Multifaceted Interactions of Stereoacuity, Inter-Ocular Suppression, and Fixation Eye Movement Abnormalities in Amblyopia and Strabismus

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Purpose. Amblyopic and strabismus subjects experience inter-ocular suppression, impaired stereoacuity, and increased fixation instability. The purpose of the study was to investigate factors affecting suppression and stereoacuity and examine their relationship to fixation eye movement (FEM) abnormalities.

Methods. We recruited 14 controls and 46 amblyopic subjects (anisometropic = 18, strabismic = 14, and mixed = 14) and 11 subjects with strabismus without amblyopia. We utilized the dichoptic motion coherence test to quantify suppression, and stereoacuity was assessed using the Titmus Fly test. We recorded FEMs using high-resolution video-oculography and classified subjects that did not have nystagmus (n = 27) versus those with nystagmus (n = 32; fusion maldevelopment nystagmus [FMN], n = 10) and nystagmus that did not meet the criteria of FMN (n = 20). We also recorded FEMs under dichoptic viewing (DcV) at varied fellow eye (FE) contrasts and computed the amplitude and velocity of the fast and slow FEMs and vergence instability.

Results. Inter-ocular suppression and stereoacuity deficits were closely correlated with an amblyopic eye (AE), visual acuity, and strabismus angle. Subjects with nystagmus displayed more pronounced stereoacuity deficits than those without nystagmus. Strabismic subjects with and without amblyopia, who demonstrated a fixation switch at 100% FE contrast, had lower inter-ocular suppression than subjects lacking a fixation switch under DcV. Amplitude of fast FEMs and velocity of slow FEMs, and vergence instability were increased as the FE contrast was lowered in both amblyopic and strabismic subjects.

Conclusions. The current study highlights the intricate relationships between AE visual acuity, eye deviation, and FEM abnormalities on suppression and stereoacuity deficits and underscores the need to evaluate FEM abnormalities while assessing dichoptic treatment outcomes.

Keywords: amblyopia, strabismus, fixational eye movements (FEMs), suppression, stereoacuity

Amblyopia, a neurodevelopmental disorder, results from discordant binocular visual input in early life, often due to causes like anisometropia, strabismus, and visual deprivation. It is characterized by reduced visual acuity, typically in one eye, without ocular anomalies. Amblyopic and strabismus subjects, even without amblyopia, experience impaired binocular and inter-ocular visual functions, such as reduced depth perception (stereoacuity)[1] and inter-ocular suppression, where the contribution of a strabismic or amblyopic eye is limited during binocular viewing.[2–8] The pattern of visual function deficits in amblyopia is complex and not solely explained by its clinical type and severity.[9–13] The multifaceted nature of visual function deficits in amblyopia is highlighted by studies that show severe amblyopia is associated with more significant stereo-acuity deficits and inter-ocular suppression.[14–21] Interestingly, individuals with resolved visual acuity losses after patching or newer binocular treatments may still experience stereopsis deficits and inter-ocular suppression.[15,22–27]

Besides visual sensory functions, unstable fixation is seen in patients with amblyopia and strabismus.[28–33] Our investigations have revealed that the unstable fixation can be attributed to nystagmus, including fusion maldevelopment nystagmus, or due to alterations of physiologic involuntary fixation eye movements (FEMs).[5,31,32,34] FEM characteristics, along with the type of amblyopia, are associated with the specific pattern of monocular and binocular visual function deficits. For instance, strabismic/mixed amblyopia subjects with fusion maldevelopment nystagmus (FMN) are associated with greater fellow eye and binocular contrast sensitivity deficits.[35] Existing studies have revealed that individuals with strabismic/mixed amblyopia and nystagmus typically exhibit absent or poor stereopsis despite improvements in visual acuity following patching therapy. This includes individuals with treated amblyopia as well as those with no or

minimal strabismus after surgical repair.[34,36,37] However, the presence of nystagmus on inter-ocular suppression remains unclear.

Visual input and viewing conditions can affect FEMs.[38–40] FEM abnormalities in amblyopia correlate with the severity of visual acuity and stereo-acuity deficits.[32,35,41] We have previously examined FEMs under dichoptic viewing (DcV), where the fellow eye (FE) contrast is reduced while the amblyopic eye (AE) views a high contrast stimulus as used in newer binocular therapies that target inter-ocular suppression. We found that such a stimulus can result in a fixation switch where the AE is fixing on the target stimulus at low FE contrasts, further suggesting that this type of stimulus facilitates overcoming the suppression. We have also found increased fixation and vergence instability under DcV at low FE contrasts.[40] None of the studies to date have examined how changes in FEMs under DcV at varied FE contrasts correlate with inter-ocular suppression.

Our current study measured visual acuity and stereoacuity and quantified inter-ocular suppression through a psychophysical dichoptic motion coherence test.[19,25] This test involves contrast rebalancing to present full contrast signal dots to the AE while varying the contrast of noise dots to the FE, facilitating binocular combination. The degree of contrast imbalance needed for balanced performance serves as a quantifiable measure of the degree of suppression as well as the severity of amblyopia.[19] We evaluated FEMs for the presence of nystagmus and recorded FEMs under DcV at varied FE contrasts. We hypothesize that inter-ocular suppression will be present in amblyopic and strabismic subjects, irrespective of the presence of nystagmus, and that the visual acuity deficit and strabismus angle will be the primary determinants of inter-ocular suppression deficits. We hypothesize that greater inter-ocular suppression will be associated with pronounced fast and slow FEM abnormalities and vergence instability under DcV. We also assessed the relationship between the fixation switch as the FE contrast is lowered with the measured inter-ocular suppression. We hypothesize that strabismic subjects who exhibit a fixation switch where the amblyopic or strabismic eye fixates on the target in a dichoptic environment with varied FE contrasts will experience less inter-ocular suppression.

Methods

The experiment protocols complied with the tenets of the Declaration of Helsinki and were approved by the Cleveland Clinic Institutional Review Board. Informed consent was obtained from the study participants/parents or legal guardians on behalf of the minors/children. We recruited 46 subjects with amblyopia, 11 with strabismus without amblyopia, and 14 healthy controls. All the subjects had a comprehensive eye examination. The clinical and demographic parameters were extracted from a retrospective chart review, including cycloplegic refraction and strabismus angle measurements at distance and near at the time of eye movement recordings.

Visual and Stereoacuity Measurements

Psykinematix (KyberVision) software was used to generate test stimuli, displayed on a monitor with a resolution of 2560 × 1600 at 60 Hz with a brightness of 350 cd/m^2 at a distance of 3.1 m in a dark room. Monocular distant visual acuity was assessed while the non-viewing eye was occluded. Subjects viewed one randomly selected Early Treatment Diabetic Retinopathy Study (ETDRS) optotype with crowding bars – the size in arcmin was adjusted using a psychophysical staircase procedure (2-down and 1-up staircase with a proportional step size reduction of 50% before the first reversal and 25% increments and 12.5% decrements thereafter) with a total of six reversals. The thresholds were taken to be the arithmetic mean of the reversals computed in arcmin and were converted into log MAR for statistical analysis.[42] The Titmus Stereoacuity Test was used to measure stereoacuity in log arcsec. Patients with no stereoacuity were assigned a value of 3.85 log arcsec. In our cohort, 32 subjects had some to poor stereopsis (stereoacuity defined as worse than 2 log arc seconds) and 39 subjects had good stereopsis (stereoacuity defined as 2 log arc seconds or better).

Eye Movement Measurements

A high-resolution video-based eye tracker (EyeLink 1000) was used as described previously to measure binocular horizontal and vertical eye positions under monocular, binocular, and dichoptic viewing conditions.[31,43] Each subject's head was supported on a chinrest, 84 cm from the LCD screen. An infrared permissive filter was used to block visible light while allowing the non-viewing eye to be tracked. Monocular calibration and validation of each eye were done in a dark room using a 5-point constellation with best-corrected vision. The subjects fixated their gaze on a white circular target (0.5 degrees visual angle) projected against a black background on the LCD 30-inch monitor with a resolution of 2560 × 1600 at 60 Hz with brightness of 350 cd/m^2. The recordings were obtained under both eye viewing (BEV), fellow eye viewing (FEV), and amblyopic eye viewing (AEV) to categorize the amblyopic/strabismic participants per their FEM waveforms (see below Fig. 1). The eye movement recordings were also obtained under DcV, where the dot is presented independently but coincidently to each eye. Subjects viewed a target on a 3D LCD 32-inch monitor with a 1920 Å~ 1080 resolution at 120 Hz with a 111 cd/m^2 brightness. To deliver different images to the right and left eyes, we used interleaved polarization: every even line was visible only to one eye, and every odd line was visible only to the other eye, owing to opposite polarization. During the development of the program, calibrations were performed to ensure that the displayed images (to the right and left eyes) were identical at the pixel level. A total of four trials were done under DcV. The target dot (0.5 degrees visual angle) was presented at the center of the screen – the contrast of the target presented to the AE was kept at 100% contrast for all trials. In contrast, the FE contrast varied from 100% (trial 1), 50% (trial 2), 25% (trial 3), and 10% (trial 4). Each trial lasted 45 seconds, and the subjects took breaks between trials.

Eye Movement Analysis

The eye positions were analyzed using MatLab (MathWorks). Blinks and partial blinks were identified and subsequently eliminated. Using the Engbert and Kleigl algorithm, fixational saccades and quick phases of nystagmus were identified.[44–46] We pooled together the quick phases and fixational saccades due to their similar dynamic characteristics, as described in our previous study.[47–49] Drifts and slow phases were defined as epochs between fixational saccades and quick phases in patients without and with nystag-

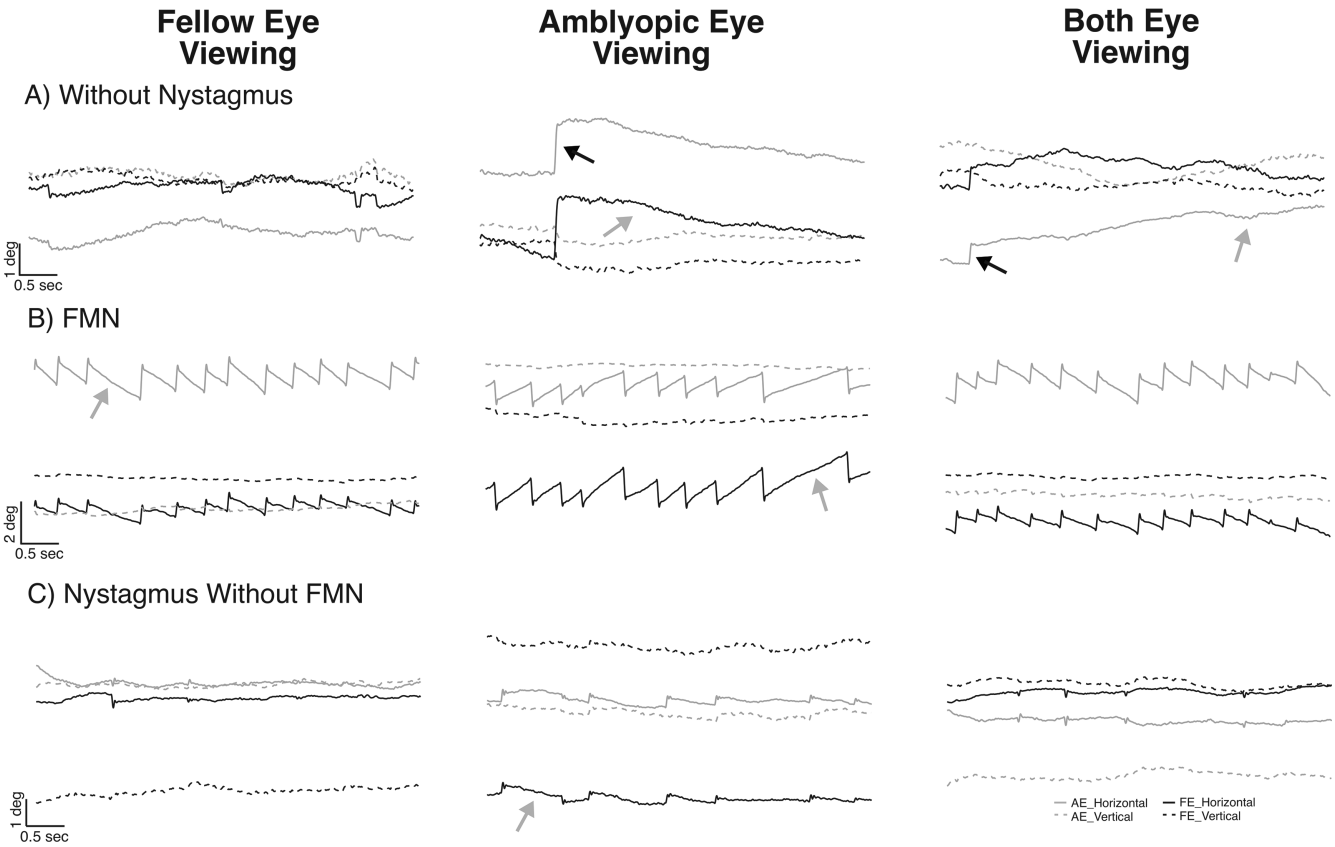

Figure 1. Figure 1 illustrates examples of eye movements during 5 seconds under 3 different conditions: (1) fellow eye viewing on the left column, (2) amblyopic eye viewing in the middle column, and (3) both eye viewing on the right column. Examples are taken from three participants: (**A**) a subject without nystagmus in the *top row*, (**B**) a subject with fusion maldevelopment nystagmus (FMN) in the *middle row*, and (**C**) a subject with nystagmus without FMN in the *bottom row*. The x-axis represents time, whereas the y-axis shows the horizontal positions (*solid line* = *black* = fellow eye and *grey* = amblyopic eye) and vertical eye positions (*dotted line* = *black*; fellow eye and *grey* = amblyopic eye).

mus, respectively.[31,43] The composite amplitude (degrees) and median velocity (degrees/s) of fast and slow FEMs for each eye were calculated as Composite = [Horizontal^2 + Vertical^2]$^{1/2}$. We computed the 10th, 25th, 50th, 75th, and 90th percentiles of the composite amplitude and velocity of the FE and AE for each subject obtained during each DcV trial.

