixels was recorded and the main experimental stimuli were adjusted by this degree to ensure alignment. This was carried out at the beginning of each session, although magnitudes did not change notably between sessions. Larger angle ocular deviations were corrected with prisms (incorporated into refractive correction) to grossly align images to each eye prior to the above alignment calibration.

Participants were instructed to fixate in the center of the stimulus throughout the test. Brightly colored (red presented to the right eye and green presented to the left eye) blindspot fixation markers ( $1^\circ$  circles presented  $15^\circ$  temporally on each screen along the horizontal midline; see Figure 1) became highly visible if accurate central fixation was not maintained. For one observer (AH), fixation was also monitored with a ViewPoint EyeTracker (Arrington Research, Scottsdale, AZ) when mapping suppression with LM stimuli. Any fixation losses (greater than 1 deg) prevented this observer from responding. Results were comparable to the main experiment, as can be seen in Figure A2.

The point of subjective equality (PSE) in the perceptual matching task was measured at each location of the visual field tested. Participants increased or decreased sector modulation until it perceptually matched the surrounding ring presented to the preferred eye. Staircases (one-down, one-up) were initiated randomly from either halfway between a physical modulation match and maximum adjustable modulation or halfway between a modulation match and minimum adjustable modulation. An audio cue signalled once each response was made, and a longer

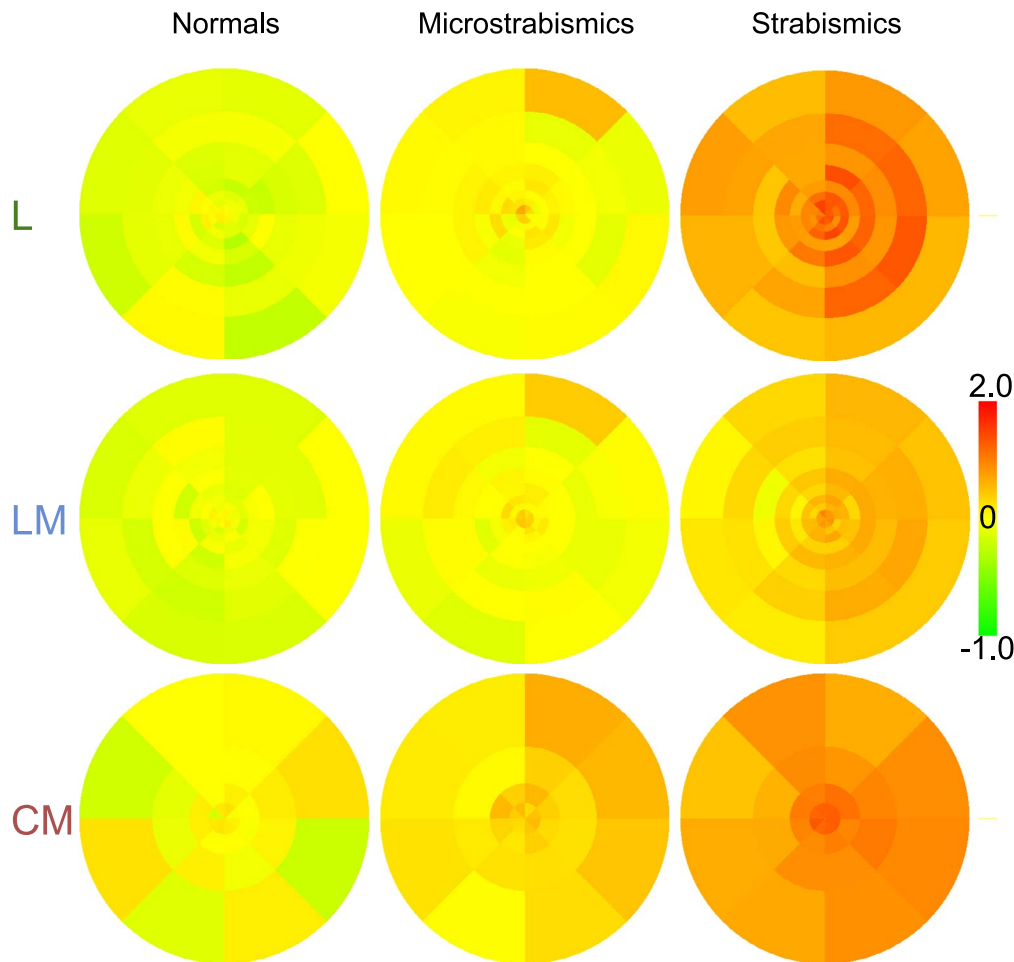


Figure 3. Colored suppression maps averaged across participants within each group (normals, microstrabismics, strabismics) for different stimulus types (L, LM, CM). Color bar to the right of the Figure applies to all maps. A red sector shows deepest suppression, yellow no suppression, and green facilitation.

audio cue sounded when six reversals were complete, after which the staircase was terminated and a new sector was adjusted. Step size was initially 0.1 (of a maximum 1.0 modulation; see Analysis section), reducing to 0.05 after two reversals. In each experimental run, 64 (L or LM) or 32 (CM) staircases were completed (i.e., one for each sector). Sector presentation order was systematically counterbalanced across four to six runs to evenly distribute the effects of practice, adaptation, and fatigue. This involved working clockwise from the outside ring in, for at least two runs, and anticlockwise from the inside ring out, for at least two runs. The average was taken of equal numbers of anticlockwise and clockwise runs. Runs were carried out on different days for each participant.

## Analysis

Mean match thresholds (PSEs) for four to six experimental runs for each stimulus type (L, LM, and

CM), sector orientation, and eccentricity were calculated for each participant. These values constitute our estimates of depth of suppression, which were normalized across stimulus type using the following equation:

$$S_{\text{norm}} = \frac{(M_{\text{match}} - M_{\text{baseline}})}{M_{\text{baseline}}} \quad (2)$$

where  $S_{\text{norm}}$  is the normalized depth of suppression.  $M_{\text{match}}$  is the PSE modulation of the sector and  $M_{\text{baseline}}$  is the baseline modulation of the surrounding ring.

Suppression values were plotted using color-coded maps. For L and CM stimuli, the range of normalized depth of suppression is from  $-1.0$  to  $2.0$  (asymmetry due to lowering of the baseline modulation from 0.5 for given individuals as described in the Stimuli section above to allow for measurement of deeper suppression). All normalized color-coded suppression maps (Figure 3) therefore have a range of  $-1$  (green: maximum facilitation) to  $2.0$  (red: maximum suppression).

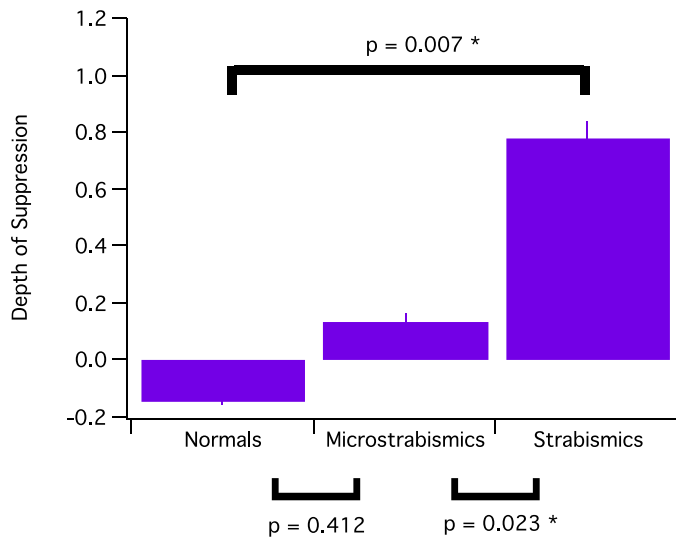


Figure 4. Suppression depth averaged across all sectors and all stimulus types for the three participant groups. The  $p$  values show a significant (asterisk) difference between microstrabismics and strabismics, and normals and strabismics. Error bars show  $\pm 1$  SE ( $-1$  for normals).

sion), with 0 (yellow) representing a physical match between the sector and surrounding ring modulation.

In order to investigate hemifield suppression, the average of all sectors in each half of the measured visual field either side of the vertical midline (see exceptions below for AH and CMa) was taken. The hemifield with the deepest average suppression was arranged for all participants to be on the right side of the suppression map for statistical analysis. For two strabismics (AH and CMa) entire maps were rotated clockwise by one sector, in order to superimpose the clearly defined hemifield suppression regions with those of other participants (see colored suppression maps in Appendix: Figures A1 and A2, respectively). The Appendix shows individual suppression maps with the actual arrangement of measured suppression maps prior to any adjustment.

Visual performance in spatial vision discrimination tasks in anisometropic and strabismic amblyopes has been shown to be distinctly different (Levi & Klein, 1982a, 1982b; McKee, Levi, & Movshon, 2003; Song, Levi, & Pelli, 2014). Mixed amblyopes (with both strabismus and anisometropia) show behavior akin to strabismic amblyopes in terms of binocular performance (e.g., McKee et al., 2003). Therefore, despite participant JB having no manifest deviation, anisometropia, and microstrabismus, she is included in the strabismic category as she had strabismus surgery for large-angle esotropia when she was 5 years old.

Data from the nine binocularly abnormal participants (four with strabismus and five with microstrabismus) were compared to those previously reported for four binocularly normal (unblurred)

participants (from Chima et al., 2015). A mixed design repeated measures analysis of variance (ANOVA) was performed. In the overall statistical analysis, which included all stimulus types, adjacent sectors for L and LM stimuli were averaged to provide information about 32 sectors, equivalent to the number used for CM stimuli. Participant group was a between-subjects factor (three levels: normal, microstrabismus, and strabismus), and within-subjects factors were stimulus type (three levels: L, LM, or CM), orientation (Orientations 1–4; see Figure 2), and eccentricity (eight levels across the visual field at  $\pm 1.30^\circ$ ,  $2.90^\circ$ ,  $5.95^\circ$ , and  $12.00^\circ$ ). Statistical outcomes of ANOVAs comparing L and LM stimuli were similar, whether data were averaged across 32 or 64 sectors.

