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Reduced Monocular Luminance Promotes Fusion But Not Mixed Perception in Amblyopia

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Purpose. The purpose of this study was to understand how monocular luminance reduction affects binocular balance and examine whether it differentially influences fusion and mixed perception in amblyopia.

Methods. Twenty-three normally sighted observers and 12 adults with amblyopia participated in this study. A novel binocular rivalry task was used to measure the phase duration of four perceptual responses (right- and left-tilts, fusion, and mixed perception) before and after a neutral density (ND) filter was applied at various levels to the dominant eye (DE) of controls and the fellow eye (FE) of patients with amblyopia. Phase durations were analyzed to assess whether the duration of fusion or mixed perception shifted after monocular luminance reduction. Moreover, we quantified ocular dominance and adjusted monocular contrast and luminance separately to investigate the relationship between changes in ocular dominance induced by the two manipulations.

Results. In line with previous studies, binocular balance shifted in favor of the brighter eye in both normal adults and patients with amblyopia. As a function of the ND filter's density, the duration of fusion and mixed perception decreased in normal controls, whereas that of fusion but not mixed perception increased significantly in patients with amblyopia. In addition, changes in binocular balance from luminance reduction were more significant in more balanced amblyopes or normal observers. Furthermore, shifts in binocular balance after contrast and luminance modulation were correlated in both normal and amblyopic observers.

Conclusions. The duration of fusion but not mixed perception increased in amblyopia after monocular luminance reduction in the FE. Moreover, our findings demonstrate that changes in ocular dominance from contrast-modulation and luminance-modulation are correlated in both normal and amblyopic observers.

Keywords: amblyopia, luminance, fusion, mixed perception, interocular suppression, binocular rivalry

A neural disorder that impairs vision, amblyopia arises from abnormal visual development during the critical period when neural plasticity peaks.[1] Abnormal visual experience from anisometropia (blur), strabismus (misalignment), as well as pattern deprivations from congenital cataract and ptosis,[2,3] can disrupt visual information and misguide how the brain learns to process visual information from both eyes,[4] inducing amblyopia.[5] There are both monocular and binocular deficits associated with amblyopia. For instance, the visual acuity of the amblyopic eye (AE) is worse than that of the fellow eye (FE), and this difference is not optically correctible.[2] In addition, amblyopia exhibits imbalanced suppression between the two eyes[4,6]; the FE severely suppresses the weight of the AE's input to binocular vision,[5] thereby diminishing stereopsis,[7] hand-eye coordination,[8,9] self-perception of physical competence,[10] and reading performance.[11] The recovery of monocular deficit does not ensure the recovery of binocular vision. To illustrate, even if the difference in visual acuity between the eyes is reduced from the standard patching therapy that occludes the FE for months or years,[12] improvement in binocular functions, such as stereopsis[13] and fusion,[14] does not always follow. For this reason, both clinicians and researchers have recognized the need to develop novel therapeutic strategies that target binocular functions of amblyopia.

Luminance affects how the visual system processes information from two eyes in both normal[15] and amblyopic vision.[16–19] If luminance is reduced in both eyes, the response of the visual system gets attenuated. Similarly, when the luminance of one eye is dimmed with a neutral density (ND) filter, its weight of the input becomes attenuated, thereby shifting interocular suppression in favor of the brighter eye. This is so because modifying the input of one eye, such as by changing its contrast or luminance, can influence the net balance of interocular suppression. In normal vision, reduced luminance in one eye disrupts binocular balance[16–19] and stereopsis[20] to a similar extent regardless of which eye gets dimmed because their natural state of binocular vision is balanced. However, in amblyopia, not only does luminance affect binocular balance but also induces different changes depending on which eye gets dimmed.[5,21,22] A recently proposed therapeutic strategy for mitigating amblyopic imbalance involves dimming the FE, potentially benefiting stereopsis[23] and balance.[16–19] The influence of differential levels of luminance on the process of how input from two eyes gets combined has been modeled using computational statistics. According to the contrast gain-control model, reducing luminance of the FE not only reduces the weight of said eye in binocular combination but also its inhibitory influence on the AE's weight. In other words, reducing luminance of the FE decreases its gain control on the AE, thereby lifting the suppression on the AE. In light of these perceptual and modeling studies,[17,18,24] modulation of the FE's luminance has been proposed as an effective strategy for treating binocular visual deficits in amblyopia.[18,19]

Increasing the weight of the poor eye to amblyopic binocular vision indeed benefits binocular balance[16–19] and stereoscopic performance.[23] However, there are two perceptual possibilities after the weight of the AE has increased. First, due to reasons such as the AE's increased internal noise,[25,26] which can disrupt visual input, information from both eyes might not get combined properly, inducing mixed perception (e.g. diplopia). Another possibility is an increased frequency of fusion because both eyes with similar weights could process visual information in a normal fashion. However, most psychophysical studies have only measured binocular visual functions where either fusion or mixed perception can be induced but not both[17–19,27–30] because binocular combination and rivalry (e.g. suppression and mixed perception) have been thought to be mutually exclusive.[31–35] According to a model from Georgeson and Wallis,[36] fusion and mixed perception can be separately induced depending on the parameter of the visual stimulus, such as disparity[32,37,38] or orientation difference between the stimuli shown to two eyes.[39] This model states that when visual inputs from two eyes are compatible, fusion is induced; if fusion fails, the input from one eye is suppressed (i.e. rivalry)[37,40]; when both fail, double vision (i.e. mixed perception) will occur. Nevertheless, there are some instances where these three perceptual states can coexist even if the stimulus remains static[41,42] when the difference in the stimulus between two eyes is not too large. Using a perceptual test that evokes the three perceptual states with static stimuli could resolve whether changes in interocular balance in favor of the poorer eye are accompanied by an increased occurrence of fusion rather than mixed perception.