Fixation stability was quantified by calculating the bivariate contour ellipse area (BCEA), which encompasses 68% of fixation points, using the following equation:

$$BCEA = \pi X^2 \sigma_x \sigma_y \sqrt{1 - p^2}$$

where 2.291 is the X^2 value (2 degrees of freedom) corresponding to a probability of 0.68, σ_x and σ_y are the horizontal and vertical standard deviations of eye position, respectively, and p is the product-moment correlation of two position components.[30,33,50]

Vergence BCEA values were also calculated for all subjects (left XY position – right XY position) on data obtained in each trial under dichoptic viewing at various levels of FE contrast (10%, 25%, 50%, and 100%).[51] A log10 transformation was used for statistical analysis.

The eye position traces obtained during BEV, FEV, and AEV were evaluated to categorize the amblyopic/strabismic participants per their FEM waveforms, that is, subjects were classified based on the presence or absence of nystagmus. Figure 1 illustrates the FEM traces obtained under BEV, FEV, and AEV conditions for 5 seconds. Similar to the control subjects, amblyopic subjects who did not exhibit nystagmus demonstrated inter-saccadic drifts between fixational saccades. Subjects with nystagmus were assessed for the presence of FMN, which serves as an indicator of disruption of binocularity in early infancy. FMN is characterized by a nasally directed slow phase and temporally directed fast phase during monocular viewing. We have found that amblyopic subjects can have nystagmus that does not meet the criteria of FMN. These patients exhibited jerk nystagmus with dynamic quick-phase overshoots predominantly observed during AEV. Additionally, there is no reversal direction of nystagmus between amblyopic and FEV. A notable difference that sets them apart from patients with Infantile Nystagmus Syndrome is that the slow-phase velocities are either decreasing or constant, in contrast to the increasing eye velocity commonly seen in Infantile Nystagmus. Furthermore, patients with nystagmus without FMN did not display the dissociated vertical deviation often observed in cases of FMN.

We classified amblyopic and strabismus without amblyopic subjects per their FEM characteristics (without nystagmus = 27, FMN = 10, and nystagmus no FMN = 20). The subjects were classified according to the clinical amblyopia type using the criteria from the Pediatric Eye Disease Investigator Group (PEDIG) studies[52] and their corresponding FEM

Table 1. Demographics of Subjects With Amblyopia and Strabismus Without Amblyopia

Subject ID	Gender	Age	Type	FEM	VA (AE)	VA (FE)	Refraction (OD)	Refraction (OS)	Strabismus_Distance (△)
1	F	5	Aniso	No Nyst.	0.37	0.03	+1.0 + 0.75 × 080	+1.0 + 2.5 × 095	Ortho
2	F	9	Aniso	No Nyst.	1.04	0.03	+0.50 + 0.25 × 030	+3.0	Ortho
3	M	11	Aniso	No Nyst.	1.05	0.07	+2.5 + 1.0 × 075	Plano	Ortho
4	F	6	Aniso	No Nyst.	0.19	−0.06	+3.75	+0.50	Ortho
5	M	8	Aniso	No Nyst.	0.35	−0.03	+2.5 + 0.75 × 080	+0.25	Ortho
6	F	13	Aniso	No Nyst.	0.56	−0.02	+3.0 + 1.5 × 115	+0.50 + 0.75 × 080	Ortho
7	F	12	Aniso	No Nyst.	0.00	0.00	−1.75 + 1.75 × 085	−4.00 + 2.25 × 095	Ortho
8	F	15	Aniso	No Nyst.	0.40	0.13	Plano	+2.00	Ortho
9	F	12	Aniso	No Nyst.	0.43	−0.06	+1.75 + 0.50 × 110	+5.50 + 2.00 × 080	Ortho
10	M	11	Aniso	No Nyst.	0.27	0.16	+4.75 + 0.75 × 090	+5.5 + 1.25 × 080	Ortho
11	F	11	Aniso	No Nyst.	0.31	0.00	+1.25 + 1.50 × 115	+3.50 + 1.50 × 073	Ortho
12	M	11	Aniso	No Nyst.	0.83	−0.02	+3.75 + 1.25 × 045	Plano + 0.25 × 090	Ortho
13	F	15	Aniso	No Nyst.	0.45	−0.02	−0.25 + 1.0 × 085	−2.25 + 6.0 × 085	Ortho
14	M	8	Aniso	No FMN	0.34	0.00	+3.25	+4.75	Ortho
15	M	15	Aniso	No FMN	0.15	−0.06	−0.5 + 0.5 × 070	+3.5 + 1.75 × 110	Ortho
16	M	6	Aniso	No FMN	0.13	0.00	+3.0 + 0.5 × 085	−0.25 + 0.75 × 080	Ortho
17	F	9	Aniso	No FMN	0.33	0.07	Plano + 4.00 × 095	+0.25 + 2.25 × 080	Ortho
18	M	6	Aniso	No FMN	0.51	0.00	+6.0	+2.0	Ortho
19	F	39	Strab	No Nyst.	0.44	−0.02	−1.25 + 0.75 × 010	−1.75 + 1.25 × 165	X(T) 2
20	F	7	Strab	No Nyst.	0.17	0.04	+1.75 + 1.0 × 065	+1.25 × 0.75 × 130	RE(T) 10
21	M	11	Strab	No Nyst.	0.25	0.02	−0.25 + 0.75 × 085	Plano + 0.75 × 090	RH(T) 10, RX(T) 6
22	M	6	Strab	No FMN	−0.16	0.00	+2.5 + 0.25 × 070	+2.25 + 0.25 × 020	E(T) 6-8
23	F	8	Strab	No FMN	0.28	0.00	+2.0	+2.0	X(T) 12
24	F	32	Strab	No FMN	0.40	0.04	+7.00 + 0.50 × 147	+7.00 + 0.50 × 057	RHT 8, RET 2
25	M	13	Strab	No FMN	0.50	0.12	Plano + 1.0 × 085	−0.25 + 1.0 × 102	E(T) 4, RH(T) 6
26	F	17	Strab	FMN	0.15	0.00	+3.50 + 2.50 × 090	+3.00 + 2.0 × 090	X(T) 6, RHT 6
27	M	17	Strab	FMN	0.17	0.05	+2.5 + 1.0 × 015	+2.5 + 0.5 × 170	Flick DVD
28	M	11	Strab	FMN	0.41	0.20	−0.5 + 0.75 × 085	−0.25 + 1.5 × 100	X(T) 30
29	F	54	Strab	FMN	0.17	−0.02	Plano + 2.50 84	+0.50 + 2.00 × 115	RX(T) 18-20, DVD
30	F	49	Strab	FMN	0.16	0.12	−0.5 + 0.75 × 155	−1.0 + 0.5 × 060	Ortho with glasses
31	F	24	Strab	FMN	0.25	0.15	Plano	Plano	LET Flick
32	F	22	Strab	FMN	0.01	−0.09	+7.50	+6.50 + 0.75 × 030	Flick LHT
33	F	9	Mixed	No Nyst.	0.23	0.03	+2.5 + 2.25 × 087	Plano + 2.0 × 080	ET 10
34	F	13	Mixed	No Nyst.	0.24	−0.04	−2.25 + 0.75 × 101	−3.25 + 1.50 × 078	Flick E, 2 RHT
35	F	7	Mixed	No Nyst.	0.60	0.12	+2.00 + 1.50 × 110	+2.75 + 2.75 × 090	X(T) 10
36	M	12	Mixed	No Nyst.	0.99	−0.11	+5.5 + 2.25 × 070	+0.75	Ortho with glasses
37	M	5	Mixed	No FMN	0.41	0.06	+4.0 + 0.5 × 080	+3.0 + 0.5 × 080	RE(T) 4
38	F	6	Mixed	No FMN	0.91	0.02	−8.5 + 3.0 × 095	−0.75	RX(T) 16, LHT 5
39	F	7	Mixed	No FMN	0.08	−0.07	+3.25 + 1.25 × 075	+4.75 + 0.50 × 110	LET 10-12
40	F	38	Mixed	No FMN	0.65	−0.14	+3.50 + 0.50 × 030	+1.75	Ortho with glasses
41	M	12	Mixed	No FMN	1.14	0.21	+3.25 + 2.25 × 080	+0.75 + 0.75 × 080	10 RET
42	M	8	Mixed	No FMN	0.33	−0.04	+1.5 + 2.5 × 105	Plano + 0.75 × 078	RX(T) 14, LH(T) 6
43	F	14	Mixed	No FMN	0.19	−0.13	−1.0	+2.5 + 0.5 × 096	LXT 50, RH(T) 5
44	F	12	Mixed	No FMN	0.25	−0.06	+4.50 + 2.00 × 075	+4.00 + 1.00 × 105	E(T)
45	M	6	Mixed	FMN	0.64	0.30	+5.5 + 1.75 × 091	+6.5 + 2.0 × 089	E(T) 4
46	M	34	Mixed	FMN	0.75	0.35	−2.50 + 2.75 × 090	−0.50 Sphere	X(T) 18, RHypo(T) 20
47	F	13	Strab No Amb	No Nyst.	−0.08	−0.05	−0.50 + 0.50 × 030	−0.75 + 0.25 × 135	XT 16
48	F	57	Strab No Amb	No Nyst.	0.14	0.14	−0.75 + 0.75 × 165	−0.25 + 0.50 × 075	X(T) 16, LH(T) 3
49	M	52	Strab No Amb	No Nyst.	−0.06	−0.03	−7.00 + 2.00 × 103	−6.75 + 0.75 × 066	Ortho with glasses
50	F	11	Strab No Amb	No Nyst.	0.00	0.00	−2.50 + 0.75 × 004	−2.75 + 0.50 × 002	X(T) 16
51	M	9	Strab No Amb	No Nyst.	−0.09	−0.04	+0.25 + 0.75 × 100	+0.25 + 0.75 × 100	RX(T) 8, Flick RHT
52	M	16	Strab No Amb	No Nyst.	0.04	−0.08	−1.00 + 0.50 × 095	−0.75 + 0.75 × 103	X(T) 20-25
53	F	9	Strab No Amb	No Nyst.	0.04	0.01	+0.75 + 0.75 × 080	−3.75 + 5.25 × 085	X(T) 12-14
54	F	13	Strab No Amb	No FMN	0.16	0.13	+3.00 + 1.75 × 070	+2.75 + 2.75 × 100	X(T)8
55	F	13	Strab No Amb	No FMN	−0.13	−0.06	+1.0 + 0.50 × 100	+1.0 + 0.50 × 080	RXT 8, Flick LHT
56	F	31	Strab No Amb	No FMN	0.00	−0.04	+2.75 + 1.25 × 070	+3.25 + 0.75 × 080	E(T) 8
57	F	6	Strab No Amb	FMN	0.11	0.13	+1.25 + 0.50 × 090	+1.25 + 0.50 × 090	LX(T) 8, Bilat. DVD

(Aniso, anisometropic amblyopia; at least one of the following criteria must be met: (a) ≥ 0.50 D difference between eyes in spherical equivalent or ≥ 1.50 D difference between eyes in astigmatism in any meridian. Strab, strabismic amblyopia; at least one of the following criteria must be met, and criteria are not met for mixed amblyopia: (a) heterotropia at distance (with or without spectacles), (b) history of strabismus surgery, and (c) history of strabismus that has resolved with glasses and/or surgery. Mixed, mixed amblyopia; both of the following criteria must be met: (a) criteria for strabismus (see above), (b) ≥ 1.00 D difference between eyes in spherical equivalent or ≥ 1.50 D difference between eyes in astigmatism in any meridian. Strab No Amb, strabismus without an amblyopia component. F, female; M, male; C, control; FEM, fixational eye movement; FMN, fusion maldevelopment nystagmus; No FMN, subjects who had nystagmus that did not meet the criteria of FMN whereas no Nyst, subjects without nystagmus. Ortho, Orthotropia; (), intermittent deviation; XT, exotropia; ET, esotropia; HT, hypertropia, and HypoT, hypotropia (preceded by L – left and R – right). VA, visual acuity; FE, fellow eye; AE, amblyopic eye).

waveforms, as outlined in Table 1. The cohort consisted of 18 individuals with anisometropic amblyopia (13 without nystagmus and 5 with nystagmus but no FMN), 14 with mixed amblyopia (4 without nystagmus, 8 with nystagmus but no FMN, and 2 with FMN), and 14 with strabismic amblyopia (3 without nystagmus, 4 with nystagmus but no FMN, and 7 with FMN). Subjects with a strabismus component were divided into two subgroups based on a deviation angle:

those with an eye misalignment greater than 8Δ ($n = 22$) and those with an eye misalignment less than 8Δ ($n = 17$).