## Results

We aim to address four principal questions:

1. Is measured interocular suppression different between normal and binocularly abnormal participants?
2. Are there specific patterns of suppression for strabismic and microstrabismic participants?
3. Does the addition of dynamic luminance noise affect the measured magnitude of suppression in strabismic and microstrabismic participants?
4. Do CM stimuli provide a more sensitive test for suppression than LM stimuli in participants with abnormal binocular vision?

### The effect of participant group on suppression depth

Differences in depth and extent of suppression between participant groups can be seen in Figure 3, where the color maps change from green to yellow to orange–red for normal, microstrabismic, and strabismic groups, respectively. A summary of mean quantified results from Figure 3 for different participant groups is provided in Figure 4. There is a significant main effect of participant group,  $F(2, 10) = 6.19$ ;  $p = 0.018$ . Significantly deeper levels of suppression are found for strabismic, than microstrabismic ( $p = 0.023$ ) and normal participants ( $p = 0.007$ ).

### The effect of eccentricity on suppression depth: Hemifield and central patterns

There is a significant overall main effect of eccentricity for all groups combined,  $F(1.77, 17.65) = 7.02$ ,  $p$

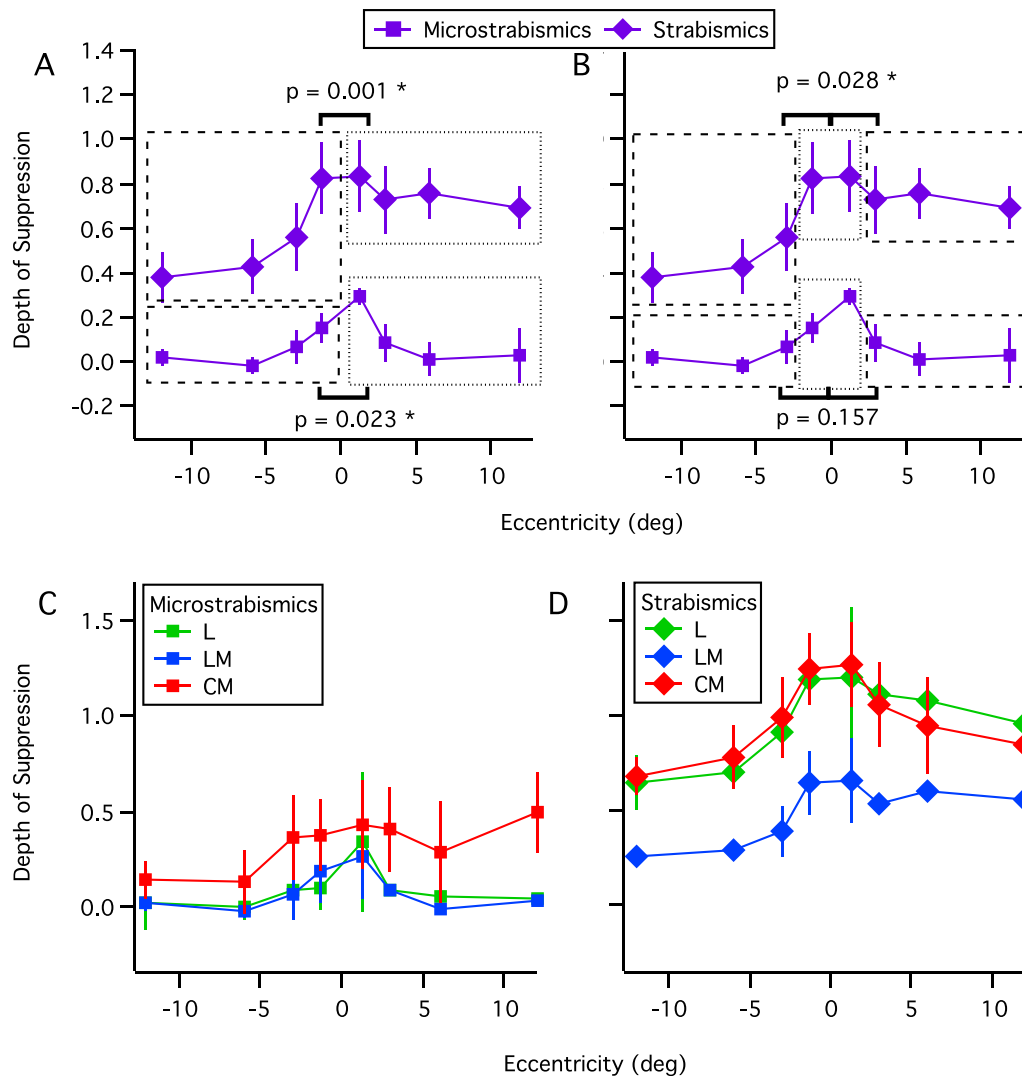


Figure 5. (A) and (B) show the same plots of suppression across eccentricity averaged across all stimulus types for microstrabismics (small squares) and strabismics (large diamonds). (A) significant ( $p$  values with asterisks) differences between one hemifield (dashed box) and the other (dotted box). (B)  $p$  values for central (dotted box) compared with peripheral (dashed box) sectors. (C) and (D) show data for individual stimulus types for microstrabismic and strabismic observers, respectively. Error bars show  $\pm 1$  SE.

$= 0.007$ . Previous investigators have described hemifield and central patterns of suppression in strabismic participants (Travers, 1938; Irvine, 1948; Jampolsky, 1955; Herzau, 1980; Sireteanu et al., 1981), or only a central suppression pattern in microstrabismic participants (Sireteanu et al., 1981; Hallden, 1982; Mehdorn, 1989; Babu et al., 2013). This gives a sound *a priori* basis for the statistical investigation of simple effects across eccentricity for each group.

The effects of eccentricity (averaged across stimulus type) for each participant group are summarized in Figure 5. Suppression values averaged across the four orientations are taken at each eccentricity, as there is no significant effect of orientation on depth of measured suppression,  $F(1.43, 14.32) = 3.12$ ,  $p = 0.078$ .

Testing across eccentricity in the microstrabismic group shows significant hemifield suppression,  $F(1, 10) = 7.13$ ,  $p = 0.023$  (Figure 5A), but no significant central suppression. The section below looking more closely at the effect of noise on suppression with L and LM stimuli (see Figure 8A) shows significantly deeper suppression in the central two, compared to all other sectors,  $F(1, 10) = 5.56$ ,  $p = 0.040$ . For CM stimuli only, significant hemifield suppression is found in microstrabismics,  $F(1, 10) = 8.24$ ,  $p = 0.017$ . Measured CM suppression for microstrabismics is also spread over a larger central area than for L or LM stimuli (Figure 5C).

For the strabismic group, Figure 5A shows significantly deeper suppression in one hemifield than the

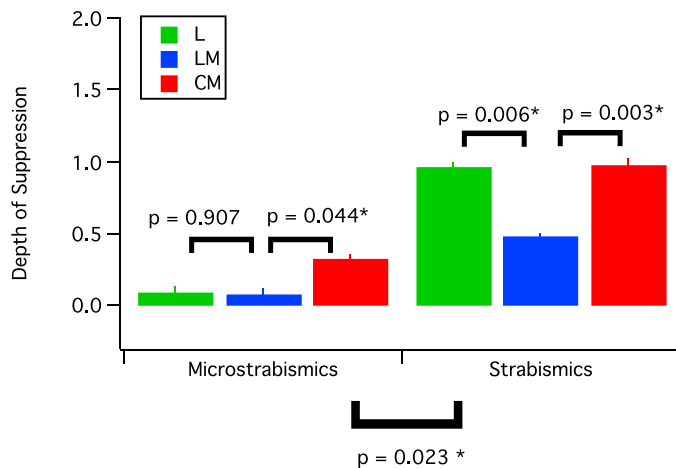


Figure 6. Suppression depth averaged across all stimulus types within microstrabismic and strabismic participant groups. The  $p$  values describe whether or not differences were significant between stimulus types within groups, and also between groups (below abscissa). Error bars show  $\pm 1$  SE.

other,  $F(1, 10) = 23.06$ ,  $p = 0.001$ , and statistically deeper central suppression,  $F(1, 10) = 6.54$ ,  $p = 0.028$  (Figure 5B). These patterns are consistent for all stimulus types (Figure 5D). The depth of suppression measured however, is significantly lower when dynamic noise is added to L stimuli (L vs. LM) for the strabismic group,  $F(1, 10) = 11.82$ ,  $p = 0.006$ , but not for the microstrabismic group,  $F(1, 10) = 0.014$ ,  $p = 0.907$ .

Individual suppression maps within the strabismic group show localized suppression agreeing with results from previous studies (i.e., extending from the strabismic eye's central visual field to the point in the amblyopic eye visual field corresponding to the non-strabismic eye's fovea; Harms, 1937; Travers, 1938; Jampolsky, 1955; Herzau, 1980; Sireteanu & Fronius, 1981; Sireteanu et al., 1981). Only one observer (CMc) showed a slightly deeper left than right hemifield suppression, likely to reflect the ocular misalignment prior to her strabismus surgery (see Table 1).