Therefore, in this study, we developed a psychophysical task that can induce perceptual states of rivalry, fusion, and mixed perception using static stimuli. This task was inspired by a recent study proposing that fusion and rivalrous perceptual states are not mutually exclusive but can both originate from a single, static stimulus across tri-stable interocular dynamics.[43] We aimed to investigate whether reducing monocular luminance could benefit both binocular balance and the perceptual outcome. Luminance was modulated by placing an ND filter on one of the two eyes because it does not affect the Michelson contrast of an image; the maximum and minimum levels of luminance would be both affected equally. We hypothesized that luminance reduction would differentially affect mixed perception and fusion in normal and amblyopic observers. We also modulated contrast in one eye and explored whether the resulting changes in ocular dominance would be correlated with those induced by monocular luminance modulation.[18]

METHODS

Participants

Twenty-three observers (mean ± SD = 24.3 ± 1.2 years old; 5 male subjects; details in Table 1) with normal or corrected to normal vision ($\leq$0.00 logMAR) and 12 anisometropic amblyopic observers (mean ± SD = 28.3 ± 5.8 years old; 5 male subjects; details in Table 2) with best-corrected vision were recruited in this study. A subset of them participated in each experiment of the study. Amblyopia was defined based on the Preferred Practice Patterns of the American Academy of Ophthalmology[12] with an interocular best-corrected visual acuity (BCVA) difference of two or more than two lines (0.20 logMAR). All the amblyopic observers were diagnosed by ophthalmologists at the Eye Hospital of the Wenzhou Medical University and had no other ocular abnormalities, including structural anomalies or fixation problems. All observers were tested at their BCVA by wearing spectacles during the experiment. Subjects were naive to the purpose of the study except for the primary author and provided written informed consent before the experiment. The study followed the Declaration of Helsinki and was approved by the Ethics Committee of Wenzhou Medical University (approval number: 2023-053-K-01).

Apparatus

Experiments 1 and 2 were respectively conducted on a MacBook Pro (13-in., 2017; Apple, Inc., Cupertino, CA, USA) and an Alienware (EYE666 11th Gen Intel Core i7-1165G7, 2.80 GHz) computer. The stimuli were generated by running MATLAB R2016b (version, 9.1.0 MathWorks, Inc., Natick, MA, USA) and Psychotoolbox extension 3.0.14.[44] Gamma-corrected head-mounted goggles (GOOVIS, AMOLED display, NED Optics, Shenzhen, China) were used to dichoptically present the stimuli. The goggles had a resolution of 1920 × 1080 pixels, a refresh rate of 60 hertz (Hz) and a maximal luminance of 150 cd/m^2. The pixels per degree of the goggles' screen was 41.6.

Stimuli and Procedure

At the display screen's maximal luminance, a novel binocular rivalry paradigm was used. It induced four perceptual responses that represent suppression, mixed perception, and fusion. Each test block contained two parts, the alignment trial and the test phase, which lasted for 180 seconds. In both parts, there was a thin pixelated binary noise frame (see Fig. 1A) that facilitated convergence and fusion. During the alignment trial, subjects were asked to adjust the location of one-half of the cross using the keyboard, eventually combining two separate parts of the cross into a seamless whole. Then, subjects began the test phase. Two gratings shown separately to the two eyes (size = 4.2 × 4.2 degrees) were surrounded by a circular cosine envelope (window = 2.8 × 2.8 degrees), which blurred their edges. Randomly assigned for each test block, the orientation of the grating for one eye had a positive orientation relative to the horizontal axis, whereas the other had a negative orientation. By continuously pressing certain keys of the keyboard, subjects would report whether they perceived one of the four percepts (see Fig. 1A): (1) right or (2) left tilt of the binocularly perceived grating (suppression), (3) horizontal grating with no tilt (fusion), and (4) piecemeal (partially mixed) or

Table 1. Details of 23 Normal Observers

Subject	Age/Sex	Refraction OD/OS	VA (logMAR) OD/OS	RDS (Arcsec)	Expt
N1	24/F	−4.50/−0.25*30 −4.75/−0.50*130	−0.06 −0.06	20	1, 2A, 2B
N2	24/F	−6.00 −5.00	−0.1 −0.16	20	1, 2A, 2B
N3	23/F	−3.00/−1.25*5 −2.75/−1.25*170	−0.1 −0.1	20	1, 2A, 2B
N4	24/F	−4.00/−0.50*140 −2.75/−1.00*20	−0.08 −0.08	30	1
N5	23/F	−4.00/−0.25*143 −3.50/−0.75*145	−0.1 −0.1	20	1
N6	24/F	−0.75/−0.50*50 −1.25/−1.00*175	0 0	25	1
N7	25/F	−3.75 −3.75/−1.00*10	0 0	25	1
N8	24/F	Plano +0.50	−0.06 −0.08	20	1
N9	28/F	−2.25 −2.75/−0.25*47	0 0	20	1
N10	23/M	−3.25 −3.50	−0.1 −0.1	25	1
N11	24/F	−3.75/−0.50*35 −4.00/−1.00*135	0 0	25	1
N12	23/M	−1.75 −1.75	0 0	20	1
N13	25/F	−0.75/−0.25*35 −0.75	−0.1 −0.1	20	1
N14	25/F	−3.25 −3.25/−1.00*170	−0.18 −0.1	20	1, 2A, 2B
N15	24/F	−2.25/−0.25*90 −1.75/−0.50*85	0 0	20	1, 2A, 2B
N16	24/F	−4.00/−1.25*3 −3.25/−0.75*150	0 0	20	1, 2A, 2B
N17	24/M	−4.00/−1.25*3 −3.25/−0.75*150	−0.08 −0.1	20	1, 2A, 2B
N18	25/M	−2.00/−0.50*40 −2.25/−0.50*165	−0.16 −0.16	20	1, 2A, 2B
N19	23/F	−3.75/−0.50*10 −3.00/−1.00*175	−0.1 −0.02	20	1, 2A, 2B
N20	26/F	−4.75 −4.75	−0.1 −0.2	20	1, 2A, 2B
N21	23/F	−5.00/−0.50*100 −5.50	0 0	20	2B
N22	25/F	−1.75/−1.25*75 −0.75/−1.25*75	−0.02 −0.04	20	2B
N23	26/M	−0.25/−0.25*180 0.00/−0.25*55	0 0	20	2B