Dichoptic Motion Coherence Test

The Dichoptic Motion Coherence Test assesses interocular suppression by measuring motion coherence thresholds at various contrast levels. The stimuli used were variations of those used by other labs.[19,53] The test was exclusively performed using the Film-type Patterned Retarder (FPR) LCD Display++, and passive polarized glasses were required to view the display. Stimuli were presented using Metropsis (Cambridge Research Systems, Rochester, Kent, UK).

Each session began with horizontal and vertical alignment of the dichoptic nonius lines. Subjects were shown an image of how the cross should appear for each eye and both eyes together; the image to one eye was the bottom and left side of the cross, whereas the image to the other eye was the top and right side of the cross. Participants were tasked with illustrating their perceived image based on this stimulus. For subjects who were not able to view the entire cross, the contrast of the image of the nonius cross that was presented to the FE was reduced. In instances involving strabismic subjects, efforts were made to align the images between the two eyes according to the subjects' responses. Successful alignment yielded an image of a cross with a central cut-out square, surrounded by four additional squares and a high-contrast border, perceptible in both eyes. With proper alignment, the image was a cross with a square cut out of the center, surrounded by four additional squares and a high-contrast border that was visible in both eyes. However, intriguingly, the perception of the nonius cross segment presented to the AE proved frequently transient, even with contrast reduction in the FE, particularly within the strabismic cohort. Subjects with strabismic amblyopia (including older participants) vocalized the fleeting nature and changing the location of the nonius cross segment as observed by the AE during the alignment procedure. We have shown that eye deviation undergoes alterations in dichoptic environments in strabismic subjects, particularly at low FE contrasts.[40] Due to the transient visibility and variable location of the nonius cross, as reported by multiple strabismic subjects, coupled with the changing eye deviation in the dichoptic environment, a decision was made to maintain the target dot location without adjustment based on nonius cross measurements. This choice was implemented to ensure consistency in the visual stimulus throughout the current experiment.

The visual stimulus used in the experiment included random dot kinematograms presented to either the right or left eye. These kinematograms comprised 100 dots with an individual dot diameter of 0.5 degrees. Among these dots, signal dots moved uniformly in a specific direction, whereas noise dots moved randomly. The stimulus was displayed at the center of the screen and was enclosed by a rectangular reference frame with zero disparity. This visual setup was presented against a uniform mid-gray background, maintaining an average luminance of 60 cd/m. To adjust the visibility of the dots, their luminance was adjusted by modulating it relative to the background, using the Michelson contrast formula. The formula is calculated as follows: Dot luminance contrast (%) = 100 * ((Ldots - Lbackground) / Lbackground). In this context, Ldots represent the luminance of the dots, whereas Lbackground indicates the luminance of the background. The signal dots were presented to the AE in the experiment, whereas the noise dots were presented to the FE.[25]

Additionally, two small black squares with zero disparity are placed above and below the reference frame to assist with fusion. The participants were shown a stationary image of a "Lion" on the right side and a "Pikachu" image on the stimulus display's left side. They were instructed to indicate the coherent motion direction of the signal dots verbally, and the examiner pressed the right or left key on the button box, representing rightward or leftward motion, respectively. Before initiating the experiment, the stimulus was presented without the use of polarized glasses to ensure that the participant understood the task and could accurately determine the direction of the coherent motion dots. Inter-ocular suppression was measured dichoptically, and the participants wore polarized glasses while viewing the stimulus.

Throughout the experiment, signal and noise dots were presented simultaneously, requiring the participant to assess the motion direction of the signal dots. The contrast of signal dots shown to the AE remained constant at 100%, whereas the contrast of noise dots displayed to the fellow fixing eye varied across 5 levels (100%, 90%, 75%, 62.5%, and 56.7%). The task's difficulty level was increased by decreasing the proportion of signal dots relative to noise dots.[53] To maintain a total of 100 dots perceived by the participant, when the number of signal dots decreased in AE, the noise dots increased in the FE, and vice versa. The motion coherence threshold is the proportion of signal-to-noise dots at which a participant can accurately identify the motion direction of the embedded signal elements. A 1-down and 1-up adaptive staircase (step size increase of 24% and decrease of 48% and 8%, before and after the first reversal, respectively) was utilized to determine the motion coherence threshold at various levels of noise contrast in the FE.[53]

Figure 2 plots the results of the dichoptic motion coherence test in a control subject and three amblyopia subjects. The x-axis represents the contrast level of noise dots presented to the FE. In contrast, the y-axis represents the motion coherence threshold (number of signal dots) obtained using the staircase method. The black arrows on each image square, where the number of signal dots is reduced, indicate the signal dot with 100% contrast. As the FE contrast approaches that of the AE, the number of signal dots to detect the direction of motion increases, as would be expected in control and amblyopic subjects. However, the required signal dots are much higher for amblyopic subjects, including at lower FE contrasts of 62.5% and 75%. Previous studies evaluating the dichoptic motion coherence threshold have computed binocular and dichoptic motion coherence thresholds with a total testing time of 1 hour. These studies reported no statistically significant difference in binocular motion coherence threshold between controls and amblyopic/strabismic subjects.[19] In the current study, there were no statistically significant differences observed between the number of signal dots required to discriminate motion at 56.7% FE contrast between controls (median dots = 1) and amblyopic/strabismic subjects (median dots = 1.7, $P > 0.05$). Thus, the dichoptic motion coherence threshold testing was limited to noise dots at 56.7% and higher FE contrast levels, as most amblyopic/strabismic subjects were expected to have abnormalities at those contrast levels. This modification allowed us to reduce the testing time to about 10 to 12 minutes, which was much more feasible for the younger study participants.

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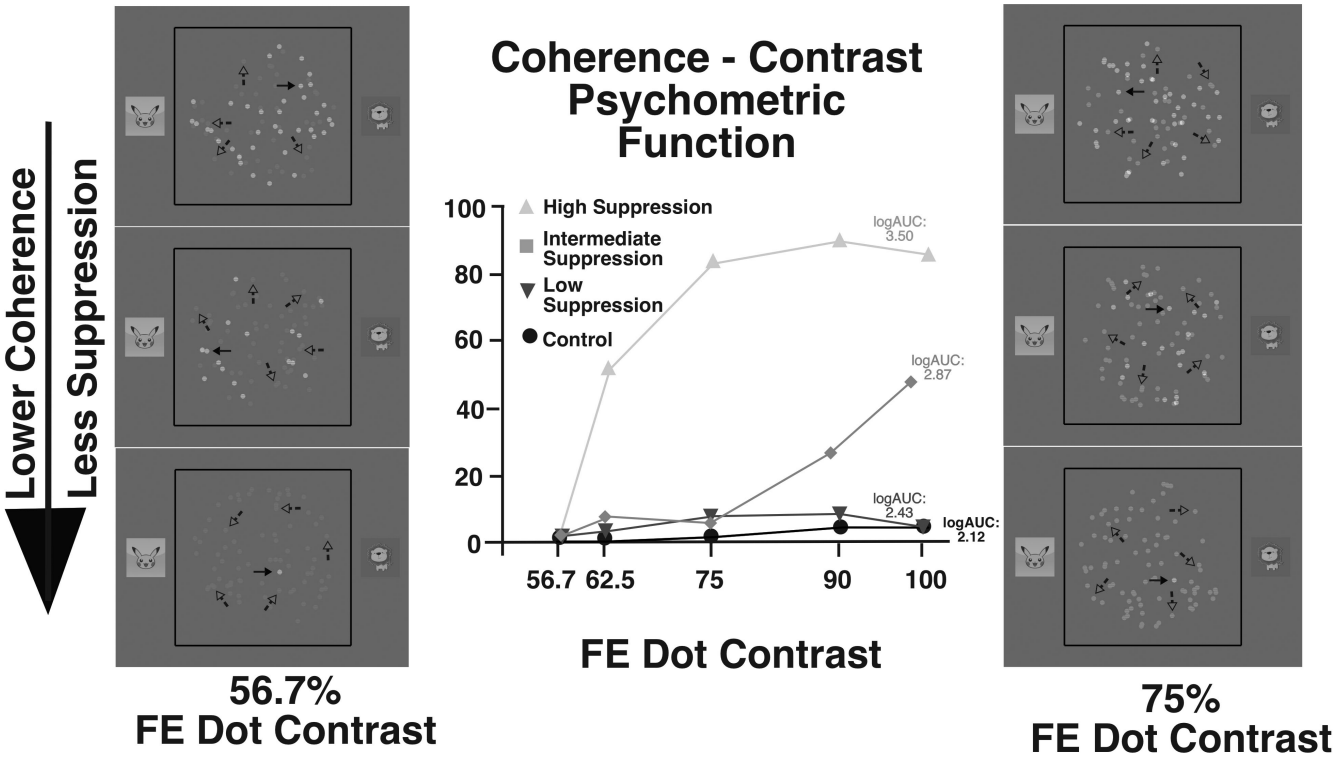

Figure 2. Figure 2 illustrates the schematic representation of the dichoptic stimulus on both the *right* and *left* sides of the graphs. On both sides, the *dots* carrying the coherence signal (depicted as *white dots* in this example) were presented to the amblyopic eye at 100% contrast. Furthermore, on the *left side* of the figure, noise dots with 56.7% contrast (depicted as *light grey dots*) were presented to the fellow eye, whereas on the right side, noise dots with 75% contrast (depicted as *grey dots*) were also presented to the fellow eye. The *solid* and *dashed arrows* indicate the motion direction of the signal and noise dots, respectively. In the plots located in the *center* of the figure, the results of the dichoptic motion coherence test are displayed for a control subject (2.12 logAUC) and a subject with low suppression (2.43 logAUC), and a subject with intermediate suppression (2.87 logAUC) and a subject with high suppression (3.50 logAUC). The x-axis represents the contrast level of noise dots presented to the fellow eye. In contrast, the y-axis represents the motion coherence threshold (number of signal dots) obtained using the staircase method.

To quantify inter-ocular suppression, we computed the area under the curve (AUC) using a third-order polynomial that was fitted to the log of number of the signal dots required to detect the motion direction at each FE contrast noise level for each participant. Subjects were grouped into either low, intermediate, or high suppression groups. Subjects in the low suppression group had log AUC ≤ 2.45 ($n = 11$), the intermediate suppression group ($n = 20$) had log AUC > 2.45 and < 3, whereas the high suppression group had a cumulative log AUC ≥ 3 ($n = 26$).

Statistical Methods

The statistical analysis was performed using SPSS Statistics (version 25). An unpaired *t*-test test was used to compare the age between control versus amblyopic/ strabismic subjects and the visual acuity of AE across anisometropic versus strabismic/mixed amblyopia. The normality of data was evaluated using the Kolmogorov–Smirnov test. A 1-way ANOVA was performed to assess the inter-ocular suppression deficits as a function of the severity of amblyopia groups, clinical subtype groups, stereoacuity groups, and per the FEM waveform groups. A 1-way ANOVA was also performed to evaluate the stereoacuity deficits as a function of the severity of the amblyopia groups, clinical subtype groups, inter-ocular suppression groups, and per the FEM waveforms. Post hoc analyses were conducted on statistically significant differences using Bonferroni correction.

Hierarchical multiple regression analyses were conducted to determine the factors influencing stereoacuity and suppression deficits. We evaluated suppression (dependent variable) as a function of continuous independent variables, namely the age of the subject, visual acuity deficit of the amblyopic eye in log MAR, clinically measured strabismus angle in prism diopters, and stereopsis in log arc sec. To test the effect of the compound variable FEM waveform, that is, subjects without nystagmus and those with nystagmus (for the purpose of analysis, we combined patients with FMN and nystagmus without FMN into the nystagmus group), we used hierarchical regression where we started with the entire first model that incorporates all the continuous independent variables as described above and FEM waveform information (model 1). In contrast, in model 2, the compound variable waveform was removed while the remaining continuous independent variables were retained. We determine the change in model performance by evaluating changes in R^2 (ΔR^2) and F (ΔF) and whether the change is statistically significant.

Similarly, we evaluated stereo-acuity deficits using the hierarchical multiple regression analyses, incorporating the same variables as above in conjunction with suppression. The use of hierarchical regression, with model 1 incorporat-

ing all variables, including FEM waveform information, and model 2 excluding the compound variable while retaining other continuous independent variables, allows for a systematic assessment of the contribution of FEM waveform to the model's performance. For all multiple regression models, there was linearity as assessed by partial regression plots and a plot of studentized residuals against the predicted values. The independence of residuals was assessed by a Durbin-Watson statistic, which was less than 2.4 for all the regression models. There was homoscedasticity, as evaluated by visual inspection of a plot of studentized residuals versus unstandardized predicted values. There was no evidence of multicollinearity, as assessed by tolerance values greater than 0.1 with VIF values less than 3. There were no studentized deleted residuals greater than ±3 standard deviations. The assumption of normality was met, as assessed by a Q-Q Plot. We performed a 1-way Kruskal Wallis ANOVA test to evaluate percentile data of composite amplitude and velocity of FEMs. Post hoc analyses were conducted on statistically significant differences using Bonferroni correction. All statistical tests had a critical alpha value of 0.05.