### The effect of stimulus type on measurement of suppression

Figure 6 illustrates suppression values (averaged across all sectors) for each stimulus type for the two binocularly abnormal groups. For the microstrabismic group, suppression measured using L and LM stimuli is mild and very similar, whereas suppression measured using CM stimuli is significantly deeper than that found when using LM stimuli,  $F(1, 10) = 5.32$ ,  $p = 0.044$ . For the strabismic group, suppression is significantly reduced when measured using LM, compared to L

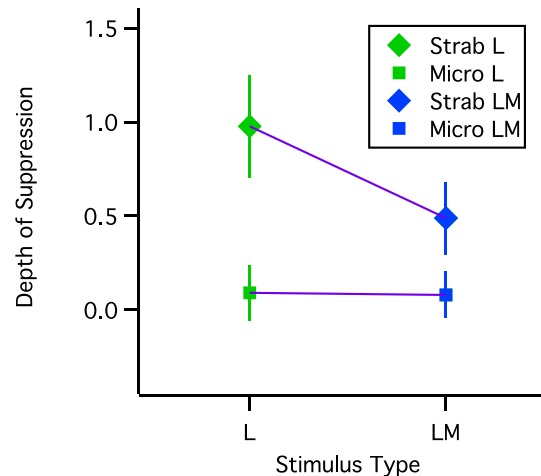


Figure 7. Suppression depth averaged across all sectors for each stimulus type, plotted for microstrabimics ("micro") and strabimics ("strab"). Error bars show  $\pm 1$  SD across all sectors.

stimuli,  $F(1, 10) = 11.82$ ,  $p = 0.006$ , suggesting that the addition of noise reduces suppression in these participants. In strabismic participants, suppression measured with CM stimuli is significantly deeper than that measured with LM stimuli,  $F(1, 10) = 15.76$ ,  $p = 0.003$ , both types of stimulus containing similar dynamic noise.

### The effect of noise and modulation polarity on L stimuli suppression for different participant groups

To enable comparison across the three stimulus types above, results obtained for 32 CM sectors were compared against 32 L and LM sectors, created by combining pairs of sectors. In the present section, suppression measured for L and LM stimuli only are examined, using all 64 sectors available, to give a more complete analysis of the effects that adding dynamic noise has on suppression measurement.

A mixed-design repeated measures ANOVA was again performed across participant group (three levels: normal, microstrabismic, and strabismic), with within-subjects factors of stimulus type (two levels: L and LM), orientation (four levels; see Figure 2), and eccentricity (16 levels). The effects described above are essentially reinforced. That is, there is a significant overall effect of eccentricity,  $F(2.92, 29.25) = 4.71$ ,  $p = 0.009$ ; a significant difference between strabismic and microstrabismic participant groups,  $F(2, 10) = 6.10$ ,  $p = 0.019$ ; and a near-significant interaction between stimulus type and participant group,  $F(2, 10) = 3.85$ ,  $p = 0.057$ . Figure 7 shows that adding noise reduces measured suppression for the strabismic group,  $F(1, 10) = 11.82$ ,  $p = 0.006$ , but has little effect on measured

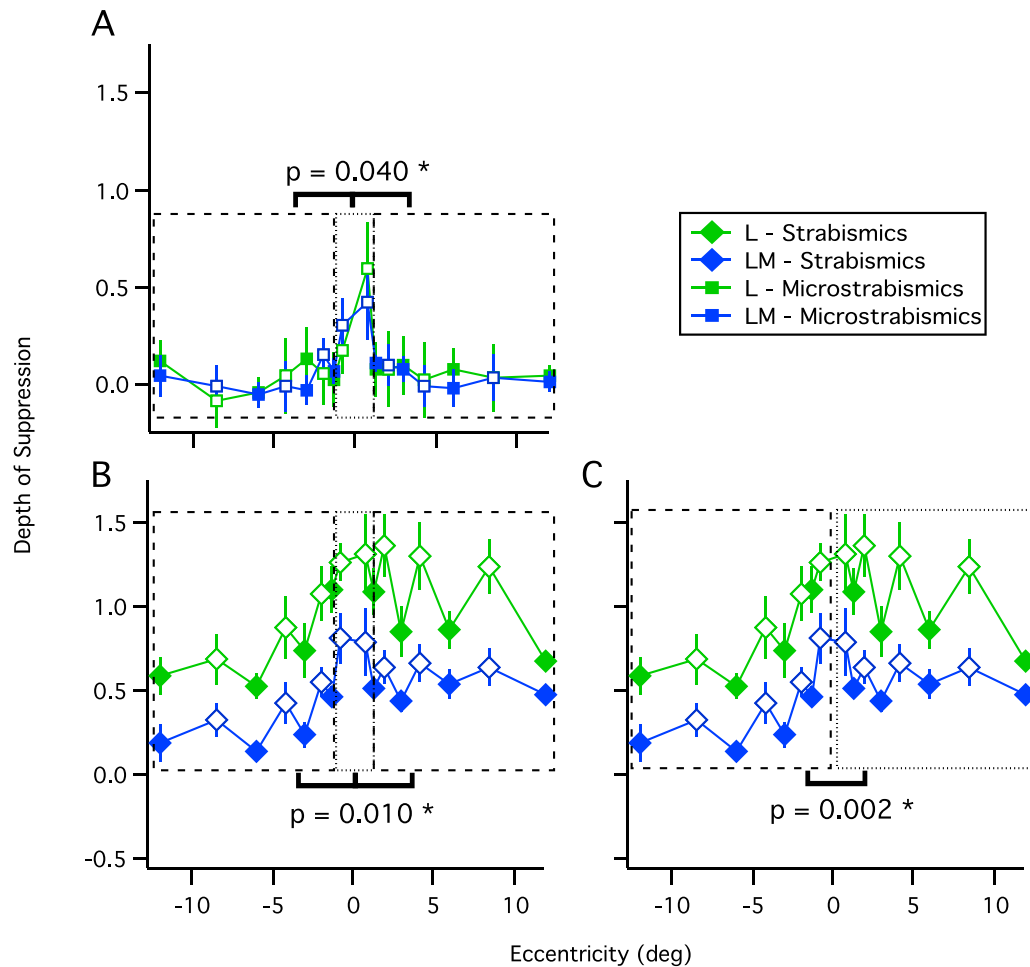


Figure 8. Suppression depth across eccentricity for L (green) and LM (blue) stimuli for (A) microstrabismics (small squares) showing significantly (asterisk) deeper central (dotted box) suppression compared with peripheral sectors (dashed box). Both (B) and (C) show significant central and hemifield (respectively) suppression for strabismics (large diamonds). Open symbols and closed symbols represent modulation increment and decrement sectors, respectively. Error bars show  $\pm 1$  SE.

suppression for the microstrabismic group,  $F(1, 10) = 0.014$ ,  $p = 0.907$ .

Eccentricity effects for the full 64 sectors using L and LM stimuli are described in Figure 8. Figure 8A depicts significant central suppression measured for microstrabismics,  $F(1, 10) = 5.56$ ,  $p = 0.040$ . Figure 8B and C, respectively, show that for strabismics, measured suppression is deeper in the central, than peripheral visual field,  $F(1, 10) = 5.15$ ,  $p = 0.047$ , and also deeper in one hemifield than the other,  $F(1, 10) = 25.64$ ,  $p < 0.001$ .

This analysis also reveals a difference between eccentricity effects for strabismic and microstrabismic groups not revealed by analysis of the 32 averaged sectors in Figure 5. Figure 8B and C show significant effects of luminance polarity on measured suppression values only for the strabismic group,  $F(1, 10) = 8.81$ ,  $p = 0.014$ . Note the zig-zag suppression patterns, which arise from stronger suppression measured of luminance modulation increment (white) than luminance modulation decrement (black) stimulus rings. No significant effect of sector polarity is found for the microstrabismic group,  $F(1, 10) = 0.77$ ,  $p = 0.400$ .

lution decrement (black) stimulus rings. No significant effect of sector polarity is found for the microstrabismic group,  $F(1, 10) = 0.77$ ,  $p = 0.400$ .

### LM versus CM stimulus suppression

Finally, do CM stimuli provide a more sensitive test for suppression than LM stimuli in participants with abnormal binocular vision? Figure 5C and D shows that measured suppression is deeper at all eccentricities with CM (red) compared to LM (blue) stimuli (both with dynamic noise) for microstrabismics and strabismics, respectively. This result is confirmed statistically when the average of all LM and all CM sectors are compared for both microstrabismics and strabismics (compare blue and red bars for LM and CM stimuli in Figure 6). This suggests that for mild anomalies of binocular vision, CM stimuli would reveal greater levels of suppression.

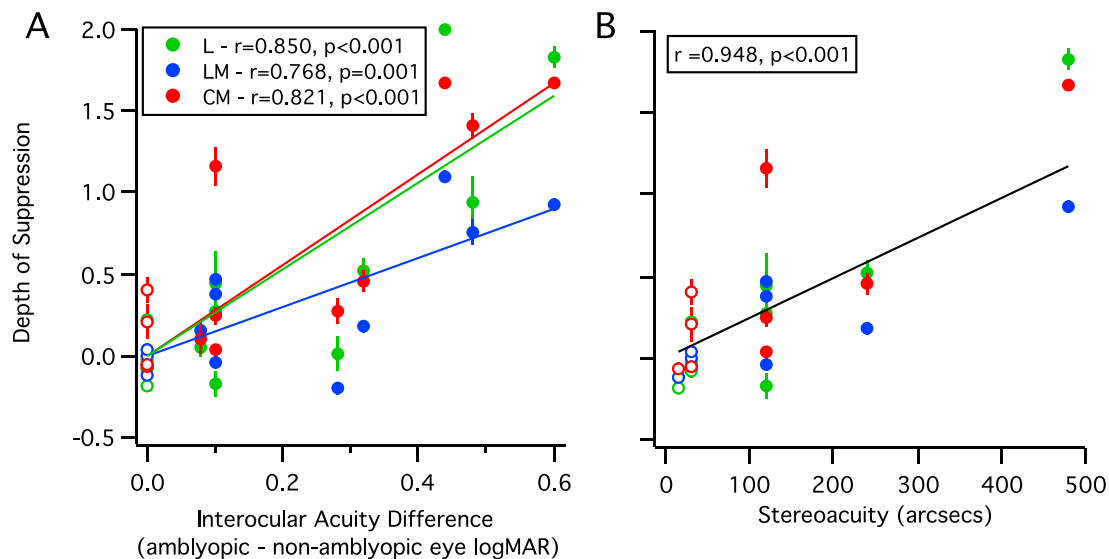


Figure 9. Suppression depth (averaged across all sectors for each participant) plotted against interocular logMAR visual acuity difference for (A) L, LM, and CM stimuli. Legends show Pearson's correlation coefficient ( $r$ ) with significance values for each stimulus type. (B) Depth of suppression against stereoacuity, measured with the Toegepast Natuurwetenschappelijk Onderzoek (TNO) stereotest. The slope is fit to average of L and LM (first-order) stimuli data, as stereoacuity is also measured with first-order stimuli. Open symbols represent data from binocularly normal observers. All error bars show  $\pm 1$  SE of the mean.