Expt, experimentl F, female; M, male; OD, right eye; OS, left eye; RDS, Randot stereoacuity; VA, visual acuity.

superimposed (entirely mixed) sum of two gratings (mixed perception). The perceptual response was recorded in milliseconds.

All subjects were asked to perform a practice test to be familiarized with the task. The practice test was used to establish which eye was more perceptually dominant. Then, the subjects completed two blocks for each experimental condition. The phase duration of each percept throughout each block was recorded in all conditions (representative data in Fig. 1B). Luminance was reduced in one eye using the ND filter (0-, 1.3-, 1.7-, and 2-ND for luminance transmittance of 100%, 5%, 2%, and 1%, respectively) rather than changing the display of the screen because the screen's limited resolution prevented us from doing so. The filter was placed before the normal observers' dominant eye (DE) and the amblyopic observers' FE. These ND filters were selected in light of previous studies demonstrating that binocular vision of several amblyopes does not respond readily to intermediate degrees of ND filters (for example 1-ND).[17,19] We had confirmed that the ND filter independently affected luminance without perturbing the Michelson contrast of the stimulus.

There were four different parameters of stimuli: luminance, spatial frequency, interocular orientation difference, and contrast ratio between the eyes. These four parameters were varied in the study depending on the goal of each experiment. The similarities and differences in configuration of the stimulus, procedures, and aims of the two

Table 2. Clinical Details of 12 Observers With Anisometropic Amblyopia

Patient	Age/Sex	Refraction OD/OS	VA (logMAR) OD/OS	RDS (Arcsec)	Squint	History	Expt
A1	22/M	0.00/−0.50*30 0.00/−5.00*175	−0.1 0.4	400	Ø	Detected at 8 years old, patched for several days, barely wearing glasses	1, 2A, 2B
A2	34/F	+6.00/−1.75*160 −0.25/−0.25*35	0.7 −0.1	400	Ø	Detected at 12 years old, patched occasionally for several months, have worn glasses until 25 years old since diagnosis	1, 2A, 2B
A3	32/F	+3.50/−1.50*165 −1.00	0.5 0	200	Ø	Detected at 8 years old, patched occasionally for 1 month along with bead threading, barely wearing glasses	1
A4	18/M	−8.25/−1.75*5 0.00/−2.50*175	0 0.4	400	Ø	Detected at 9 years old, patched for 1 year along with bead threading, have been wearing glasses since diagnosis	1, 2A, 2B
A5	24/F	−0.75/−0.25*180 +3.00/−0.75*60	0 0.2	200	Ø	Detected at 13 years old, have worn glasses for 1 week after diagnosis, no patching	1, 2A, 2B
A6	23/M	+3.00/−0.50*130 +0.25/−0.25*35	0.6 0	200	Ø	Detected at 9 years old, patched for 1 month along with bead threading, have worn glasses for 1 year since diagnosis	1, 2A, 2B
A7	34/F	+1.00/−0.75*5 −2.00/−0.25*60	0.2 −0.1	100	Ø	Detected at 12 years old, patched for 1 year along with bead threading, occasionally wearing glasses since diagnosis	1, 2A
A8	38/F	+2.25/−2.00*170 −0.50/−0.50*175	0.4 0.1	600	Ø	Detected at 13 years old, have worn glasses until 28 years old since diagnosis, no patching	1
A9	28/F	+0.75/−0.50*50 +6.50/−1.25*45	−0.1 0.5	200	Ø	Detected at 13 years old, patched for 3 months, barely wearing glasses	1, 2A, 2B
A10	30/M	−7.00/−0.75*135 −5.00/−0.75*58	0.3 0.06	80	Ø	Detected at 14 years old, have been wearing glasses since 13 years old, no patching	2B
A11	28/F	Plano +3.00/−2.25*10	0 0.5	200	Ø	Detected at 18 years old, no patching, barely wearing glasses	2B
A12	29/M	+4.00 +2.25	0.42 0.14	400	Ø	Detected at 13 years old, occasionally wearing glasses since 12 years old, no patching	2B

Expt, experiment; F, female; M, male; OD, right eye; OS, left eye; RDS, Randot stereoacuity; VA, visual acuity.

experiments are summarized in the subsections below and Table 3.