Results

We examined the inter-ocular suppression, stereo-acuity deficits, and FEMs in 14 controls, 46 amblyopic subjects, and 11 strabismus without amblyopia subjects. There were no differences in age (years) (age range = 5–57 years) between

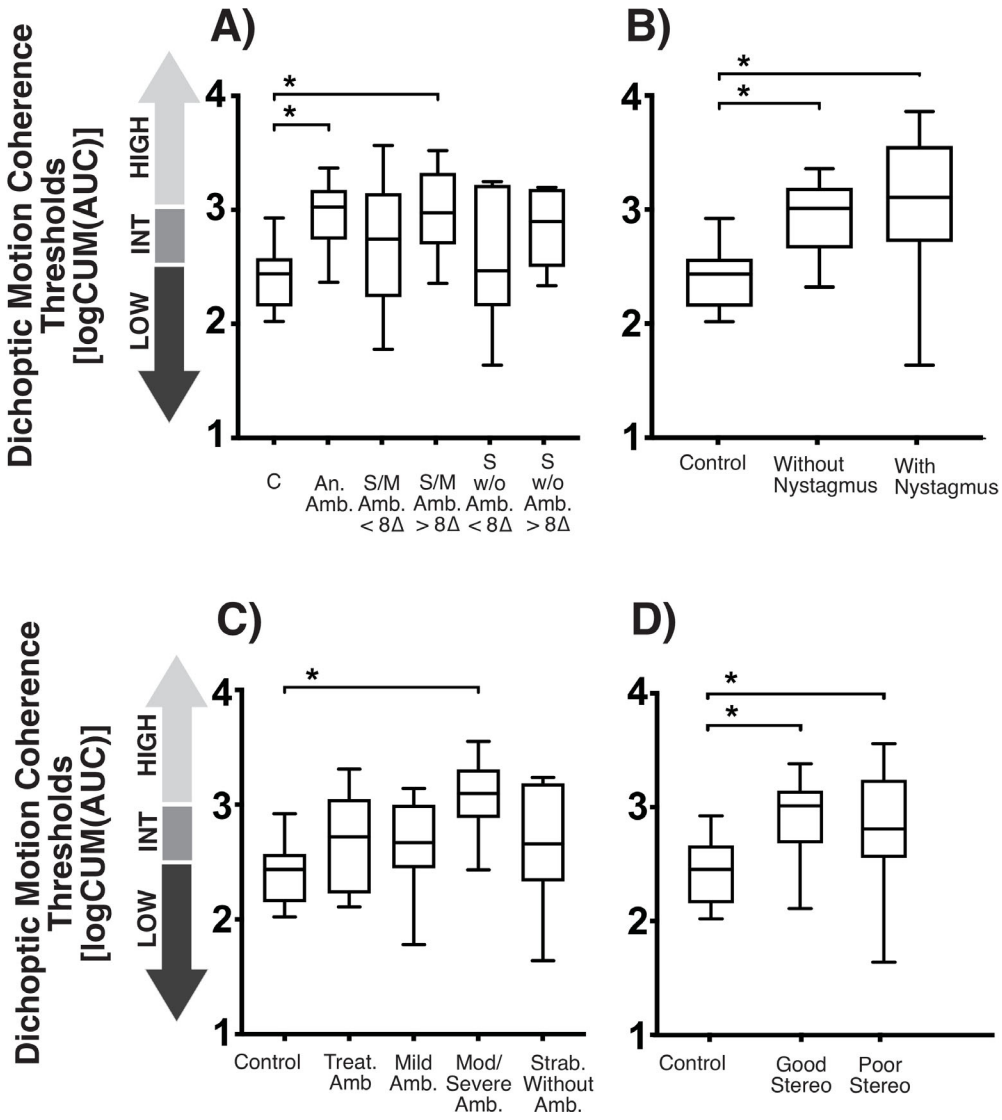

Figure 3. Figure 3 illustrates the box-whisker plots of interocular suppression across various groups. The y-axis represents suppression using the area under the curve (AUC) values. In (**A**), the data were categorized per types of amblyopia: An. Amb = anisometropic amblyopia; S/M Amb = strabismic and mixed amblyopia; and S w/o Amb. = strabismus without amblyopia. Subjects with a strabismus component were further divided into two subgroups based on the degree of eye misalignment, using a threshold of 8Δ (**A**); (**B**), the subjects were categorized per FEM waveforms; (**C**), the subjects were categorized per the visual acuity deficits in the amblyopic eye: Control, Treat Amb = treated amblyopia; Mild Amb = mild amblyopia; Mod/Severe Amb = Moderate and Severe Amblyopia; and Strab. Without Amb. = strabismus without amblyopia; (**D**), the subjects were categorized per the stereoacuity deficits. In the box-whisker plots, *solid lines* represent median values, while dotted lines correspond to quartiles. The figure also depicts the post hoc analysis indicating statistically significant multiple pairwise comparisons between the various groups (*).

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controls (12.2 ± 9.76) versus amblyopia and strabismus without amblyopia (15.9 ± 12.9) subjects ($P = 0.12$). The visual acuity (log MAR) showed no significant differences among anisometropic amblyopia (0.43 ± 0.29 log MAR) versus strabismic/mixed amblyopia groups (0.38 ± 0.30 log MAR, $P = 0.44$).

Factors Affecting Inter-Ocular Suppression in Amblyopia and Strabismus Without Amblyopia

Our study aimed to explore the relationship between interocular suppression and different subtypes of amblyopia and in cases of strabismus without amblyopia, as shown in Figure 3A. As expected, amblyopic subjects with and without strabismus, and those with strabismus without amblyopia, exhibited increased inter-ocular suppression compared to controls, indicated by higher dichoptic motion coherence thresholds (log AUC values, $P = 0.004$).

Amblyopic and strabismic subjects without amblyopia can have nystagmus with and without FMN.[31] In Figure 3B, we categorized subjects according to the FEM waveform characteristics. We found that subjects with and without nystagmus had greater dichoptic motion coherence thresholds than controls ($P = 0.004$). Figure 3C illustrates the extent of inter-ocular suppression per the visual acuity deficit of the AE. We found interocular suppression was more pronounced in subjects with moderate to severe amblyopia ($P = 0.0002$). In Figure 3D, the amblyopic and strabismic subjects were characterized based on their stereoacuity levels. Interestingly, regardless of the extent of their stereoacuity deficit, amblyopic and strabismic subjects exhibited higher suppression levels than controls ($P = 0.0007$). Figure 3 also depicts the post hoc analysis indicating statistically significant multiple pairwise comparisons between the various groups.

We ran a hierarchical multiple regression analysis to delve deeper and evaluate how the presence of nystagmus and other clinical parameters affect suppression. In the first model, visual acuity of AE and FE, clinically measured strabismus angle, the extent of anisometropia (difference in spherical equivalent between the two eyes), age, stereoacuity deficits, and multi-categorical waveform characteristics (without and with nystagmus) were included. In contrast, multi-categorical waveform variable information was removed in the second model (Table 2). The first model with waveform information F (7, 67) = 6.41, $P < 0.0001$, adj. $R^2 = 0.42$, and the second model without the waveform information F (5, 67) = 7.96, $P < 0.0001$, adj. $R^2 = 0.39$ predicted inter-ocular suppression. In both models, increasing visual acuity deficit of the AE and clinically measured strabismus angle were statistically significant factors that contributed to the prediction of suppression deficits. However, there was not statistically significant R^2 and F change ($\Delta R^2 = -0.03$, $\Delta F = 1.93$) after removal of the waveform information in the second model (see Table 2). In other words, the inclusion of a multi-categorical variable waveform in the first model did not improve the ability of the model to predict the extent of inter-ocular suppression. Interestingly, stereoacuity deficit and inter-ocular suppression measured using dichoptic motion coherence showed a weak inverse correlation, likely because poor stereoacuity does not always occur with greater suppression as shown in the subsequent results.

Table 2. Evaluation of Extent of Suppression Using a Hierarchical Regression Model

	Model 1 With Waveform Unstandardized (Standardized) Coefficients	Model 2 Without Waveform Unstandardized (Standardized) Coefficients
Constant	2.72***	2.78***
AE visual acuity	0.49 (0.38)***	0.56 (0.44)***
Strabismus angle	0.01 (0.34)***	0.01 (0.39)***
Refractive error difference	0.00 (0.01)	0.03 (0.12)
Age	−0.04 (−0.13)	−0.00 (−0.10)
Stereopsis	−0.12 (−0.26)	−0.09 (−0.20)
No nystagmus	0.24 (0.29)	NA
Nystagmus	0.25 (0.31)	NA
	R^2, $F = 0.42$, 6.41***	R^2, $F = 0.39$, 7.96*** ΔR^2, $\Delta F =$ −0.03, 1.93

(AE, amblyopic eye and FE, fellow eye. In the table, statistical significance is denoted by asterisks: a single asterisk (*) indicates $P < 0.05$, and three asterisks (***) represent $P < 0.001$).

Factors Affecting Stereoacuity Deficits in Amblyopia and Strabismus Without Amblyopia

We computed the stereoacuity deficits in anisometropic amblyopia, strabismic/mixed amblyopia, and strabismus without an amblyopia component, as illustrated in Figure 4A ($P < 0.0001$). Strabismic/mixed amblyopic subjects had the most pronounced stereoacuity deficits. In Figure 4B, subjects were categorized based on FEM waveform characteristics. Our analysis revealed that subjects with nystagmus exhibited greater stereoacuity deficits than controls and those without nystagmus ($P < 0.0001$). Figure 4C illustrates the extent of the stereoacuity deficit in amblyopic subjects per the visual acuity deficit of the AE. We found stereoacuity deficits were most pronounced in subjects with moderate to severe amblyopia ($P < 0.0001$). In Figure 4D, the box and plots illustrate the stereoacuity deficits within groups categorized based on the extent of suppression. Amblyopic and strabismic subjects had increased stereoacuity deficits regardless of the extent of suppression ($P < 0.0001$). Figure 4 also depicts the post hoc analysis indicating statistically significant multiple pairwise comparisons between the various groups.

To further explore this complex relationship, we conducted a hierarchical multiple regression analysis to identify the factors that could predict the extent of stereoacuity deficits. In the initial model, we included factors such as visual acuity in the amblyopic eye, clinically assessed strabismus angle, anisometropia extent (difference in spherical equivalent between the eyes), age, extent of suppression, and multi-categorical waveform characteristics (with and without nystagmus). The second model, however, excluded information related to FEM waveforms (Table 3). Regression coefficients and standard errors can be found in Table 3. The first model with waveform information F (7, 67) = 11.969, $P < 0.000$, adj. $R^2 = 0.58$, and the second model without the waveform information F (5, 67) = 4.640, $P < 0.001$, adj. $R^2 = 0.27$ predicted stereoacuity deficits. The variable visual acuity AE in both models was statistically significant, whereas the strabismus angle was statistically significant in the second model. However, there was a statistically significant R^2 and F