An alternative way to indicate sensitivity would be to examine slopes of depth of suppression measured for each stimulus type versus degree of binocular anomaly. A steeper slope would indicate higher sensitivity to change in suppression depth with treatment, or with disease progression. In Figure 9A average suppression depth (averaged across all central sectors for CM, and across central two rings for L and LM, thus covering the same area of the visual field) for each individual participant is plotted against interocular visual acuity difference using standard clinical acuities.

Referring to Figure 9A, significant positive correlations exist between depth of suppression and interocular visual acuity difference for L ( $r = 0.850$ ,  $p < 0.001$ ) and LM ( $r = 0.768$ ,  $p = 0.001$ ) stimuli. Slopes are significantly steeper for L than LM stimuli (L slope value  $2.65 \pm 0.39$ , compared to LM slope value of  $1.49 \pm 0.27$ ;  $p < 0.001$ ). This result suggests that suppression measured using L stimuli would be more sensitive to changes in binocularity if a suitable starting measure can be made. If suppression is too deep to obtain a reliable measure with L stimuli, LM stimuli may be more suitable, such as in deep amblyopia.

When comparing the two dynamic noise stimuli (LM and CM) for measurements of suppression, CM slopes are significantly steeper (LM:  $1.49 \pm 0.27$ , CM:  $2.77 \pm 0.38$ ;  $p = 0.002$ ), indicating that suppression measured using CM stimuli is significantly more sensitive to change. Suppression is also consistently deeper at all interocular acuity differences when measured with CM than LM stimuli. As the use of CM results in a deeper suppression measure than LM stimuli, CM stimuli

would be particularly useful for measuring suppression in microstrabismics (see Figure 5B). Again, suppression depth is significantly positively correlated with interocular visual acuity difference for LM ( $r = 0.768$ ,  $p = 0.001$ ) and CM ( $r = 0.821$ ,  $p < 0.001$ ) stimuli.

Figure 9B shows data for depth of suppression data for L, LM, and CM stimuli plotted against those participants for whom stereoacuity could be measured (i.e., four binocularly normal and for five of the nine binocularly abnormal). As stereoacuity was measured using only first-order stimuli, averaged suppression values for L and LM stimuli only were compared with clinical random dot stereoacuity values. A strong positive correlation ( $r = 0.948$ ,  $p < 0.001$ ) is found.

## Discussion

In this study, suppression is found in localized areas within the central  $24^\circ$  of visual field for adult participants with abnormal binocular vision. Careful alignment of the stimuli for each participant, along with highly visible blind spot markers, enabled presentation of our stimuli to localized regions of the visual field. That localized regions of suppression were indeed measured suggests that fixation was maintained. In addition, when actual eye movement recording for one participant (AH) was conducted, the main findings were replicated. As in previous studies, noiseless L stimuli have been used. In addition, the present study uses LM and CM stimuli to assess suppression. The

novel method outlined in the present study as well as previous studies (Babu et al., 2013; Chima et al., 2015) has the advantage of presenting similar stimuli to corresponding retinal points, which elicits strongest suppression (Schor, 1977; Kilwinger et al., 2002), as opposed to some current clinical measures such as the Worth 4-dot test and Sbisá Bar assessment that use strongly dissociative measures.

## The extent of microstrabismic and strabismic suppression

In the present study, strabismics show deep central and also hemifield suppression. Previous investigators who used standard L stimuli have also reported scotomata extending from the strabismic eye's central visual field to the point in the amblyopic eye visual field corresponding to the nonstrabismic eye's fovea (Harms, 1937; Travers, 1938; Jampolsky, 1955; Herzau, 1980; Sireteanu & Fronius, 1981; Sireteanu et al., 1981). Studies that do not correct for the ocular deviation (Harms, 1937; Campos, 1982; Hallden, 1982; Gottlob et al., 1992), thereby not stimulating corresponding retinal points, have reported only central suppression. Presenting similar stimuli to corresponding retinal points, Babu et al. (2013) also reported central symmetric suppression for all participants (four microstrabismics, six strabismics, and six anisometropes), despite their correction of strabismus. However, asymmetry across the visual field may have been uncovered for the strabismics in that study, if individual suppression maps had been aligned and analyzed in a similar way to the current study.

Microstrabismic suppression is significantly shallower than that measured for strabismic participants. When using L and LM stimuli, suppression is localized to the very central sectors (within  $0.75^\circ$  from the fovea; see Figure 8A), with none seen outside of this area. This is in agreement with findings of other studies (Sireteanu & Fronius, 1981; Sireteanu et al. 1981; Hallden, 1982). In contrast, Mehdorn (1989), using phase-difference haploscopy, found no suppression in microstrabismics, attributing this lack of measured suppression to the adaptation mechanism of harmonious abnormal retinal correspondence (hARC). Joosse et al. (1997) also found no suppression in microstrabismics (defined as less than  $8^\circ$  or 14 prism diopters deviation). However in their study, monocular detection thresholds during binocular viewing were measured across the visual field. Suppression of the true fovea in this condition would still be highly favorable to prevent diplopia. We believe that the suprathreshold interocular contrast-matching task used in the present experiment is more akin to how information from the eyes is combined in real world circumstances.

## The effect of adding noise to L stimuli

Suppression depth in strabismic participants is lower when measured in the presence of dynamic noise (i.e., for LM versus L stimuli). Thus LM stimuli may be valuable when assessing suppression in patients with deep amblyopia, bringing it into the measurable range and revealing patterns across the visual field. These findings are reinforced by examining individual suppression plots of participants with large interocular acuity differences (e.g., CMc in Figure A3 and JB in Figure A4). In a previous study in binocularly normal participants with imposed interocular blur, suppression was also deeper for L than LM stimuli (Chima et al., 2015). Dynamic noise may introduce temporal transients as does the introduction of motion or flicker, which clinically have been found to break down suppression in amblyopia (e.g., Scheiman & Wick, 2008), perhaps in a similar way to continuous flash suppression (Wolfe, 1986; Tsuchiya & Koch, 2005; Yang & Blake, 2012).

Strabismic but not microstrabismic suppression is reduced with the addition of dynamic noise. Adding stimulus noise to strabismic amblyopic eyes where internal noise is greater than in normal eyes (Levi & Klein, 2003; Baker, Meese, & Hess, 2008) would result in less of a difference between eyes for LM than for L stimuli. In microstrabismus, the noise was likely to be above internal noise for both eyes, resulting in minimal difference in measured suppression.

An unexpected finding is that strabismic suppression of L (and to a lesser degree LM) incremental sectors is deeper than for decremental sectors (see Figure 8B). Some observers in Babu et al.'s (2013) study also showed deeper suppression for increment than decrement L stimuli. This polarity asymmetry of suppression does not occur for CM stimuli, where the mean luminance is unchanged across rings or in microstrabismic participants. In a luminance contrast discrimination task, Zele, Wood, and Girgenti (2010) found that amblyopes have better decrement than increment discriminability. Similar effects have also been observed in normal participants for a range of first- and second-order stimuli (Lu & Sperling, 2012). More sensitive perception of decrements compared to increments in the amblyopic eye, combined with local visual field adaptation (e.g., Peli, 1990; McIlhagga & Peterson, 2006), could account for shallower measures of suppression for decremental than incremental sectors. A statistically significant asymmetry was not found in either binocularly normal or microstrabismic observers, which suggests that luminance-polarity dependant suppression is a feature associated with greater degrees of amblyopia or with greater depths of measurable suppression.

## Suppression depth and clinical findings

Larger interocular differences in visual acuity correlate positively with deeper measures of interocular suppression (Figure 9A), agreeing with the results of previous studies (Sireteanu & Fronius, 1981; Agrawal et al., 2006; Li et al., 2011; Narasimhan et al., 2012; Li et al., 2013). This significant correlation in amblyopia does not prove a causal relationship, however present results are not in line with a previous suggestion that weak suppression is required to prevent diplopia in deep amblyopia (Holopigian et al., 1988). Recent models suggest an imbalance in inhibitory and excitatory interactions between amblyopic and non-amblyopic eyes (e.g., Meese et al., 2006; Ding et al., 2013). In these models, deeper amblyopia is associated with a greater imbalance in interocular interactions. Specifically, the more inhibition is exerted on the weaker eye, the stronger the difference between the eyes. The stronger eye dominates perception until the signal strength from the weaker eye is increased, so that the signal from each eye contributes equally to perception. In the present study we demonstrate that this can occur in specific areas of the visual field. Further agreement with this model is evidenced with the strong correlation between increased depth of suppression and decreased stereo-acuity (Figure 9B). A similar but weaker relationship was found in amblyopes for an interocular global motion task (Li et al., 2011). Thus a greater imbalance between the eyes increases chances of suppression and decreases chances for fine fusion of spatial images.

## LM and CM stimuli suppression

The present study is the first to compare depth and extent of amblyopic suppression in response to LM and CM stimuli. For all but one participant (AR), suppression was deeper with CM compared with LM stimuli. Use of CM stimuli has advantages as it provides a more sensitive method to detect suppression in suspected amblyopes, and is not vulnerable to differential increment versus decrement suppression measures found for L or LM stimuli.

Although in this study the sector sizes differed, depending on whether LM or CM stimuli were used, in normal observers with imposed interocular blur this difference did not affect measured suppression depth (Chima et al., 2015). Also in this study, LM and CM noise amplitudes chosen were set at 0.25 and 0.50, respectively. With imposed interocular blur in normal vision, measured suppression decreased as LM noise amplitude increased, as did visibility (as measured by multiples above detection threshold; Chima et al., 2015). If that result holds in strabismic participants, the

differences found between LM and CM suppression measures would still exist.