Experiment 1: Phase Duration of the Four Perceptual Responses. During the pilot experiment, we found that normal observers could not perceive all four perceptual states if we fixed the spatial frequency and orientation difference of the stimuli across subjects. Some of them could not perceive fusion, whereas others could not see mixed perception at all. This was because the bandwidth of orientation tuning[43] and spatial frequency[45] that permits fusion was highly individualistic. Because interocular luminance difference would induce binocular imbalance in normal observers, we predicted that phase durations of mixed perception and fusion would decline after monocular luminance reduction. If mixed perception and fusion were minimal even when luminance was unobstructed (i.e. 0-ND), then no decrease would be detected. Therefore, we first optimized the spatial frequency (within 0.65–0.85 c/deg) and orientation difference (within 11–16 degrees) of the stimuli for normal subjects (luminance levels: 0-ND and 1.3-ND on DE; $n = 13$) in one session. This enabled observers to perceive all four perceptual states with less than a 10% difference in proportions of phase duration between fusion and mixed perception during each test block. In another session, the spatial frequency (0.75 c/deg) and orientation difference (13 degrees) were consistent across subjects (luminance levels: 0-, 1.3-, 1.7-, and 2-ND on DE). Ten normal observers were tested under this condition to confirm the necessity of individualizing the stimulus parameters and further verify the outcome we obtained under the individualized condition. In these two sessions, the contrast ratio of the two gratings remained at 1 (50% contrast to both eyes).

As for amblyopic observers, we tested them at various luminance levels by placing 0-, 1.3-, 1.7-, and 2-ND filters on their FE. The spatial frequency (0.75 c/deg) and orientation difference (13 degrees) remained fixed, but they were tested at contrast ratios of 0.5 (100% contrast to AE, 50% to FE; $n = 9$) and 1 (50% contrast to both eyes; $n = 7$). The design was made because we assumed that their mixed perception and fusion would be minimal when the luminance of both eyes was at its maximum due to the FE's strong suppression on the AE. Therefore, there was no reason for us to optimize the stimuli for each of them at 0-ND condition. Patients with amblyopia who only reported seeing the percept shown to FE at the contrast ratio of 0.5 (50% contrast to the FE) did not participate in another contrast condition during which the contrast ratio was set at 1 because they had a severe imbalance.

Experiment 2: Ocular Dominance Index . In experiment 2, we examined the effect of changing contrast, luminance, or both on ocular dominance in normal and amblyopic observers. By doing so, we measured how ocular dominance responded to interocular luminance difference (experiment 2A) and whether changes in ocular dominance from contrast modulation and from luminance modulation

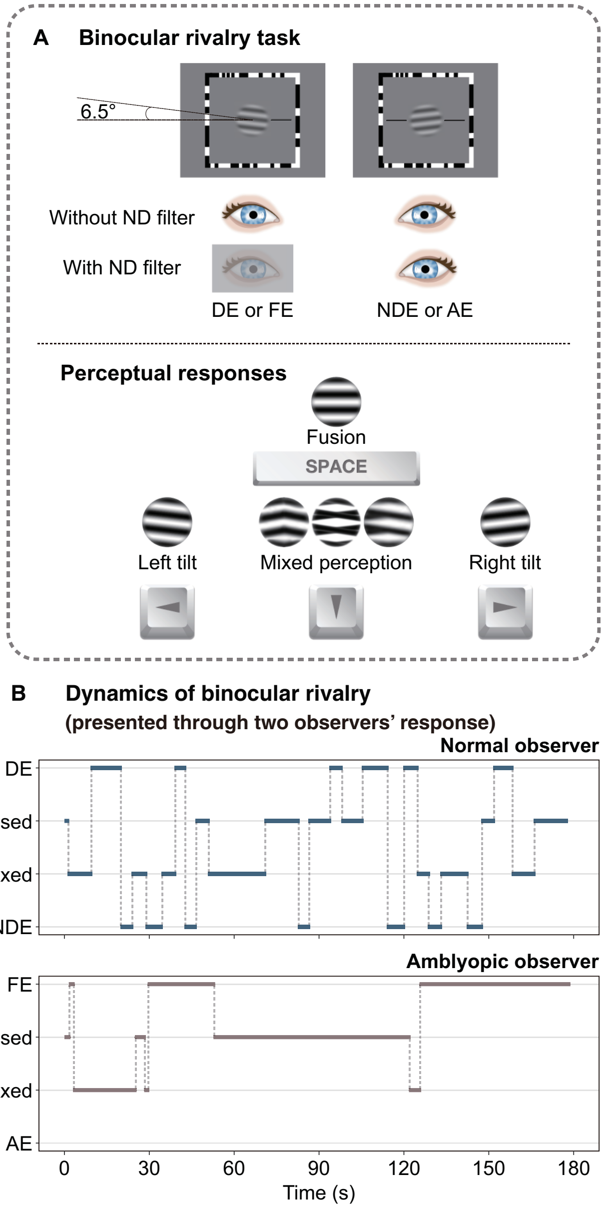

Figure 1. A binocular rivalry task with four choices of response. (**A**) Two sinusoidal gratings with the same size and spatial frequency but opposite orientations were dichoptically presented to two eyes. ND filters with different densities were placed before the dominant or fellow eye, allowing light transmittance of 100% (0-ND), 5% (1.3-ND), 2% (1.7-ND), and 1% (2-ND). Subjects reported what they perceived using the keyboard. (**B**) Time-series plots showing the perceptual dynamics of one representative control and one amblyope from one test.

were correlated (experiment 2B). We measured subjects' phase durations of percepts and converted them into ocular dominance index (ODI; see Equations 2 and 3). Spatial frequency (0.75 c/deg) and orientation difference (13 degrees) remained fixed across all subjects.