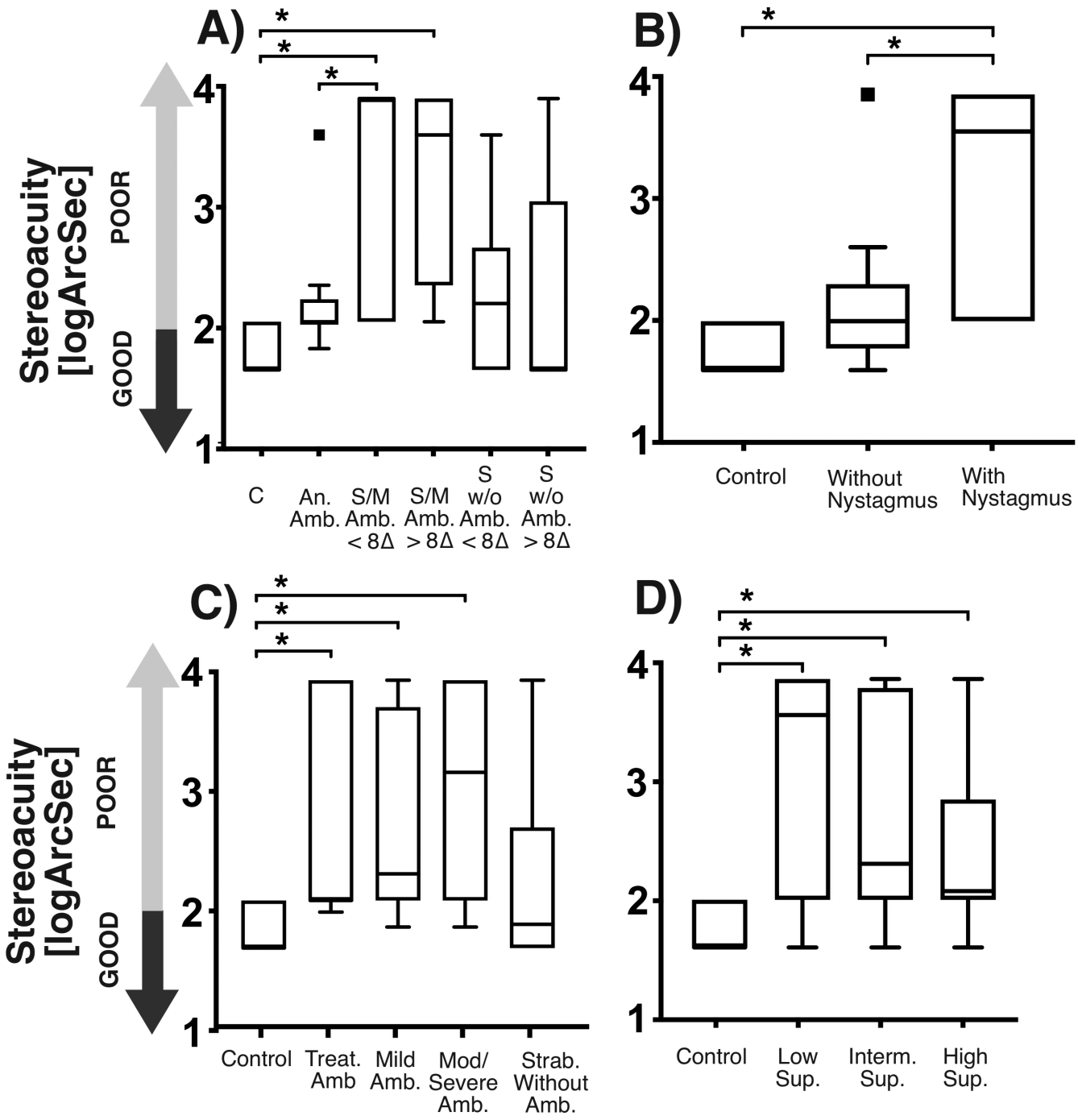

Figure 4. Figure 4 illustrates the box-whisker plots of stereoacuity deficits across various groups. The y-axis represents the stereoacuity deficits. In (**A**), the data were categorized per types of amblyopia: An. Amb = anisometropic amblyopia; S/M Amb = strabismic and mixed amblyopia; and S w/o Amb. = strabismus without amblyopia. Subjects with a strabismus component were further divided into two subgroups based on the degree of eye misalignment, using a threshold of 8Δ (**A**); (**B**), the subjects were categorized per FEM waveforms; (**C**), the subjects were categorized per the visual acuity deficits in the amblyopic eye: Control, Treat Amb = treated amblyopia; Mild Amb = mild amblyopia; Mod/Severe Amb = moderate and severe amblyopia, and Strab. Without Amb. = strabismus without amblyopia; (**D**), the subjects were categorized per the extent of suppression. In the box-whisker plots, *solid lines* represent median values, whereas the *dotted lines* correspond to quartiles. The figure also depicts the post hoc analysis indicating statistically significant multiple pairwise comparisons between the various groups (*).

change ($\Delta R^2 = -0.31$, $\Delta F = 22.31$) after removal of the compound variable waveform information (see Table 3). In other words, the inclusion of multi-categorical variable waveform in the first model improved the performance of the model by being able to predict 76 % variation in stereoacuity deficits compared to the second model which predicted only 52 % of the variation in stereoacuity deficits.

Table 3. Evaluation of Stereoacuity Using a Hierarchical Regression Model

	Model 1 With Waveform Unstandardized (Standardized) Coefficients	Model 2 Without Waveform Unstandardized (Standardized) Coefficients
Constant	2.70***	3.27***
AE visual acuity	0.82 (0.30)***	1.12 (0.41)***
Strabismus angle	0.01 (0.16)	0.03 (0.36)***
Refractive error difference	0.00 (0.00)	0.01 (0.02)
Age	0.00 (0.11)	0.01 (0.17)
Suppression	−0.42 (−0.20)	−0.52 (−0.25)
No nystagmus	0.13 (0.07)	NA
Nystagmus	1.13 (0.65)***	NA
	R^2, $F = 0.58$, 11.969***	R^2, $F = 0.27$, 4.64***
		ΔR^2, $\Delta F = -0.31$, 22.31***

(AE, amblyopic eye and FE, fellow eye. In the table, statistical significance is denoted by asterisks: a single asterisk (*) indicates $P < 0.05$, and three asterisks (***) represent $P < 0.001$).

Fixation Switch and Inter-Ocular Suppression and Stereoacuity Deficits in Amblyopia and Strabismus

Typically, in strabismic amblyopia, the FE is fixing on the target and the AE is deviated. We have previously reported that there can be a fixation switch where AE is fixing on the target under DcV. The fixation switch can occur at 100% FE contrast or when the FE contrast is lowered. Figure 5 plots FEMs from 3 subjects with co-existing strabismus (subject 1 [subject_ID: 41] had FE fixing at all four contrasts without a fixation switch; subject 2 [subject_ID: 37] had alternating fixation noted at 50%, 25%, and 10% FE contrasts with AE fixing for most of the trial at 10% FE contrast, whereas subject 3 [subject_ID: 55] had alternating fixation noted at all FE contrasts including 100% FE contrast). Subject 1 without the fixation switch had greater inter-ocular suppression, whereas subject 3 with alternating fixation at 100% FE contrasts had the least amount of inter-ocular suppression. Thus, we evaluated the inter-ocular suppression (see Fig. 5A) and stereoacuity deficit (see Fig. 5B) in the control group ($n = 14$), anisometropic amblyopia group ($n = 18$), a group with clinically measured strabismus exhibiting alternating fixation behavior from 100% FE contrast onward under DcV ($n = 7$), a group with clinically measured strabismus exhibiting alternating behavior from 50% FE contrast under DcV ($n = 11$), and a group with clinically measured strabismus without alternating behavior under DcV ($n = 15$). In total, six patients could not be included in this analysis due to missing dichoptic gaze data ($n = 4$, out of these 1 had low suppression, and 3 had intermediate suppression), and the other two subjects had strabismic amblyopia but did not have clinically measurable strabismus (both had low suppression).

Figure 6A is a box and whisker plot of cumulative log AUC of dichoptic motion coherence thresholds and Figure 6B is a box and whisker plot for stereoacuity deficits, respectively, in controls, anisometropic amblyopia, strabismic subjects with and without amblyopia per their fixation switch behavior observed under DcV. Based on our analysis of cumula-

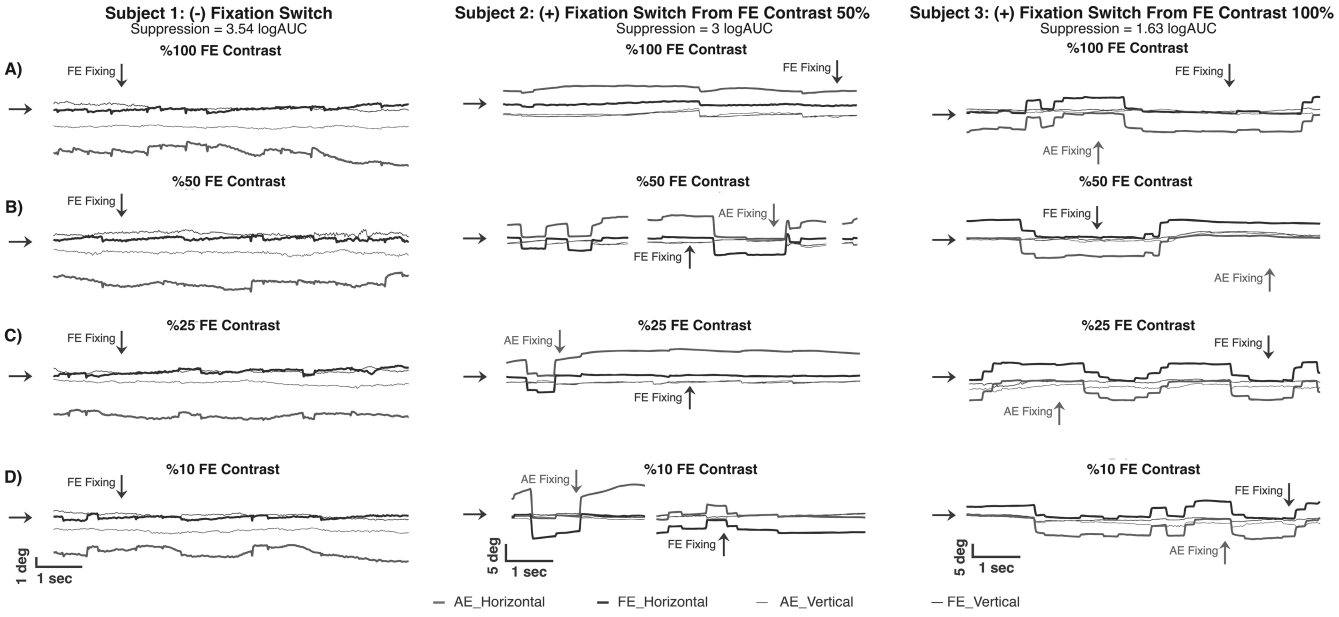

Figure 5. Horizontal and vertical eye position traces are plotted on the y-axis, representing the eye positions, while time is indicated on the x-axis. The data are presented for 3 subjects with mixed/strabismic amblyopia during DcV at fellow eye contrasts of (**A**) 100%, (**B**) 50%, (**C**) 25%, and (**D**) 10% contrast. The *solid-thick black lines* represent the fellow eye's horizontal positions, and the *grey lines* indicate the amblyopic eye's horizontal positions. The *solid-thin black lines* also represent the fellow eye's vertical positions, and the *grey lines* indicate the amblyopic eye's vertical positions. Subject 1 exhibits mixed/strabismic amblyopia without fixation switch. Subject 2, a mixed/strabismic individual, demonstrates a fixation switch (indicated by the *black arrow*) when the fellow eye fixates at 50%, 25%, and 10% contrast, whereas the amblyopic eye takes over fixation (indicated by the *grey arrow*). The primary position is represented by the *horizontal arrows* on the far left. Subject 3, another individual with mixed/strabismic amblyopia, also shows a fixation switch (indicated by the *black arrow*) when the fellow eye is fixating at 100%, 50%, 25%, and 10% contrast.

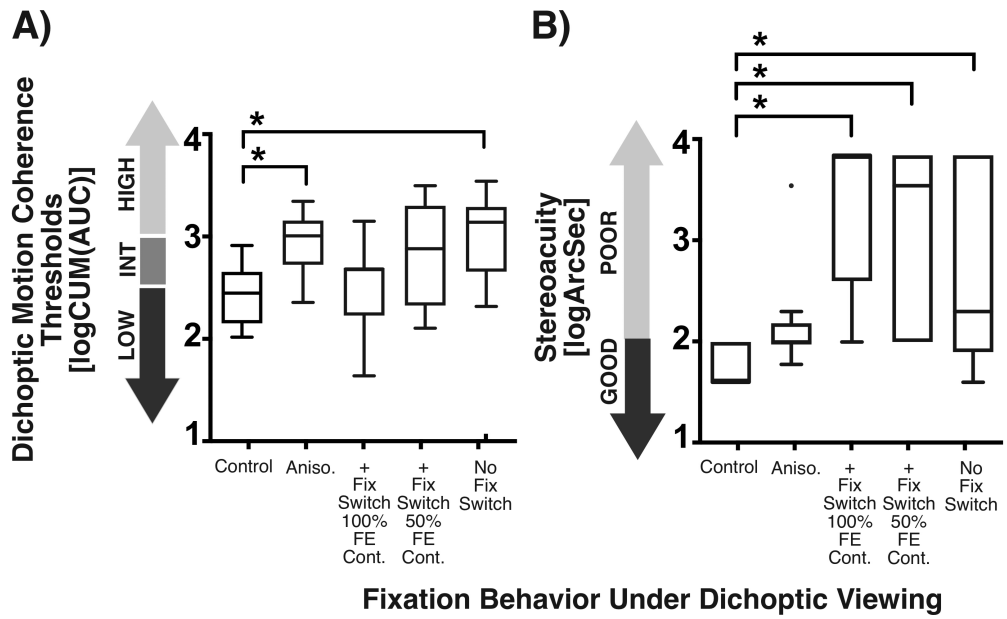

Figure 6. Figure (**A**) illustrates the relationship between the extent of suppression and fixation behaviors using box-whisker plots. The y-axis represents low, intermediate, and high suppression levels indicated by area under the curve (AUC) values, whereas fixational behaviors are depicted on the x-axis. (**B**) Illustrates the relationship between stereoacuity deficits and fixation behaviors through box-whisker plots. On the y-axis, stereoacuity deficit levels are indicated while fixational behaviors, including Control, Aniso (anisometropic amblyopia), + Fix Switch 100% FE Cont. (clinically measured strabismus exhibiting alternating fixation behavior from 100% FE contrast), + Fix Switch 50% FE Cont. (clinically measured strabismus exhibiting alternating fixation behavior from 50% FE contrast), and No Fix Switch (clinically measured strabismus without alternating behavior) are depicted on the x-axis. *Solid lines* represent median values in the box-whisker plots, whereas the *dotted lines* correspond to quartiles.

tive AUC threshold values concerning fixation switch behavior, we observed statistically significant differences. These differences were found in pairwise comparisons between the control group and subjects who did not exhibit fixation switch behavior ($P = 0.002$), as well as between the control and anisometropic amblyopia group ($P = 0.003$). When comparing stereoacuity deficits based on fixation switch behavior, we observed statistically significant differences. Differences were found in pairwise comparisons between the control group and individuals with strabismus exhibiting alternating fixation behavior at 100% FE contrast ($P < 0.0001$), at 50% FE contrast ($P = 0.0002$), and in individuals with strabismus without alternating behavior ($P = 0.0023$).