What causes deeper interocular suppression to exist in response to CM than LM stimuli? Data from a previous human fMRI study (Larsson, Landy, & Heeger, 2006), and electrophysiological studies on cat (Mareschal & Baker, 1998) and monkey (Baker et al., 2013; Li et al., 2014), show greater activity in V2 when perceiving CM, than LM stimuli, implicating V2 as a site for early stages of CM processing. Neurons in V2 are predominantly binocular and show reduced activation to strabismic eyes of monkey (Bi et al., 2011). Deeper measured suppression may mean that a greater signal increase in the amblyopic eye is required to achieve balanced binocular input for CM than for LM stimuli. This is in agreement with Zhou, Huang, and Hess (2013), who suggested that there are greater extrastriate, than striate deficits in amblyopia. Furthermore, stimulus visibility differences are not able to explain interocular blur suppression differences in response to LM and CM stimuli in binocularly normal observers (Chima et al., 2015).

Microstrabismic suppression of LM stimuli was central, but changed to a more widespread hemispheric pattern when measured using CM stimuli. If CM stimuli are processed in cortical areas after binocular combination, perception of each eye's CM image may be more broadly affected due to binocular disruption. The deeper CM suppression in both strabismic and microstrabismic participants could be explained in this way. Suppression of CM stimuli involves larger central regions than LM stimuli, possibly due to CM stimulus extraction occurring in extrastriate areas with larger receptive fields (e.g., V2; Gattass, Gross, & Sandell, 1981; Foster, Gaska, Nagler, & Pollen, 1985; Kennedy, Martin, Orban, & Whitteridge, 1985; Gattass, Sousa, & Gross, 1988) than those found in V1.

Strabismic suppression patterns for L, LM, and CM stimuli differ only in depth, with general hemispheric and central regions of suppression evident for all stimuli. Microstrabismic suppression patterns are predominantly very central; however, with CM stimuli, some hemispheric suppression is revealed. These findings may be consistent with physiological differences in which primary strabismus involves deficits at higher neural levels than does primary microstrabismus, reinforcing the idea that microstrabismus and strabismus are separate clinical entities (e.g., Helveston & von Noorden, 1967; Lang, 1974). Patients with microstrabismus have smaller interocular visual acuity differences and better disparity processing (as indicated by better performance on random dot stereo tests) than do patients with larger angles of strabismus (see Table 1). Visual deficits in strabismics are much more pronounced, and stereopsis is also severely affected.

## Conclusion

Distinct patterns of interocular suppression exist in those with abnormal binocular vision due to strabismus and microstrabismus. Participants with strabismus show central and asymmetric hemispheric suppression. Microstrabismics show central suppression, although if CM (second-order) stimuli are used, suppression can be more widespread, asymmetric, and deeper. When interocular visual acuity difference is greater, the addition of dynamic binary noise reduces measures of suppression, making it useful for quantifying deeper suppression. Microstrabismic suppression is less extensive and weaker than that found in strabismic participants. The use of CM stimuli allows for more sensitive detection of suppression in mild amblyopes or potentially in those with amblyogenic factors (i.e., disturbances to binocularity processing). Depth of suppression is correlated positively with interocular difference in visual acuity and with decreasing stereoacuity. Our results using binocularly abnormal participants are consistent with those that suggest that early stages of processing of CM stimuli involve regions of predominantly binocular input.

**Keywords:** *amblyopia, strabismus, microstrabismus, suppression, contrast-modulated*

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## Appendix

### Strabismic suppression maps

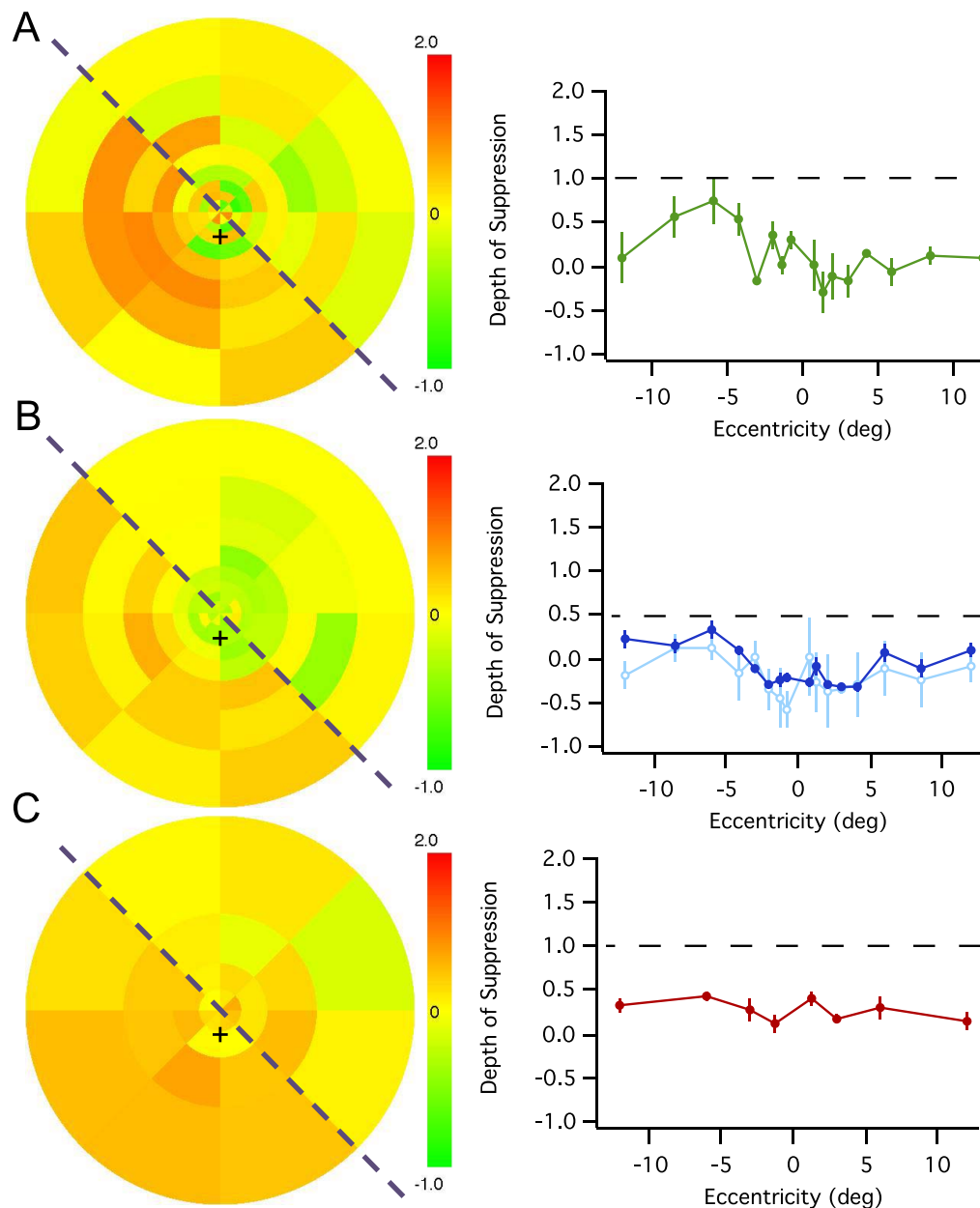


Figure A1. Data for participant AH, an exotrope with anisometropia. Visual acuity: R 0.25, L  $-0.04$  logMAR. Colored suppression maps are shown in the left column (details as described in Figure 2). Dashed lines indicate the hemifields used for statistical analysis. The black cross denotes location of the suppressing eye's fovea. The right column shows suppression averaged within the indicated hemifield, across eccentricity. (A), (B), and (C) depict maps obtained for L, LM, and CM stimuli, respectively. Black dashed lines in right column for maximum adjustable suppression. (B) also shows results of a control experiment where fixation was monitored (open light blue symbols), giving similar results to the main experiment. Error bars show  $\pm 1$  SE across four orientations, except for control experiment data averaged over two orientations.