Experiment 2A. We wondered if binocular vision would respond differently to interocular luminance differences in normal adults and patients with amblyopia. We hypothesized that if ocular dominance was more balanced, binocular vision would respond more significantly to monocular reduction in luminance. To confirm our hypothesis, we calculated subjects' ODI when using 0-, 1.3-, 1.7-, and 2-ND filters on their dominant (controls) or the fellow (amblyopes) eye. Normal observers were tested at the contrast ratio of 1, whereas amblyopes were tested at two different contrast ratios to simulate two different interocular suppression states: in the contrast ratio of 1, both eyes were shown with gratings at 50% contrast, whereas in the contrast ratio of 0.5, the AE was shown at 100% contrast and the FE at 50%. Ten normal observers and seven amblyopic observers (all from experiment 1) participated in this experiment.

Experiment 2B. Binocular balance, which can be computed as ODI from phase durations using Equations 2 and 3 (see details below), can significantly shift from changes in luminance or contrast in one eye.[16–19,37] We wanted to examine whether changes in ODI from monocular contrast modulation would be correlated with those from monocular luminance modulation. The former was computed by first measuring ODI when the contrast level (50%) was equal in two eyes (contrast ratio = 1) and ODI when the DE's or FE's contrast was lower (50%) than the non-dominant eye (NDE) or AE (100%; hence, contrast ratio = 0.5), and then computing the difference between the two ODIs. Luminance was kept at 100% during the 2 ODI measurements. The change from monocular luminance reduction was calculated by first measuring ODI when the luminance level (100%) was equal in two eyes (luminance ratio = 1) and ODI when the DE's or FE's luminance was dimmer (1%, using a 2-ND filter) than the NDE or AE (100%; hence, luminance ratio = 0.01), and then calculating the difference between the two ODIs. Contrast was kept at 50% during the two ODI measurements. Then, we analyzed whether the difference between the first pair of ODI (monocular contrast modulation) was correlated with the difference between the second pair of ODI (monocular luminance modulation). The order of the four conditions was randomized for all observers. Thirteen normal observers (10 from experiment 2A) and nine amblyopic observers (6 from experiment 2A) participated in this experiment. Patients with severe amblyopia[17,46] whose phase duration of AE remained at 0 seconds even after monocular luminance and contrast modulations did not participate in this experiment because their ocular dominance index would not change.

Data Analysis

As mentioned before, the subject's response was obtained in milliseconds during testing. The sum of 4 responses, however, did not always amount to 180 seconds because when some subjects changed their response by switching one key to another, there was a brief period of no keypress. To resolve the differing sum of the response time across subjects, we converted the total phase duration of each response to its proportion (%) relative to the sum of all responses, which was then analyzed (see details in Statistical Analysis).

In addition, the dynamics of binocular rivalry were evaluated by pooling phase durations per key press of all individuals and plotting their distributions. These were then fitted to a model of gamma distribution[47,48]:

$$g(x) = \frac{\lambda^{a} x^{a-1}}{\Gamma(a)} e^{-\lambda x},\ \lambda > 0,\ a > 0,\ x \geq 0 \tag{1}$$

Table 3. Experimental Design of the Study

			Experimental Condition				
Expt	**Group**	**Key Question**	**SF (c/deg)**	**Ori Diff (Degrees)**	**ND**	**CR**	**Outcome Measure**
1	Nor	How does percept duration change after reducing luminance in one eye?	0.65–0.85	11–16	0, 1.3	1	Phase duration
	Am					0.5, 1	
2							
A	Nor	How does ocular dominance respond to luminance reduction in one eye?			0, 1.3, 1.7, 2	1	
	Am		0.75	13			Ocular dominance index (ODI)
B	Nor	Are changes in ocular dominance from contrast- and luminance-modulation related?			0, 2	0.5, 1	
	Am						

Am, amblyopic group; CR, contrast ratio between eyes; Expt, experiment; Nor, normal group; Ori diff, orientation difference between eyes; SF, spatial frequency.

where Γ is the gamma function, x is the duration per key press of one perceptual response, and λ and α are free parameters that characterize the rate ($\lambda = \mu/\sigma^2$) and shape ($\alpha = \mu^2/\sigma^2$), where μ and σ are the mean and the standard deviation of the phase duration. Because the data assumed the asymmetrical shape of the gamma distribution, we computed the median of phase duration in controls and amblyopes for further analysis.

When binocular balance was the main outcome of interest (i.e. experiment 2), we converted the proportion data to ODI using the equations below[49,50]:

$$ODI_{Nor} = \frac{p_{DE} - p_{NDE}}{p_{DE} + p_{mixed} + p_{NDE} + p_{Fused}} \tag{2}$$

$$ODI_{Am} = \frac{p_{FE} - p_{AE}}{p_{FE} + p_{mixed} + p_{AE} + p_{Fused}} \tag{3}$$

where p_{DE}, p_{NDE}, p_{mixed}, p_{Fused}, p_{FE}, and p_{AE} are the proportions of the perceptual duration in each test block. An ODI equal to 0 represents a perfect binocular balance. An ODI larger than 0 means that the fellow (amblyopes) or dominant (controls) eye is more perceptually dominant. An ODI less than 0 means that the amblyopic or NDE is more dominant. The ODI is directly determined by the relative difference between the proportions of exclusive percepts but not those of mixed or fused percepts.