Figures 7A and 7B demonstrates the correlation between the extent of suppression and stereoacuity deficits in subjects without and with nystagmus. In the group of patients without nystagmus, stereoacuity levels appear to be independent of suppression, with most individuals exhibiting either some or good stereoacuity. However, several of these patients had high suppression levels. Most of the subjects with high suppression levels had moderate to severe amblyopia or strabismus $> 8\Delta$. Notably, only one subject without nystagmus had poor stereoacuity, severe amblyopia, and strabismus $> 8\Delta$ highlighted within a square. In contrast, a significant portion of subjects with nystagmus demonstrates poor stereoacuity levels independent of suppression levels. This includes one subject with moderate anisometropic amblyopia indicated within a black circle (on the top right). On the other hand, the two subjects indicated within gray circles (on the top left) had poor stereo-acuity with low interocular suppression. These two subjects had small angle strabismus $< 8\Delta$; one had strabismus without amblyopia, and the other had mild amblyopia. Thus, the analysis reveals that the presence of nystagmus is associated with poor stereoacuity and that stereoacuity and suppression levels are determined by a combination of factors, including visual acuity deficit and strabismus angle, and FEM waveforms.

Fast and Slow FEM Characteristics in Controls and Amblyopic Subjects Per Inter-Ocular Suppression Deficits

We have previously reported increased amplitude of fast FEMs and increased velocity of slow FEMs in amblyopic subjects with greater visual acuity, contrast sensitivity, and stereoacuity deficits.[31,32,54] We have also found that the fast and slow FEM metrics of the FE and AE are affected by viewing conditions, including under DcV at varied FE contrasts.[40] The relationship between the extent of inter-ocular suppression and FEM abnormalities seen under DcV is not clear. Thus, we evaluated the fast and slow FEMs of the FE and AE obtained under DcV at varied FE contrasts in controls, amblyopic/strabismic subjects with low, intermediate, and high suppression.

Figure 8 summarizes the normalized cumulative sum histogram of the composite amplitude of fast FEMs of FE (top) and AE (bottom) in controls (black line) and amblyopic/strabismic subjects with low suppression (dark gray), intermediate suppression (medium gray), and high suppression (light gray) obtained during DcV at varied FE contrasts. There is a rightward shift of the distribution of the amplitude of the fast FEMs of FE and AE during DcV at all FE contrasts in those with high suppression than the other groups. We

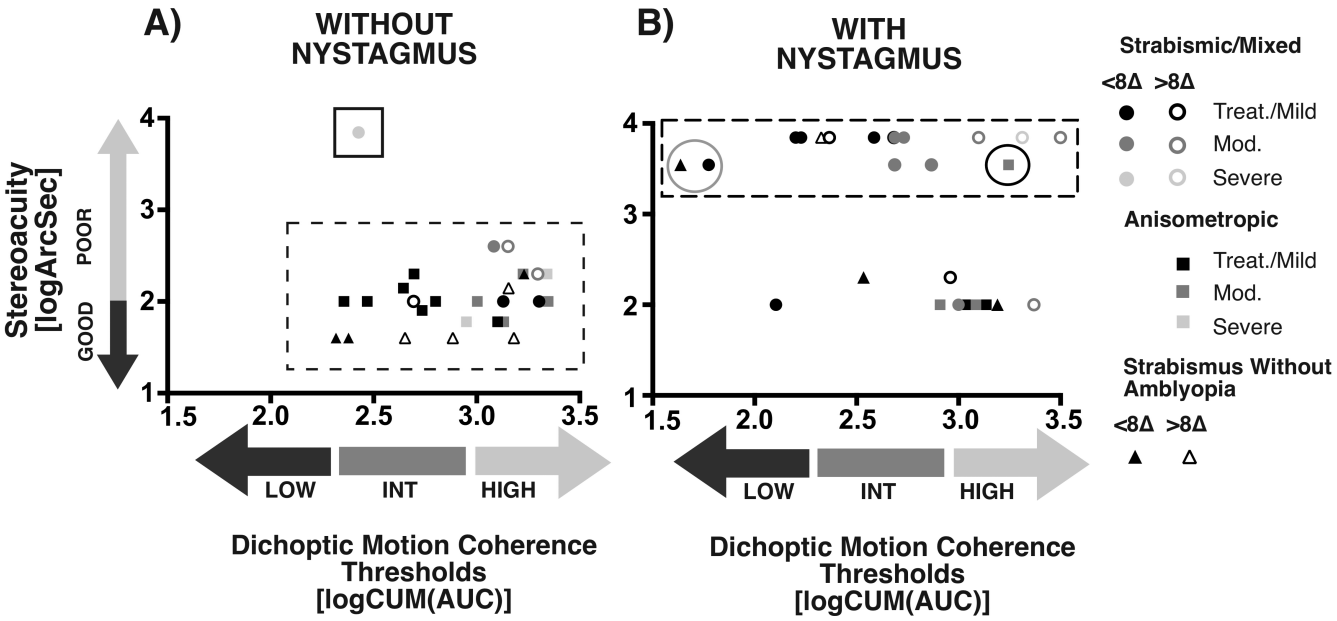

Figure 7. The Figure demonstrates the correlation between the extent of suppression and stereoacuity deficits in subjects without nystagmus (**A**) and those with nystagmus (**B**). The x-axis represents low, intermediate, and high suppression levels indicated by area under the curve (AUC) values, whereas the y-axis represents stereoacuity deficit levels. Circular symbols denote the strabismic/mixed group, whereas the square symbols represent the anisometropic amblyopia group. The triangle group signifies individuals with strabismus without amblyopia. Each group is divided based on visual acuity of amblyopic eye: the mild/treated subgroup is shown in *black*, the moderate amblyopia subgroup is shown in *grey*, and individuals with severe amblyopia are shown in *light grey*. Among those with a strabismus component, they are further classified into two categories. Individuals with clinically measured strabismus angles larger than 8Δ are depicted with *open symbols*, whereas those with angles smaller than or equal to 8Δ are represented with *closed symbols*.

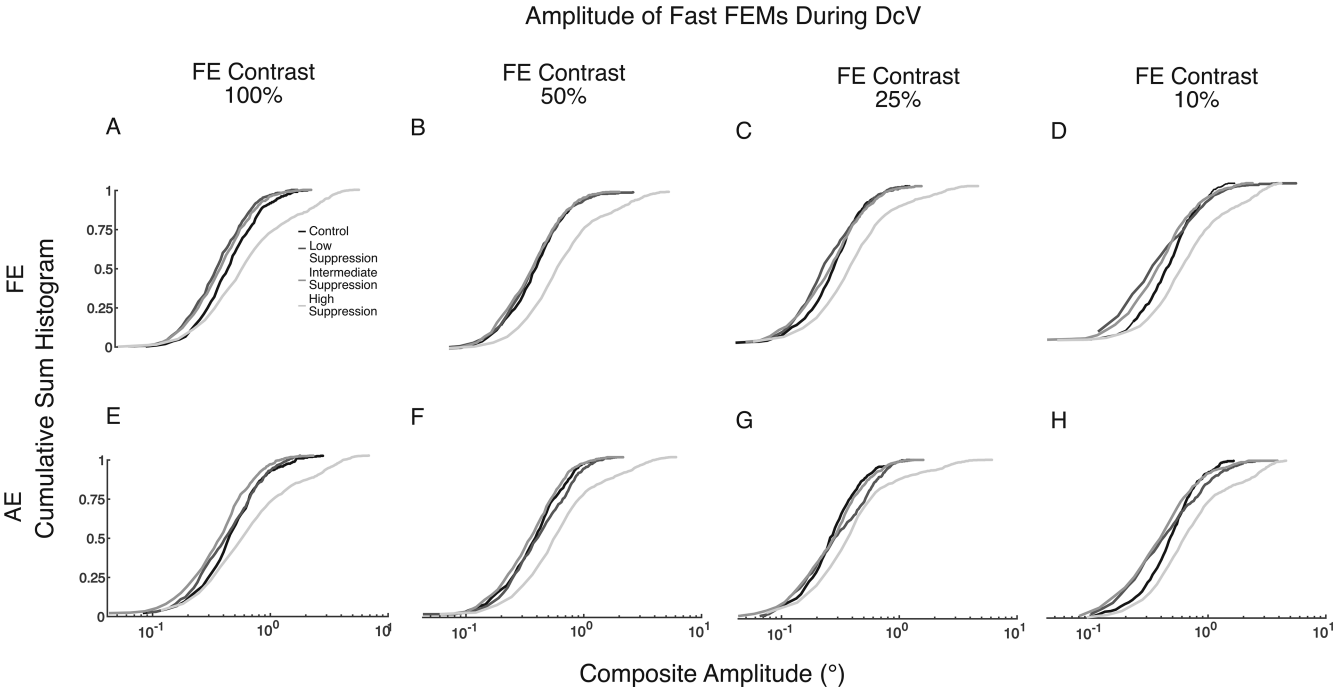

Figure 8. Cumulative sum histograms of composite amplitudes (degrees) for fast FEM of the fellow eye and amblyopic eye were obtained during DcV at different fellow eye contrasts: 100% (**A–E**), 50% (**B–F**), 25% (**C–G**), and 10% (**D–H**). The data were collected from the control group (depicted in *black*), the low suppression group (represented in *dark gray*), the intermediate suppression group (shown in *gray*), and the high suppression group (illustrated in *light gray*).

analyzed the 25th, 50th, 75th, and 90th percentiles of the amplitude of the AE and FE (see Table 4). For the majority of the percentiles, the amplitude of the FE and AE is greater regardless of FE contrast, with post hoc comparisons demonstrating statistically significant differences between subjects with high suppression and controls.

Table 4. Composite Amplitude of Fast FEM of Fellow Eye and Amblyopic Eye During DcV Across the Suppression Groups

Percentile	FE Contrast	Control	Low Suppression	Intermediate Suppression	High Suppression	Kruskal-Wallis Analysis of Variance
10th	100%	0.23 ± 0.05	0.21 ± 0.06	0.21 ± 0.07	0.39 ± 0.39	**$P = 0.032$**
		(0.23 ± 0.05)	(0.22 ± 0.08)	(0.22 ± 0.09)	(0.39 ± 0.40)	**$P = 0.016$**
	50%	0.22 ± 0.07	0.24 ± 0.12	0.19 ± 0.06	0.36 ± 0.31	**$P = 0.001$**
		(0.23 ± 0.06)	(0.23 ± 0.06)	(0.22 ± 0.09)	(0.36 ± 0.34)	$P = 0.055$
	25%	0.23 ± 0.06	0.25 ± 0.13	0.22 ± 0.09	0.36 ± 0.24	**$P = 0.006$**
		(0.22 ± 0.05)	(0.26 ± 0.10)	(0.22 ± 0.08)	(0.36 ± 0.27)	**$P = 0.034$**
	10%	0.24 ± 0.08	0.23 ± 0.07	0.23 ± 0.11	0.39 ± 0.29	**$P = 0.021$**
		(0.24 ± 0.08)	(0.24 ± 0.12)	(0.22 ± 0.09)	(0.37 ± 0.29)	**$P = 0.008$**
25th	100%	0.33 ± 0.07	0.27 ± 0.08	0.29 ± 0.11	0.50 ± 0.44	**$P = 0.008$**
		(0.32 ± 0.07)	(0.3 ± 0.1)	(0.30 ± 0.11)	(0.51 ± 0.46)	**$P = 0.021$**
	50%	0.30 ± 0.08	0.33 ± 0.16	0.29 ± 0.12	0.51 ± 0.38	**$P = 0.004$**
		(0.31 ± 0.08)	(0.34 ± 0.13)	(0.31 ± 0.14)	(0.50 ± 0.40)	**$P = 0.012$**
	25%	0.33 ± 0.08	0.34 ± 0.14	0.31 ± 0.13	0.54 ± 0.36	**$P = 0.003$**
		(0.32 ± 0.08)	(0.40 ± 0.19)	(0.32 ± 0.14)	(0.51 ± 0.38)	**$P = 0.023$**
	10%	0.32 ± 0.11	0.38 ± 0.19	0.32 ± 0.13	0.54 ± 0.39	**$P = 0.005$**
		(0.32 ± 0.10)	(0.38 ± 0.17)	(0.32 ± 0.13)	(0.53 ± 0.40)	**$P = 0.012$**
50th	100%	0.46 ± 0.11	0.43 ± 0.17	0.40 ± 0.14	0.70 ± 0.51	**$P = 0.024$**
		(0.45 ± 0.10)	(0.46 ± 0.16)	(0.42 ± 0.15)	(0.71 ± 0.54)	**$P = 0.041$**
	50%	0.41 ± 0.11	0.49 ± 0.25	0.41 ± 0.16	0.70 ± 0.46	**$P = 0.002$**
		(0.42 ± 0.12)	(0.49 ± 0.19)	(0.42 ± 0.17)	(0.71 ± 0.5)	**$P = 0.001$**
	25%	0.48 ± 0.13	0.49 ± 0.22	0.47 ± 0.20	0.76 ± 0.55	**$P = 0.010$**
		(0.45 ± 0.11)	(0.57 ± 0.25)	(0.49 ± 0.23)	(0.74 ± 0.67)	$P = 0.057$
	10%	0.46 ± 0.12	0.58 ± 0.35	0.48 ± 0.21	0.75 ± 0.46	**$P = 0.012$**
		(0.44 ± 0.12)	(0.61 ± 0.27)	(0.47 ± 0.21)	(0.73 ± 0.48)	**$P = 0.009$**
75th	100%	0.61 ± 0.16	0.62 ± 0.28	0.60 ± 0.24	0.93 ± 0.62	$P = 0.051$
		(0.61 ± 0.15)	(0.67 ± 0.24)	(0.61 ± 0.26)	(0.96 ± 0.66)	**$P = 0.048$**
	50%	0.58 ± 0.17	0.67 ± 0.33	0.58 ± 0.25	0.99 ± 0.58	**$P = 0.001$**
		(0.58 ± 0.18)	(0.71 ± 0.31)	(0.61 ± 0.25)	(0.98 ± 0.65)	**$P = 0.003$**
	25%	0.65 ± 0.19	0.69 ± 0.30	0.66 ± 0.31	1.06 ± 0.73	**$P = 0.015$**
		(0.60 ± 0.17)	(0.77 ± 0.35)	(0.67 ± 0.31)	(1.08 ± 0.88)	**$P = 0.029$**
	10%	0.65 ± 0.15	0.82 ± 0.54	0.70 ± 0.36	1.02 ± 0.55	**$P = 0.015$**
		(0.61 ± 0.15)	(0.87 ± 0.46)	(0.71 ± 0.36)	(0.99 ± 0.57)	**$P = 0.024$**
90th	100%	0.79 ± 0.22	0.83 ± 0.36	0.86 ± 0.39	1.25 ± 0.80	$P = 0.106$
		(0.80 ± 0.24)	(0.92 ± 0.38)	(0.89 ± 0.43)	(1.27 ± 0.83)	$P = 0.124$
	50%	0.72 ± 0.22	0.92 ± 0.67	0.81 ± 0.34	1.27 ± 0.74	**$P = 0.001$**
		(0.72 ± 0.24)	(0.91 ± 0.44)	(0.79 ± 0.32)	(1.34 ± 0.85)	**$P = 0.000$**
	25%	0.84 ± 0.31	0.91 ± 0.46	0.98 ± 0.62	1.48 ± 1.06	**$P = 0.024$**
		(0.80 ± 0.31)	(0.98 ± 0.41)	(0.93 ± 0.48)	(1.42 ± 1.17)	$P = 0.104$
	10%	0.83 ± 0.20	1.18 ± 0.93	1.05 ± 0.49	1.32 ± 0.64	**$P = 0.046$**
		(0.83 ± 0.21)	(1.19 ± 0.71)	(1.08 ± 0.56)	(1.36 ± 0.69)	$P = 0.062$