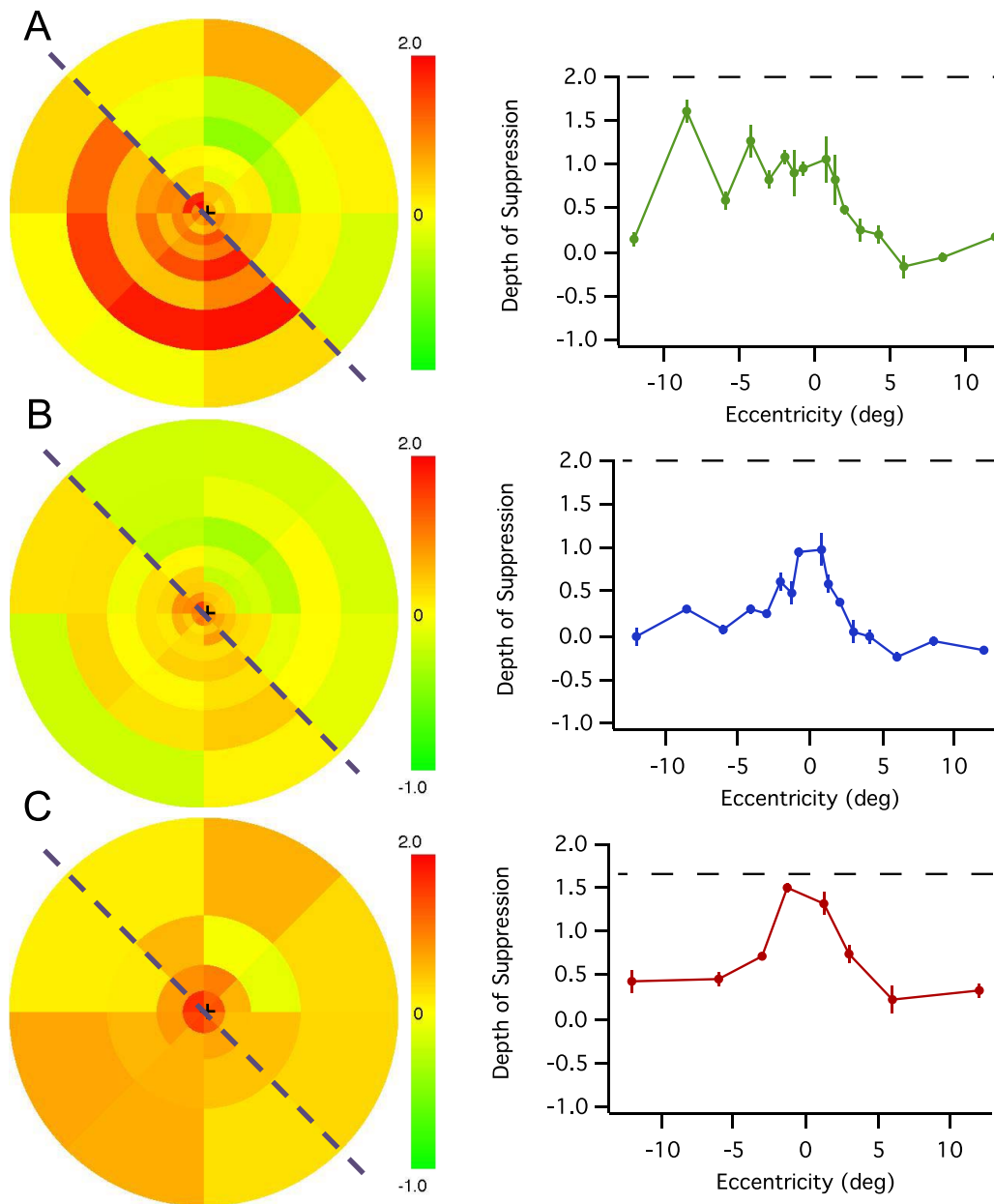


Figure A2. Participant CMA has a constant left esotropia. Visual acuity R  $-0.08$ , L  $0.4$  logMAR. The right column shows suppression averaged within the indicated hemifield, across eccentricity. All other details as in previous Figure.

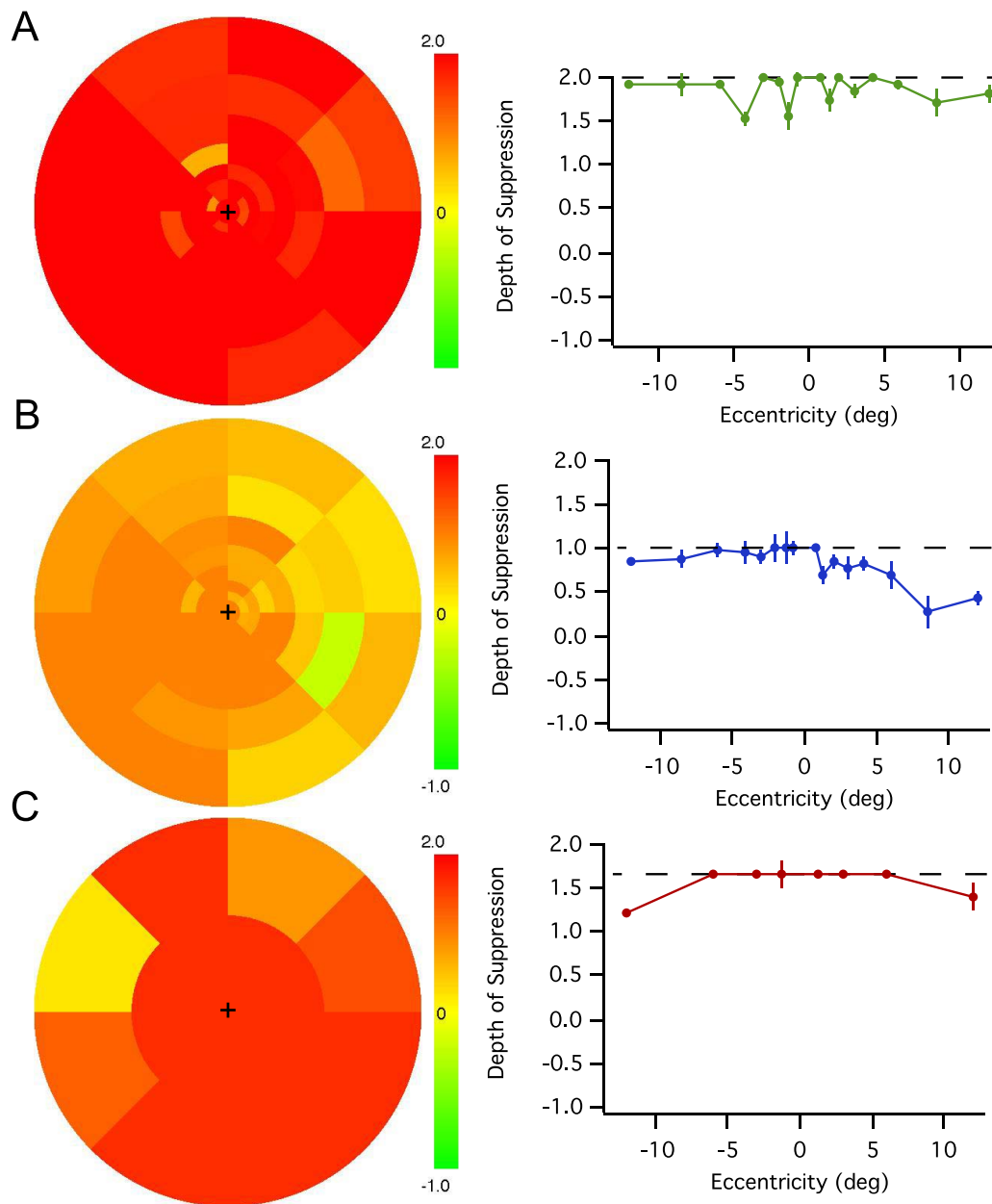


Figure A3. Participant CMc has a consecutive left exotropia. Visual acuity R  $-0.06$ , L  $0.54$  logMAR. No rearrangement of hemispheres was performed for data analysis. All other details as in previous Figure.

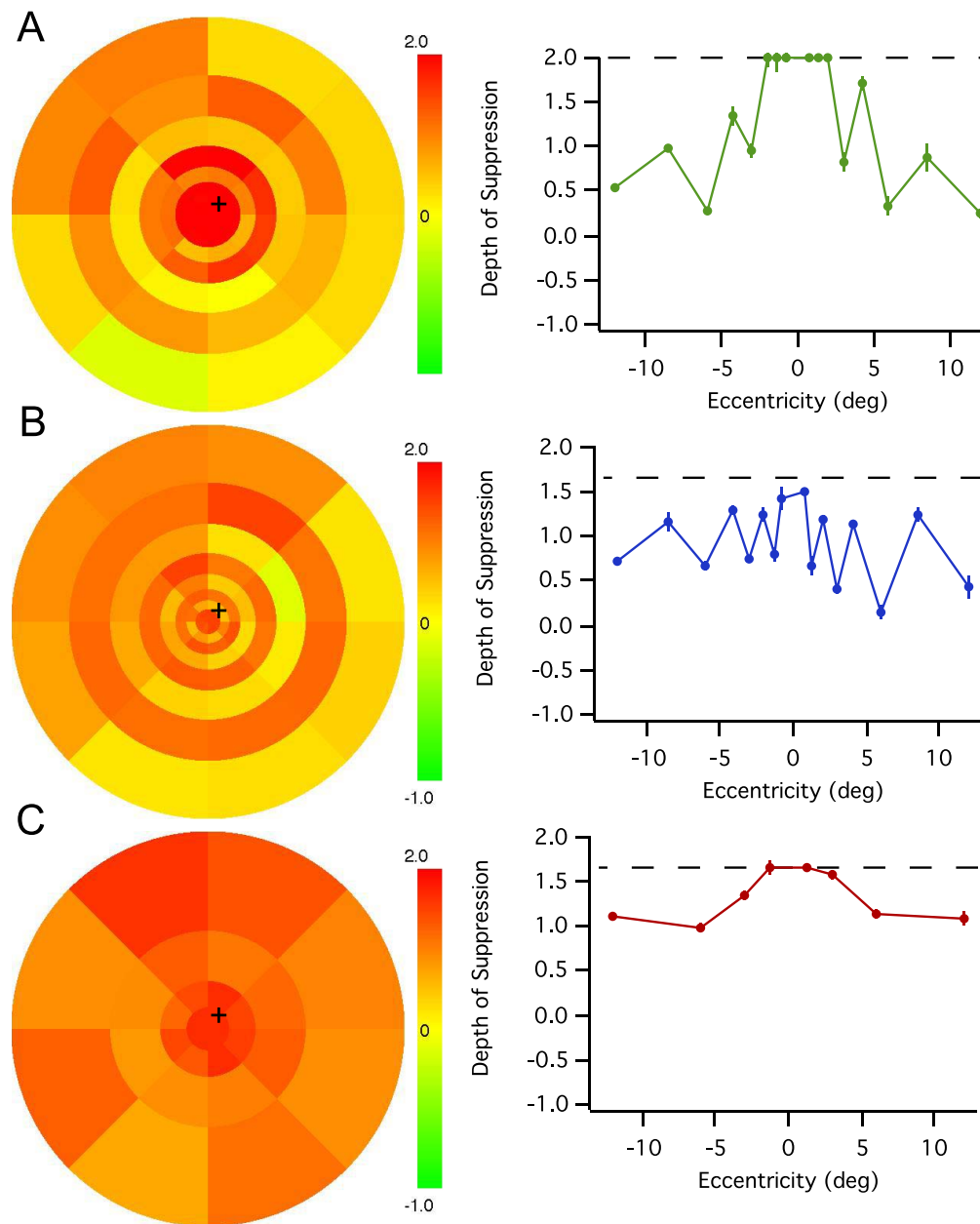


Figure A4. Participant JB is an anisometrope with a history of large-angle strabismus surgery. Visual acuity R 0.4, L  $-0.04$  logMAR. All other details as in previous Figure.