Statistical Analysis

All statistical analyses were conducted using R software.[51] The normality of data was assessed with Shapiro-Wilk's test, and homogeneity of variance with Levene's test. Data of perceptual proportions from experiment 1 were analyzed using multivariate analysis of variance (MANOVA) and post hoc pairwise tests (Tukey's Honest Significant Test). Data of ODI from experiment 2A were linearly fitted as an exponential function of four ND levels (0- to 2-ND). Then, the slope of each subject was computed from all conditions, which included two contrast ratios for patients with amblyopia (0.5 and 1) and one contrast ratio for controls (1). Due to the design, purely repeated measures analysis and purely independent analysis would be inappropriate because one pairing of conditions would have paired subjects, and the other two pairings of conditions would have unpaired subjects. Therefore, we separately performed statistical analysis using a two-tailed paired *t*-test to compare the slopes of amblyopes between two contrast ratios and an unpaired Wilcoxon signed-rank test to compare the slopes between controls and amblyopes. For these comparisons, the significance level was adjusted to 0.017 (0.05/3) to prevent type I (false positive) errors. For experiment 2B, changes in ODIs from monocular luminance modulation and those from monocular contrast modulation were computed in normal and amblyopic observers. Then, the Spearman correlation analysis was conducted to determine whether luminance-driven changes in ODIs were correlated with contrast-driven changes in ODIs for each group.

RESULTS

Experiment 1: How Does Percept Duration Change After Reducing Luminance in One Eye?

In experiment 1, we examined the effect of luminance reduction in the more perceptually dominant eye on the four perceptual responses in both normal (Fig. 2) and amblyopic observers (Fig. 3). The spatial frequencies and orientations of the stimuli were individualized in one session and remained fixed in another across subjects for normal observers at one contrast ratio. For patients with amblyopia, the spatial frequency and orientation difference of stimuli were fixed but they were tested at two contrast ratios. Figure 2A shows percept proportions in controls at two levels of luminance while viewing stimuli with individualized configurations, which were inspired by our initial belief that proportions of mixed perception and fusion had to be robust because they would significantly decrease after luminance reduction. Indeed, according to post hoc pairwise tests, proportions of DE, fusion, and mixed perception decreased with a 1.3-ND filter (P values < 0.05; see Fig. 2A), whereas the proportion of NDE increased ($P < 0.001$). Similar results are shown in Figure 2B when the stimuli remained fixed across normal observers. Except for the NDE's proportion, the other three percepts' proportions all decreased significantly as a function of the strength of the ND filter.

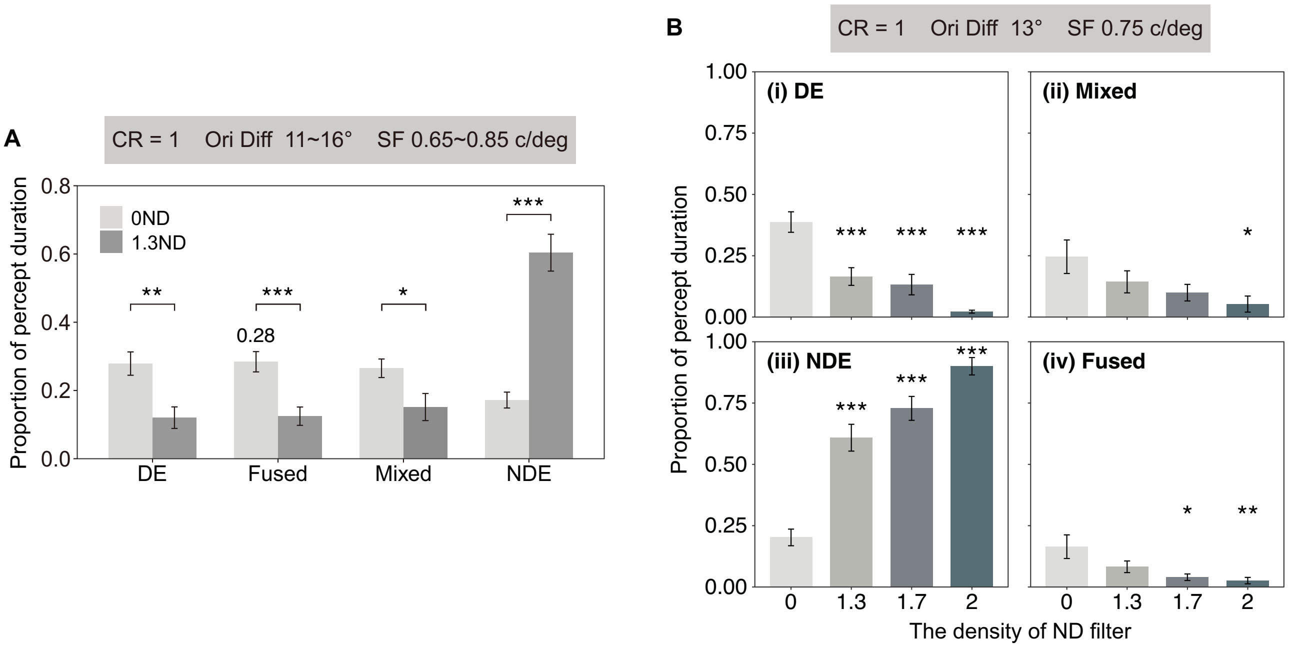

Figure 2. Bar plots showing averaged proportions of perceptual responses at different levels of luminance in normal observers. Error bars represent standard errors. Based on Tukey's post hoc pairwise tests, results with significant differences from baseline (0-ND) are labeled with asterisks: * $P < 0.05$, **$P < 0.01$, ***$P < 0.001$. (**A**) Proportions of percept durations at two luminance levels (0-ND and 1.3-ND) when the stimuli were unique ($n = 13$). For example, the mean proportion of fusion at 0-ND was 0.28 (annotated above the *light grey bar*). (**B**) Proportions of percept durations under four luminance levels (0-, 1.3-, 1.7-, and 2-ND) when the stimuli were uniform ($n = 10$). Each sub-panel represents each of the four perceptual responses at all four light levels. CR, contrast ratio; Ori diff, orientation difference; SF, spatial frequency.