(FE Contrast, fellow eye contrast varied at 100%, 50%, 25%, and 10%, whereas the amblyopic eye contrast was at 100% for all DcV trials. All the values in parenthesis are for the amblyopic eyes.

Figure 9 summarizes the normalized cumulative sum histogram of the composite velocity of slow FEMs in controls (black line) and amblyopic/strabismic subjects with low suppression (dark gray), intermediate suppression (medium gray), and high suppression (light gray) obtained during DcV at varied FE contrasts. There is a rightward shift of the distribution of the velocity of the slow FEMs of FE and AE during DcV at all FE contrasts in those with high suppression than the other groups.

We analyzed the 25th, 50th, 75th, and 90th percentiles of the velocity of the AE and FE (see Table 5). For most percentiles, the velocity of the FE and AE is greater regardless of FE contrast, with post hoc comparisons demonstrating statistically significant differences between subjects with high suppression and controls. Additionally, at the 10th, 25th, and 50th percentile, the velocity of AE was significantly higher in subjects with low suppression than in controls for both 10% and 25% contrast levels. In contrast, at the 75th percentile, the difference was significant for 25% contrast levels. At the 25th and 50th percentile, the velocity of FE was significantly higher in subjects with low suppression than in controls for 25% contrast levels.

Our study also quantified vergence instability obtained in controls and amblyopic/strabismic subjects categorized as low, intermediate, and high suppression groups at various FE contrast levels (10%, 25%, 50%, and 100%; see Table 6). The main effect of varied FE contrasts was significant (F (2.6, 150.1) = 5.8, P = 0.001), indicating that change in FE contrasts affects vergence instability. The main effect of group showed a statistically significant difference in vergence instability across suppression groups (F (3, 57) = 3.85, P = 0.014), indicating that vergence instability was different across various suppression groups. However, the interaction effect between the group and contrast level was

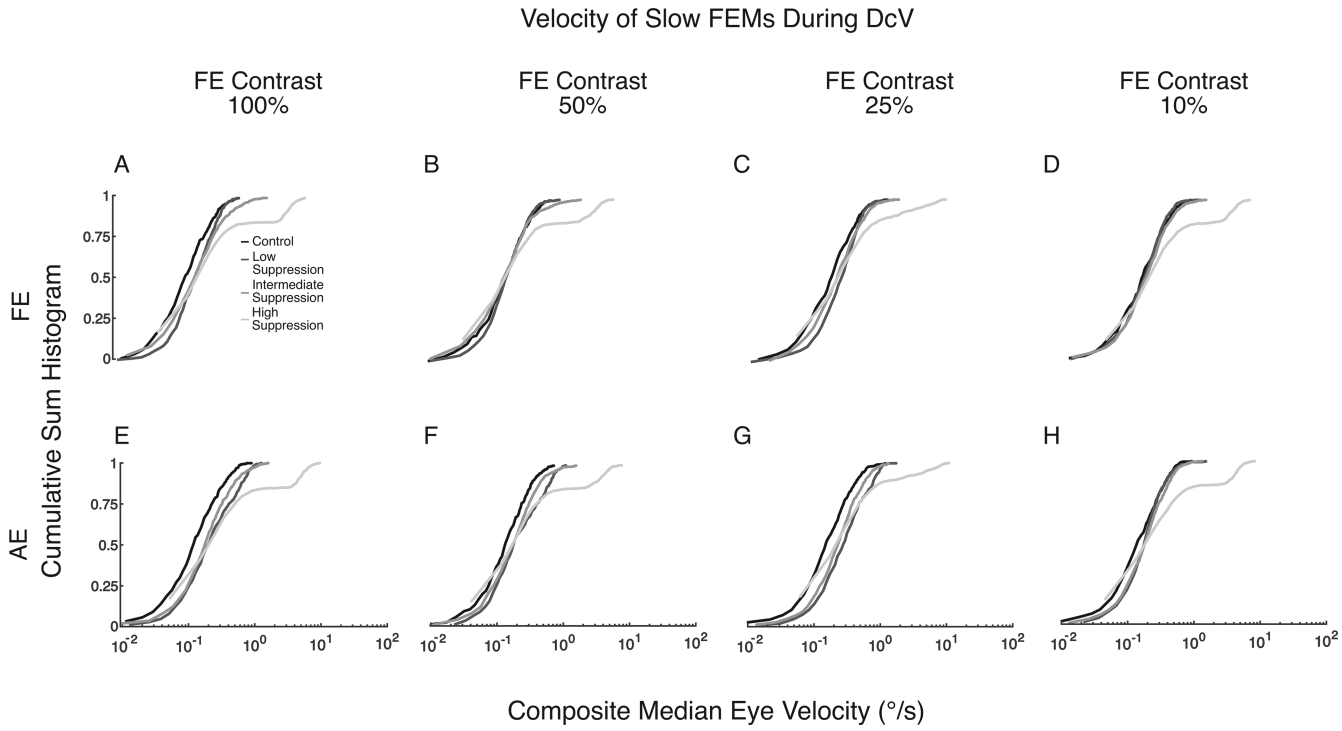

Figure 9. Cumulative sum histograms of composite velocity (degrees/sec) for slow FEM of the fellow eye and amblyopic eye were obtained during DcV at different fellow eye contrasts: 100% (**A-E**), 50% (**B-F**), 25% (**C-G**), and 10% (**D-H**). The data were collected from the control group (depicted in *black*), the low suppression group (represented in *dark gray*), the intermediate suppression group (shown in *gray*), and the high suppression group (illustrated in *light gray*).

not significant (F (7.90, 150.2) = 0.752, P = 0.64). We found significant differences in vergence instability between the control and high suppression groups at 50% FE contrast (P = 0.009) and 25% FE contrast (P = 0.016) with a borderline difference at 100% FE contrast (P = 0.05) and no difference at 10% FE contrast (P = 0.1).

We investigated vergence instability across control and stereo groups (defined by stereoacuity: ≤ log 2 arcsec and > log 2 arcsec) at different FE contrast levels (10%, 25%, 50%, and 100%; see Table 7). The main effect of varied FE contrasts was significant (F (2.6, 152.1) = 6.34, P = 0.001), indicating that change in FE contrasts affects vergence instability. The main effect of the group showed a statistically significant difference in vergence instability across controls versus good and poor stereopsis groups (F (2, 58) = 4.14, P = 0.021), indicating that vergence instability was different across various stereopsis groups. However, the interaction effect between the group and contrast level was not significant (F (5.24, 152.1) = 0.63, P = 0.684). Notably, a significant difference in vergence instability was found between the control group and the group with stereoacuity > log 2 arcsec at the 10% contrast level (P = 0.039).

Discussion

In this study, we conducted a comprehensive analysis of inter-ocular suppression and stereoacuity in subjects with amblyopia, both with and without concurrent strabismus, as well as in strabismic subjects without amblyopia. The main findings were (1) both stereoacuity deficits and inter-ocular suppression were closely linked to the visual acuity deficit of the AE and strabismus angle. (2) Inter-ocular suppression was evident in anisometropic and strabismic amblyopia as well as in strabismic subjects without amblyopia. Additionally, strabismic subjects, including those with amblyopia, who exhibited a fixation switch at 100% FE contrast under DcV, had less inter-ocular suppression than those who did not exhibit a fixation switch under DcV. (3) Stereoacuity deficits were more pronounced in subjects with nystagmus than those without nystagmus, but this relationship was not observed for inter-ocular suppression. We observed that subjects with poor stereoacuity displayed varying levels of inter-ocular suppression. This underscores the complex interplay between suppression and stereoacuity, suggesting that stereoacuity, may not always be contingent upon the level of inter-ocular suppression. (4) Eye movement abnormalities, such as increased amplitudes and velocities in both fast and slow FEMs, were more pronounced in subjects with high inter-ocular suppression.

Inter-Ocular Suppression in Amblyopia and Strabismus Without Amblyopia

In amblyopia and strabismus without amblyopia, single vision without diplopia is maintained during binocular viewing despite the inherent absence of fusion. The visual input may alternate between the two eyes in strabismus without amblyopia. In contrast, in amblyopic subjects, this is achieved through cortical mechanisms that involve continuous suppression of visual input from the amblyopic eye.[19] It has been postulated that the etiology of visual acuity deficits observed in AE may be attributed to protracted cortical suppression.[55] Inter-ocular suppression has been fairly

Table 5. Composite Velocity of Slow Fixation Eye Movements of Fellow Eye and Amblyopic Eye During Dichoptic Viewing Across the Suppression Groups