## Microstrabismic suppression maps

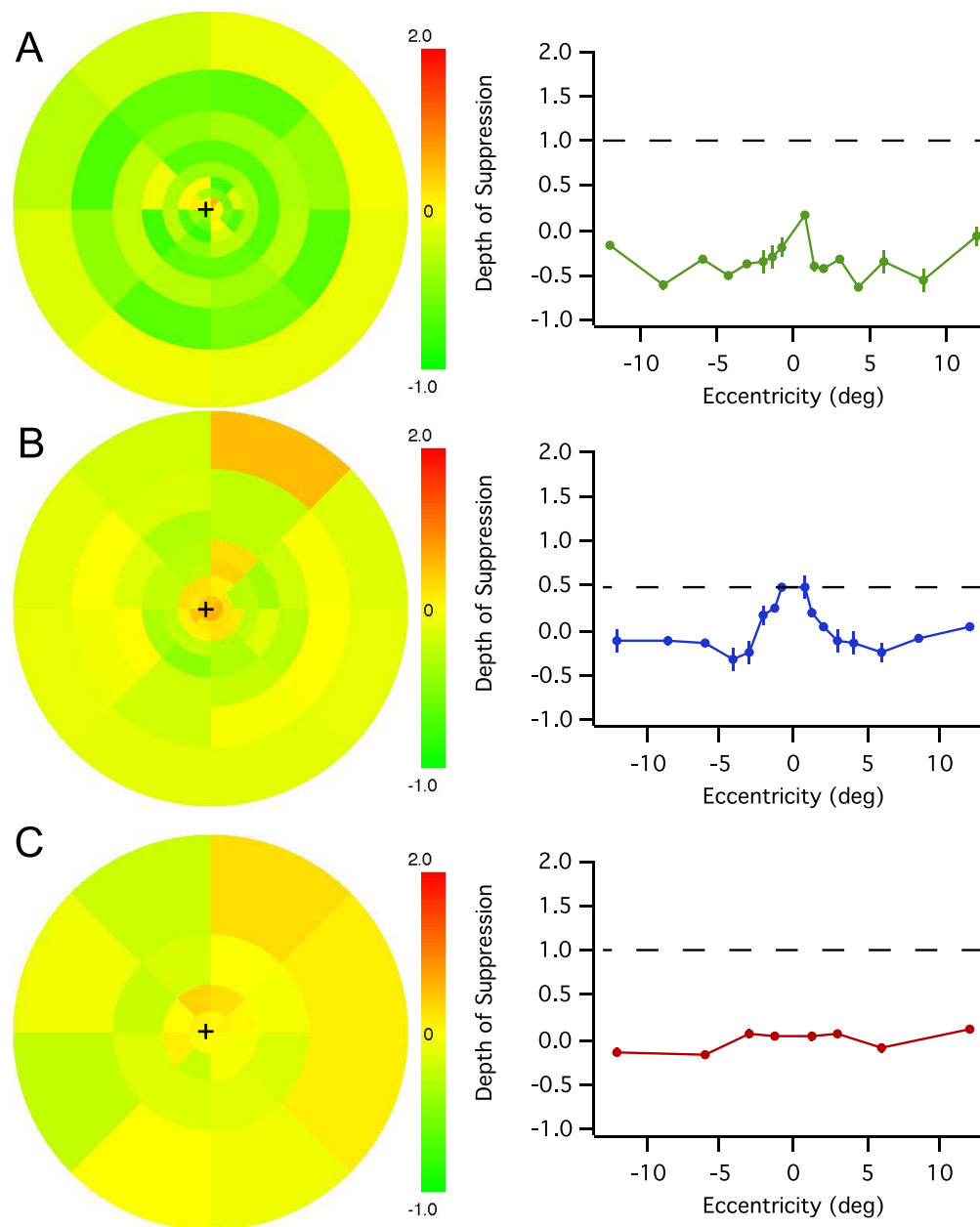


Figure A5. Participant AR has anisometropia with LE eccentric fixation and reduced stereoacuity ( $120''$ ). Visual acuity R  $-0.08$ , L  $0.02$  logMAR. All other details as in previous Figure.

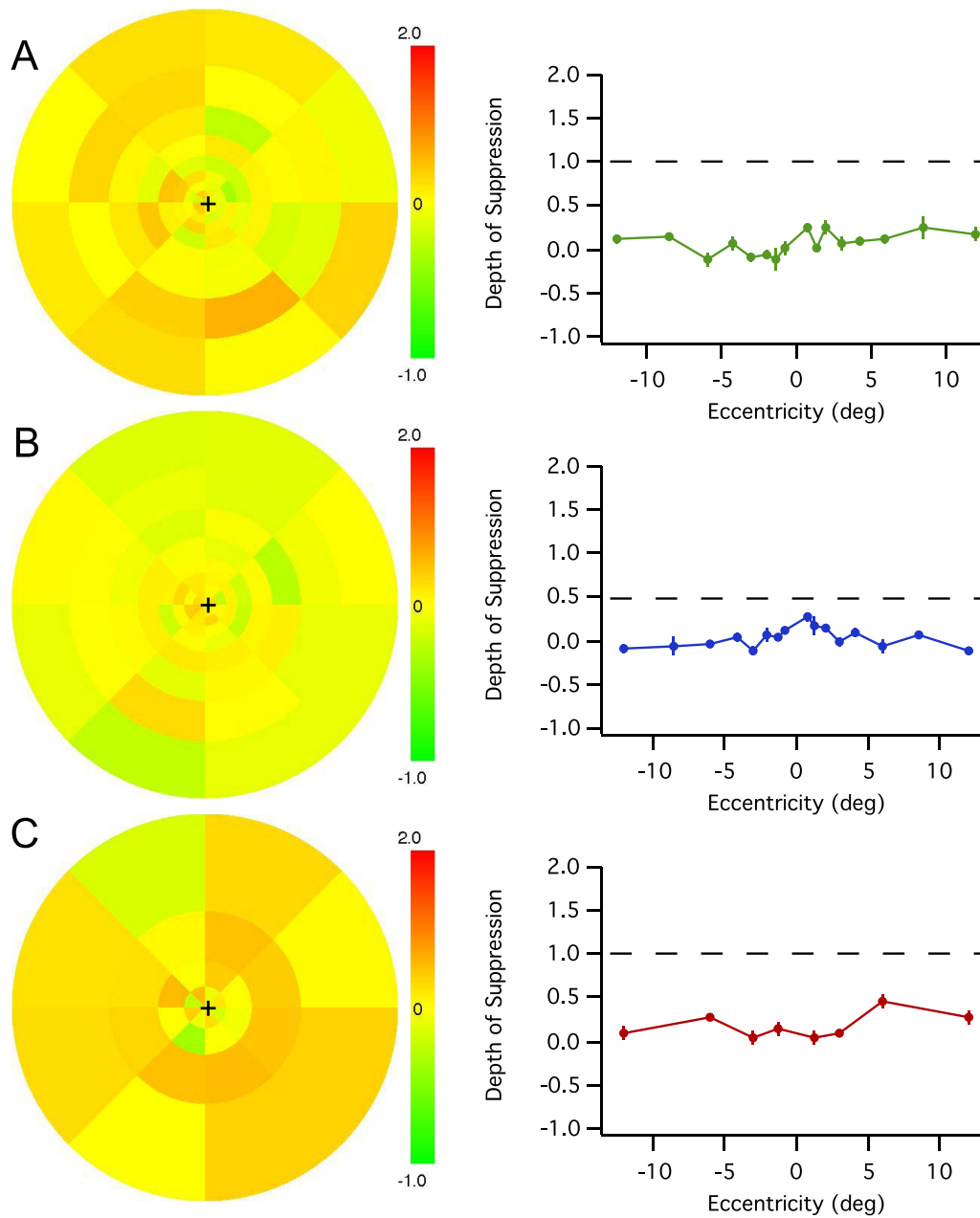


Figure A6. Participant AW has a constant manifest 6 prism dioptre left esotropia. Visual acuity R  $-0.16$ , L  $-0.06$  logMAR. All other details as in previous Figure.