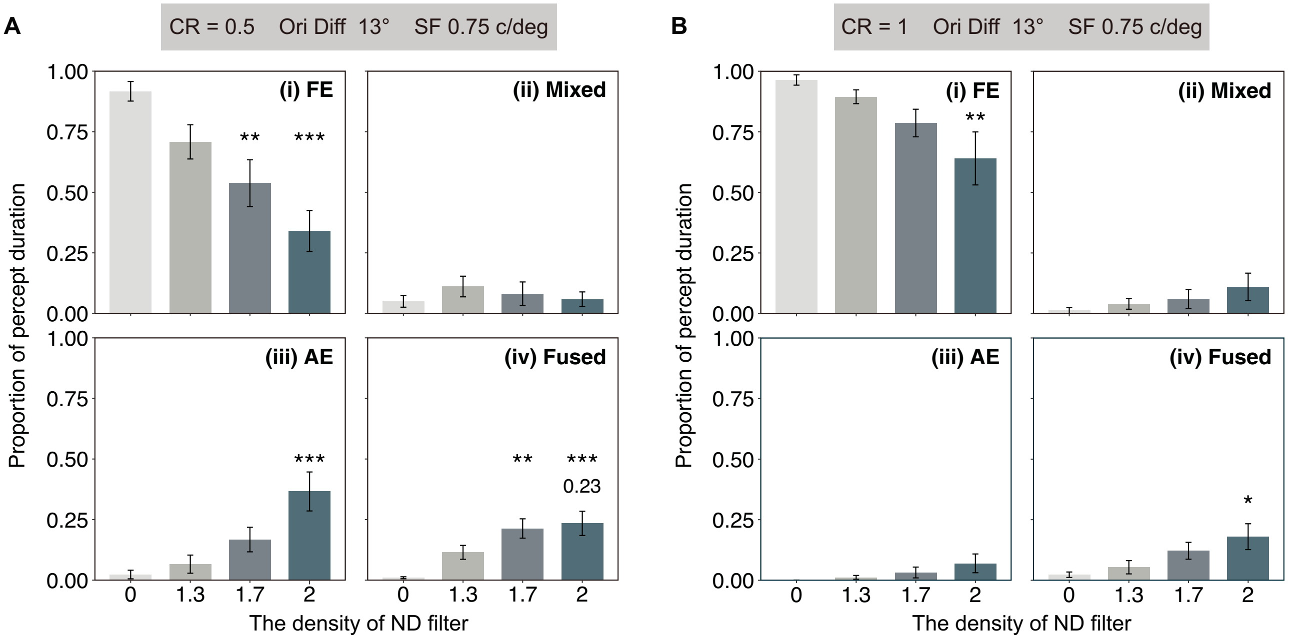

Figure 3. Bar plots showing averaged proportions of perceptual responses at four levels of luminance (with 0-, 1.3-, 1.7-, and 2-ND) in amblyopic observers. Each sub-panel represents each perceptual response at all light levels. Error bars represent standard errors. Based on Tukey's post hoc pairwise tests, results with significant differences from baseline (0-ND) are labeled with asterisks: *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$. (**A**) Proportions of percept durations when contrast ratio = 0.5 (AE at 100% and FE at 50%; $n = 9$). For instance, the mean proportion of fusion at 2-ND was 0.23 (annotated above the *dark bar*). (**B**) Proportions of percept durations when contrast ratio = 1 (AE at 50% and FE at 50%; $n = 7$). CR, contrast ratio; Ori diff, orientation difference; SF, spatial frequency.

Tukey's pairwise tests revealed significant differences (P values < 0.05) in these percepts' proportions between 0-ND (i.e. baseline) and other luminance levels (the results are shown in the asterisks in Fig. 2B). Besides, a larger variability in fusion and mixed perception at 0-ND can be observed when the stimuli were consistent across observers (see error bars of fusion and mixed perception at 0-ND in Fig. 2B) than when they were optimized for each subject (see error bars of fusion and mixed perception at 0-ND in Fig. 2A), indicating that individualizing the stimuli yielded more stable data.

Figure 3 shows the percept proportions of amblyopes at two contrast ratios (FE/AE). When the contrast ratio was set at 0.5 (AE's contrast higher; see Fig. 3A), proportions of percepts changed significantly as a function of luminance reduction except for mixed perception. According to post hoc pairwise tests, at 1.7-ND, the proportion of FE (see panel i of Fig. 3A) decreased significantly relative to 0-ND ($P = 0.007$), whereas the proportion of fusion increased significantly at 1.7-ND ($P = 0.001$; see panel iv of Fig. 3A) compared to 0-ND. When a 2-ND filter was applied, the proportion of fusion reached 0.23 (see panel iv in Fig. 3A), which was quite close to that of normal observers (proportion of 0.28; see Fig. 2A) without using the ND filter. The proportion of AE increased significantly at 2-ND relative to 0-ND ($P < 0.001$). In addition, when the contrast ratio was 1 (equal contrasts to both eyes; see Fig. 3B), the overall trend was similar. Specifically, the proportion of fusion increased significantly when 2-ND was introduced (see panel iv of Fig. 3B). However, there was no noticeable increase in AE's proportion of phase duration even at 2-ND. These findings show that if the net state of interocular suppression is more balanced (i.e. less inhibition), the relative proportions of fusion and AE can increase more readily in amblyopia.