Percentile	FE Contrast	Control	Low Suppression	Intermediate Suppression	High Suppression	Kruskal-Wallis Analysis of Variance
10th	100%	0.13 ± 0.05	0.22 ± 0.11	0.20 ± 0.15	0.64 ± 2.16	***P* = 0.034**
		(0.12 ± 0.06)	(0.29 ± 0.33)	(0.2 ± 0.11)	(0.72 ± 2.40)	***P* = 0.002**
	50%	0.15 ± 0.09	0.25 ± 0.15	0.20 ± 0.15	0.53 ± 1.56	$P = 0.190$
		(0.13 ± 0.05)	(0.33 ± 0.39)	(0.21 ± 0.12)	(0.62 ± 1.83)	***P* = 0.026**
	25%	0.13 ± 0.06	0.26 ± 0.16	0.22 ± 0.13	0.40 ± 0.86	***P* = 0.007**
		(0.13 ± 0.06)	(0.37 ± 0.38)	(0.22 ± 0.12)	(0.46 ± 1.11)	***P* = 0.007**
	10%	0.15 ± 0.05	0.24 ± 0.14	0.23 ± 0.14	0.59 ± 1.74	$P = 0.149$
		(0.13 ± 0.07)	(0.23 ± 0.06)	(0.22 ± 0.11)	(0.66 ± 2.06)	***P* = 0.006**
25th	100%	0.22 ± 0.10	0.34 ± 0.16	0.34 ± 0.23	0.82 ± 2.34	***P* = 0.017**
		(0.20 ± 0.08)	(0.44 ± 0.43)	(0.34 ± 0.18)	(0.96 ± 2.72)	***P* = 0.000**
	50%	0.25 ± 0.13	0.39 ± 0.19	0.32 ± 0.22	0.74 ± 1.91	$P = 0.260$
		(0.22 ± 0.1)	(0.50 ± 0.49)	(0.34 ± 0.20)	(0.85 ± 2.21)	***P* = 0.010**
	25%	0.23 ± 0.11	0.43 ± 0.17	0.34 ± 0.17	0.63 ± 1.21	***P* = 0.006**
		(0.22 ± 0.09)	(0.52 ± 0.47)	(0.35 ± 0.15)	(0.69 ± 1.46)	***P* = 0.002**
	10%	0.25 ± 0.09	0.38 ± 0.17	0.37 ± 0.19	0.81 ± 2.10	***P* = 0.033**
		(0.24 ± 0.10)	(0.44 ± 0.14)	(0.37 ± 0.15)	(0.91 ± 2.45)	***P* = 0.003**
50th	100%	0.43 ± 0.19	0.55 ± 0.22	0.56 ± 0.41	1.14 ± 2.78	$P = 0.083$
		(0.37 ± 0.16)	(0.68 ± 0.50)	(0.59 ± 0.30)	(1.28 ± 3.15)	***P* = 0.009**
	50%	0.42 ± 0.19	0.60 ± 0.32	0.58 ± 0.48	1.10 ± 2.46	$P = 0.206$
		(0.39 ± 0.14)	(0.75 ± 0.57)	(0.62 ± 0.35)	(1.24 ± 2.76)	***P* = 0.009**
	25%	0.45 ± 0.19	0.70 ± 0.21	0.57 ± 0.30	1.12 ± 2.11	***P* = 0.008**
		(0.41 ± 0.19)	(0.82 ± 0.52)	(0.58 ± 0.25)	(1.19 ± 2.56)	***P* = 0.005**
	10%	0.45 ± 0.21	0.62 ± 0.22	0.61 ± 0.30	1.18 ± 2.49	$P = 0.061$
		(0.43 ± 0.16)	(0.70 ± 0.21)	(0.60 ± 0.25)	(1.31 ± 2.91)	***P* = 0.004**
75th	100%	0.76 ± 0.40	0.88 ± 0.32	0.93 ± 0.65	1.58 ± 3.29	$P = 0.351$
		(0.65 ± 0.32)	(1.04 ± 0.62)	(0.97 ± 0.52)	(1.86 ± 3.78)	***P* = 0.034**
	50%	0.81 ± 0.32	0.97 ± 0.51	0.89 ± 0.70	1.55 ± 2.94	$P = 0.389$
		(0.67 ± 0.28)	(1.10 ± 0.62)	(1.05 ± 0.69)	(1.76 ± 3.33)	***P* = 0.023**
	25%	0.77 ± 0.37	1.13 ± 0.39	0.91 ± 0.51	1.86 ± 3.30	***P* = 0.025**
		(0.66 ± 0.31)	(1.20 ± 0.55)	(0.92 ± 0.38)	(1.88 ± 3.83)	***P* = 0.008**
	10%	0.79 ± 0.37	0.96 ± 0.34	0.94 ± 0.43	1.76 ± 2.94	$P = 0.071$
		(0.76 ± 0.26)	(1.06 ± 0.30)	(0.98 ± 0.35)	(1.89 ± 3.33)	***P* = 0.012**
90th	100%	1.18 ± 0.43	1.23 ± 0.44	1.40 ± 0.98	2.24 ± 3.94	$P = 0.376$
		(0.96 ± 0.46)	(1.49 ± 0.79)	(1.62 ± 1.05)	(2.66 ± 4.42)	***P* = 0.016**
	50%	1.23 ± 0.51	1.30 ± 0.79	1.40 ± 1.23	2.31 ± 3.41	***P* = 0.048**
		(1.06 ± 0.42)	(1.55 ± 0.79)	(1.71 ± 1.08)	(2.55 ± 3.81)	***P* = 0.033**
	25%	1.15 ± 0.51	1.73 ± 0.97	1.42 ± 0.80	2.64 ± 4.07	$P = 0.062$
		(1.08 ± 0.55)	(1.80 ± 0.79)	(1.45 ± 0.52)	(2.73 ± 4.50)	***P* = 0.020**
	10%	1.21 ± 0.56	1.49 ± 0.69	1.39 ± 0.63	2.41 ± 3.45	$P = 0.213$
		(1.20 ± 0.40)	(1.64 ± 0.77)	(1.47 ± 0.51)	(2.65 ± 3.93)	***P* = 0.012**

(FE, fellow eye contrast varied at 100%, 50%, 25%, and 10%, whereas the amblyopic eye contrast was 100% for all DcV trials. All the values in parenthesis are for the amblyopic eyes).

Table 6. Vergence Stability in Controls and Amblyopic and Strabismic Subjects Per Suppression Groups

FE Contrast	Control	Low Suppression	Intermediate Suppression	High Suppression	Main Effect	Interaction
100%	−0.16 ± 0.41	0.02 ± 0.45	0.03 ± 0.52	0.02 ± 0.41	F (2.635, 150.178) = 5.807,	F (7.904, 150.178) = 0.752,
50%	−0.18 ± 0.52	0.05 ± 0.47	0.03 ± 0.53	0.05 ± 0.41	$P = 0.001$	$P = 0.64$
25%	−0.05 ± 0.47	0.17 ± 0.34	0.12 ± 0.48	0.17 ± 0.44		
10%	−0.06 ± 0.36	0.11 ± 0.47	0.30 ± 0.52	0.11 ± 0.45		

well established as a mechanism for vision loss in strabismic amblyopia.[20,25,56–63] We attempted the nonius cross-alignment procedure during the experimental session to allow for alignment and fusion of the two eyes in subjects with strabismus. However, owing to the reported transient visibility and variable location of the nonius cross by multiple strabismic subjects, along with the fluctuating eye deviation in the dichoptic environment, we opted to keep the stimulus presentation unaltered, foregoing adjustments based on nonius cross measurements.[40] This could potentially have resulted in over-estimating the measured suppression in subjects with strabismus, however, within our cohort,

Table 7. Vergence Stability in Controls and Amblyopic and Strabismic Subjects Per Stereopsis Groups

FE Contrast	Control	Good Stereopsis	Poor Stereopsis	Main Effect	Interaction
100%	−0.16 ± 0.19	0.02 ± 0.46	0.17 ± 0.44	F (2.622, 152.063) = 6.340, $P = 0.001$	F (5.244, 152.063) = 0.631, $P = 0.684$
50%	−0.18 ± 0.23	0.15 ± 0.46	0.15 ± 0.45		
25%	−0.05 ± 0.23	0.29 ± 0.50	0.27 ± 0.43		
10%	−0.06 ± 0.36	0.25 ± 0.46	0.29 ± 0.45		

anisometropic amblyopia subjects also exhibited increased inter-ocular suppression, which was comparable to that seen in strabismic/mixed amblyopia subjects. Although some studies have shown evidence for suppression in anisometropic amblyopia,[57,62,64–67] other studies have found weaker suppression in anisometropic compared to strabismic amblyopia.[19,64] Most of these studies had anisometropic amblyopia participants with less visual acuity deficit than those with strabismic amblyopia. We had anisometropic, strabismic, and mixed amblyopia subjects with similar levels of visual acuity deficit which could explain the comparable levels of suppression between anisometropic versus strabismic/mixed amblyopic subjects.

It has been previously suggested that the inter-ocular suppression measured using the dichoptic technique is a direct measure of the severity of amblyopia,[68] that is, the poorer the visual acuity, the greater the suppression.[10] In our study, we found that suppression as measured using the dichoptic motion coherence threshold correlated with the severity of amblyopia – and that treated/mild amblyopic subjects and strabismic subjects without amblyopia usually have low inter-ocular suppression.[10,68,69] Indeed, clinical investigations have corroborated this notion, demonstrating that a reduction in suppression corresponds with an enhancement in the visual acuity of the AE.[68] In agreement with these studies, we found that the severity of amblyopia was the key determinant in predicting the extent of inter-ocular suppression. Suppression is also a major sensorial abnormality in humans with strabismus with and without amblyopia. We found that besides the visual acuity deficit of the AE, the strabismus angle was a key determinant of the extent of inter-ocular suppression. This agrees with previous studies that have shown that more substantial degrees of suppression are associated with large-angle strabismus cases characterized by dense amblyopia, whereas milder degrees of suppression are evident in instances of micro-strabismus unaccompanied by amblyopia.[67,70,71]

Stereoacuity Deficit in Amblyopia and Strabismus Without Amblyopia

Stereoacuity, the ability to perceive depth, is known to be compromised in strabismus, irrespective of the presence of amblyopia. Stereoacuity begins to develop around 6 months and continues to evolve through early childhood, rapidly maturing to nearly adult levels within the first 12 to 24 months of life.[72–75] There is gradual refinement in stereoacuity until adult-level perceptual discrimination is attained at ages 4 to 7 years.[76,77] Because the first 24 months of life appear to be an early critical period for the maturation of stereoacuity, this is when stereoacuity is most likely to be susceptible to disruption by a brief period of abnormal visual experience. Recent studies have also shown that the development of stereoacuity in individuals with strabismus is influenced by age of onset, the duration of constant misalignment, and age at alignment.[78–80] Previous studies have shown that the extent of visual acuity deficit in amblyopic subjects also determines the stereoacuity deficits.[81] However, this relationship is more evident in individuals with anisometropic amblyopia than those with strabismic amblyopia, highlighting its complexity.[13,15,82] Further, we and others have shown that in amblyopia, whereas recovery of visual acuity is seen to some extent with patching therapy, stereoacuity is not always restored,[13,61,83–85] particularly in strabismic amblyopia.[10,86] Thus, as expected, we found that visual acuity deficits and strabismus angle determine stereo acuity deficits.

Besides these factors, we found that the presence of nystagmus is associated with more pronounced stereoacuity deficits. FMN is a characteristic oculomotor deficit suggestive of disruption of binocularity in the first year of life. Tychsen and colleagues have shown that the severity of latent (fusion maldevelopment) nystagmus is associated with the duration of binocular decorrelation in early infancy.[87] Patients with amblyopic and strabismus without amblyopia can develop nystagmus that does not meet the criteria of FMN.[31,40] We have found that subjects with nystagmus with and without FMN have poor recovery of stereoacuity after strabismus repair[34] as well as after patching therapy.[37] Thus, existing research in both strabismic nonhuman primates and humans, along with the findings of the current study, collectively indicate that the presence of nystagmus in individuals with strabismus, whether they have amblyopia or not, is closely associated with poor or absent stereoacuity.

Relationship of Suppression, Stereoacuity Deficits, and FEM Abnormalities

Besides visual acuity deficit and strabismus, the persistent deficit in stereoacuity could also be due to active suppression of the AE by the FE.[88] Previous studies have shown that individuals with good visual acuity and stereoacuity have less inter-ocular suppression.[5,19,21,25,89–91] Interestingly, our study's multiple regression analysis revealed a weak negative correlation between stereoacuity deficits and inter-ocular suppression, a relationship notably contingent on the severity of amblyopia. None of the previous studies have evaluated FEM abnormalities in conjunction with stereoacuity deficits and inter-ocular suppression. We found patients with strabismus and amblyopia who did not have nystagmus overall had better stereoacuity deficits with inter-ocular suppression levels dependent on the severity of visual acuity deficit of the amblyopic eye and strabismus angle. On the other hand, within our cohort, the relationship between stereoacuity and suppression was more complex in patients with nystagmus. Overall, as a group, the presence of nystagmus

was associated with more marked deficits in stereoacuity. We had five amblyopic subjects and one strabismic subject without amblyopia with low inter-ocular suppression but poor/absent stereoacuity. Interestingly, all six subjects with low suppression but poor/absent stereoacuity had nystagmus with and without FMN. In other words, subjects who exhibited low levels of inter-ocular suppression but concurrently presented with poor or absent stereoacuity invariably demonstrated nystagmus. Thus, it is evident that the intricate association between stereoacuity deficits and inter-ocular suppression warrants further exploration, and the analysis of FEM waveforms holds promise in elucidating the intricate patterns of visual function deficits in strabismus and amblyopia.

Fixation Switch and Fast and Slow FEM Abnormalities Under DcV and Inter-Ocular Suppression and Treatment Implications

Our previous work has shown that fixation instability, characterized by increased amplitudes and velocities of fast and slow eye movements, is associated with more pronounced visual function deficits in amblyopia. These deficits include contrast sensitivity deficits observed in monocular and binocular viewing, visual acuity deficits in the AE, and stereoacuity deficits.[28,32,43,54,92,93] In the current study, we observed that subjects with amblyopia and strabismus with high inter-ocular suppression tend to display greater amplitude in fast eye movements, increased velocity in slow eye movements, and increased vergence instability than those with low suppression. Thus, these findings demonstrate that the FEM abnormalities are linked to inter-ocular function deficits observed in these clinical populations.

Both conventional therapy, such as patching, and emerging treatments, such as dichoptic therapy, have variable treatment outcomes.[94–98] We have previously shown that eye tracking can be helpful in predicting the treatment response of patching treatment.[37] Fixation switch behavior on eye movement recordings under DcV provides evidence that the AE can overcome the suppression at lower FE contrasts and attend to the presented target. We have previously shown that eye movement recordings can be useful in detecting fixation switches under DcV in patients with strabismus.[40] The prior study did not concomitantly evaluate inter-ocular suppression in patients with and without a fixation switch. In the current experiments, patients with strabismus exhibiting fixation switches under DcV tend to display reduced inter-ocular suppression. Another valuable measure is the evaluation of modulation of fixation eye movements under DcV.[16,25,99] Subjects experiencing a greater increase in fixation or vergence instability or more pronounced FEM abnormalities under DcV may tender amblyopia treatment less effective.[100,101] These findings are particularly relevant, as recent US Food and Drug Administration (FDA)-approved dichoptic therapies incorporate eye tracking, potentially making fixation switch and FEM abnormalities valuable markers for monitoring treatment outcomes.

In conclusion, our comprehensive study has shed light on the multifaceted interactions among visual acuity deficits, stereoacuity, inter-ocular suppression, and fixation eye movement abnormalities in the context of amblyopia and strabismus. These intricate relationships challenge conventional notions and underscore the nuanced nature of visual deficits in these clinical populations. Future studies aimed at characterizing fixation eye movement abnormalities within the framework of dichoptic treatment outcomes are warranted.

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