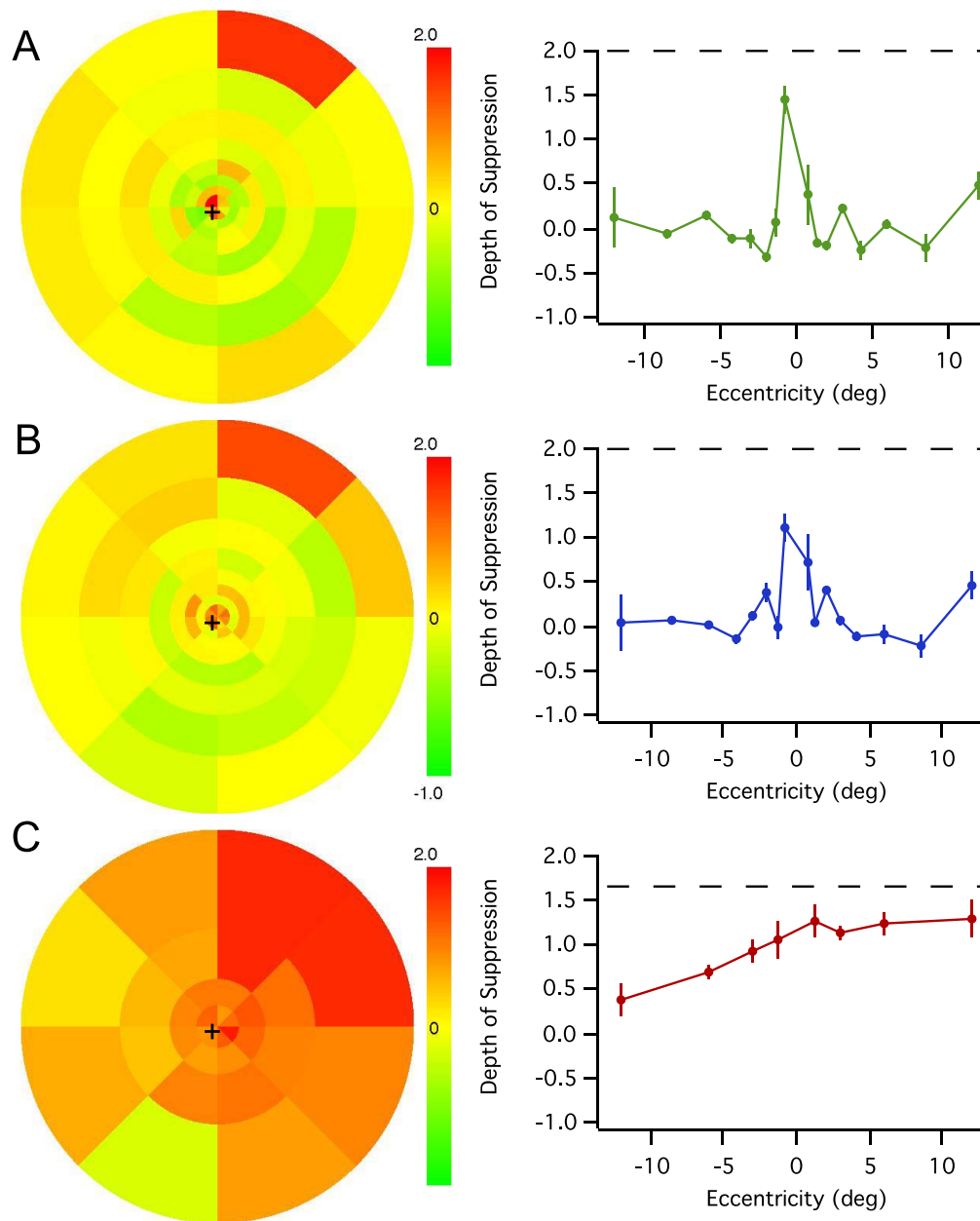


Figure A7. Participant DM has no manifest deviation, although has LE temporal eccentric fixation with reduced stereoacuity ( $120''$ ). Visual acuity R  $-0.16$ , L  $0.02$  logMAR. All other details as in previous Figure.

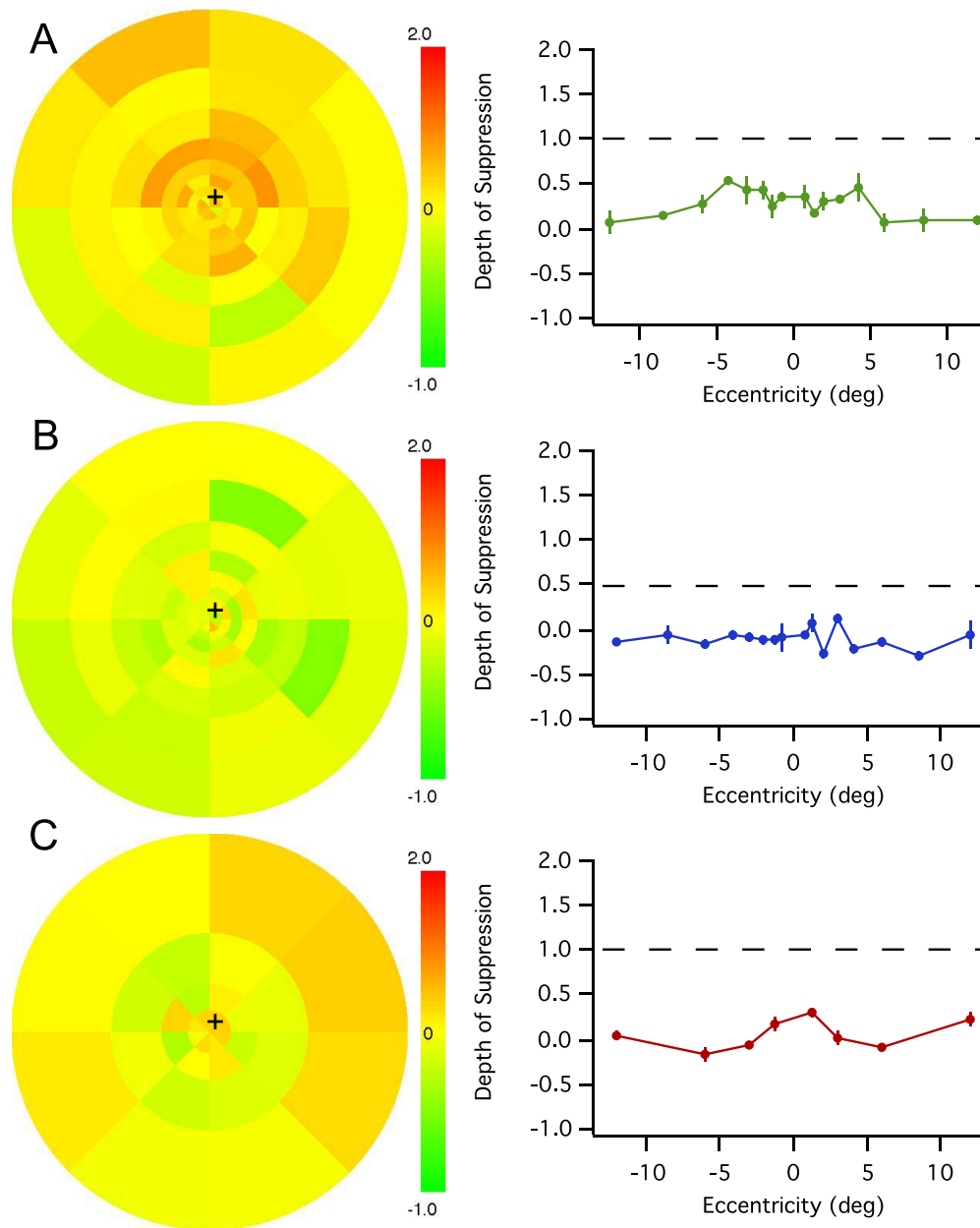


Figure A8. Participant IR is an anisometropes with reduced stereoacuity ( $120''$ ) with no manifest deviation, though had RE eccentric fixation. Visual acuity R 0.1, L 0.0 logMAR. All other details as in previous Figure.

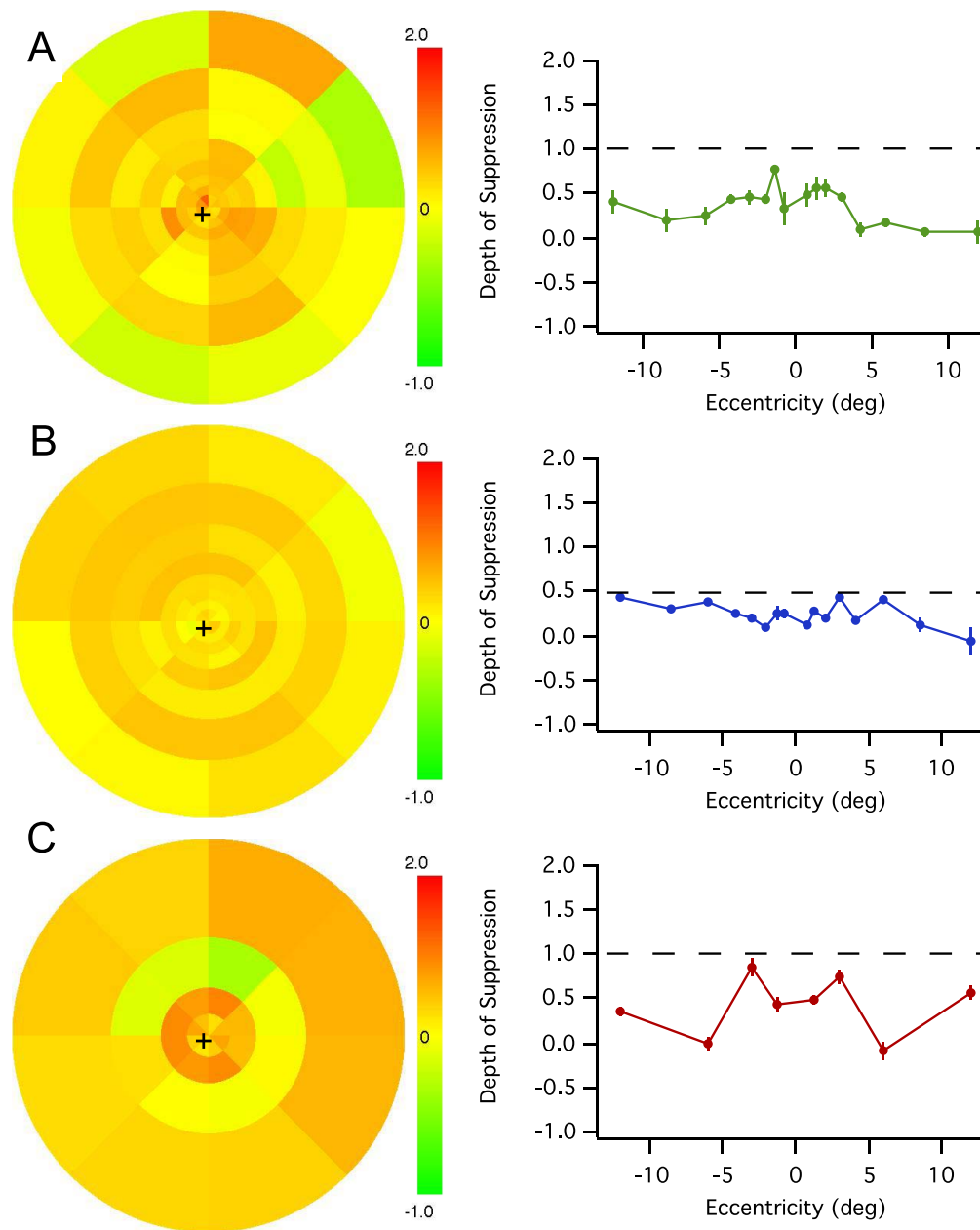


Figure A9. Participant NS has reduced stereoacuity (240'') with no manifest deviation with correction (20 prism diopter right esotropia without correction). Visual acuity R 0.12, L -0.20 logMAR. All other details as in previous Figure.