Results from the two subject groups were analyzed together using a mixed 2-way MANOVA (between-subject factor = subject group and within-subject factor = luminance level) with datasets of both groups at the same experimental conditions (spatial frequency = 0.75 c/deg, orientation difference = 13 degrees, and luminance levels: 0-, 1.3-, 1.7-, and 2-ND; see the controls' data from Fig. 2B and the amblyopes' data from Fig. 3A). The analysis revealed a significant interaction between luminance level and subject group ($F_{12,\,201} = 3.86$, $P < 0.001$), indicating that the percept proportions shifted differently between controls and amblyopes after monocular luminance reduction. Then, this interaction was independently analyzed for each percept using 2-way ANOVA, which revealed that significant interactions existed in fusion ($F_{3,\,68} = 13.53$, $P < 0.001$) and the unfiltered eye's (NDE or AE) perception ($F_{3,\,68} = 7.38$, $P < 0.001$). Together, these findings show that binocular vision responded differently to interocular luminance differences between the two groups.

Dynamics of the fusional response were also assessed. The more stable the perceptual response, the longer it lasts before it switches to another. Phase duration of fusion was pooled across all subjects (see the controls' data from Fig. 2A and the amblyopes' data from Fig. 3A). Because the data of fusion were not normally distributed, gamma distribution was used to fit the pooled fusion data (see Equation 1 in Methods for fitting details; see Fig. 4) of patients with amblyopia at each reduced luminance level (1.3-ND–2-ND; Figs. 4B, 4C, 4D) and controls at the maximum luminance level (0-ND; see Fig. 4A) as reference. The fitting was robust (R^2 values > 0.9). The observed non-normal distribution of fusion response from our rivalry task resembles previously reported distribution patterns of phase durations in binocular rivalry with three response choices without fusion.[52] The parameters of the gamma distribution can also inform the spread of the data along time (seconds) before the perceptual switch as well as the location of the peak density of the pooled data. When using a 1.3-ND filter, the rate parameter λ of the amblyopic group (see Fig. 4B) was found to be lower than that of normal observers without an ND filter (see Fig. 4A). This indicates that the phase duration of fusion was more variable before the percept switched to another in patients with amblyopia at 1.3-ND than in healthy controls. In addition, the shape parameter α was lower in patients with amblyopia at 1.3-ND compared with the normal group, demonstrating that the peak of their distributions was more to the left of the x-axis (duration) than that of unfiltered normal observers. However, when ND filters with higher densities were used (1.7- and 2-ND; see Figs. 4C, 4D), these two parameters of patients with amblyopia became closer to the controls. These results indicated that for amblyopic observers, a 1.3-ND filter was insufficient to help them achieve a similar distribution of fusional response as normal observers. Finally, due to the distribution's asymmetrical shape, the median phase duration of fusion was computed. It was found to be 2.57 seconds at 1.7-ND for patients with amblyopia (see Fig. 4C), which was slightly higher than the median fusion duration of controls at 0-ND (2.47 seconds; see Fig. 4A) and that of patients with amblyopia at 2-ND (2.06 seconds; see Fig. 4D).

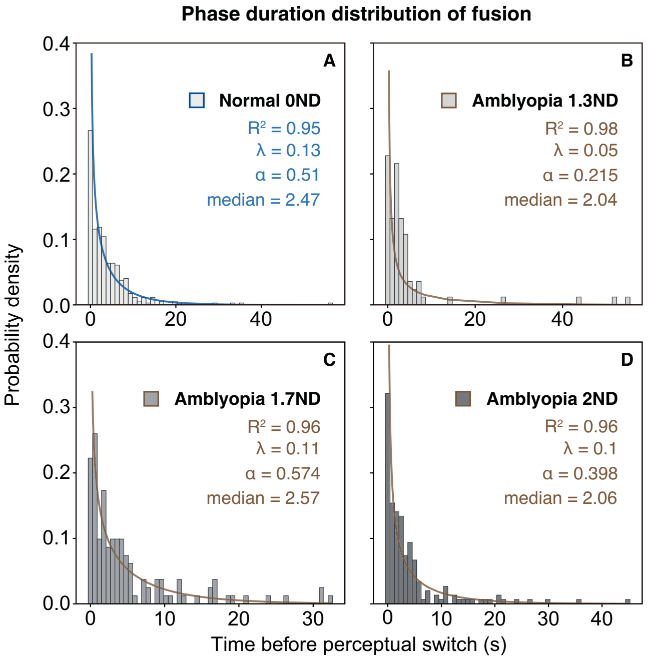

Figure 4. Distribution of phase durations for the fusional response in amblyopic (1.3-, 1.7-, and 2-ND; contrast ratio = 0.5) and normal observers (0-ND; contrast ratio = 1). The pooled data came from the controls' fusional response in Figure 2A and amblyopes' fusional response in Figure 3A. The solid curves represent the model-fit of the gamma distribution using the two parameters. R^2 was computed to quantify the goodness of the fit. (**A**) Phase duration distribution of fusion in controls at 0-ND. (**B**) Phase duration distribution of fusion in patients with amblyopia at 1.3-ND. (**C**) Phase duration distribution of fusion in amblyopes at 1.7-ND. (**D**) Phase duration distribution of fusion in patients with amblyopia at 2.0-ND.

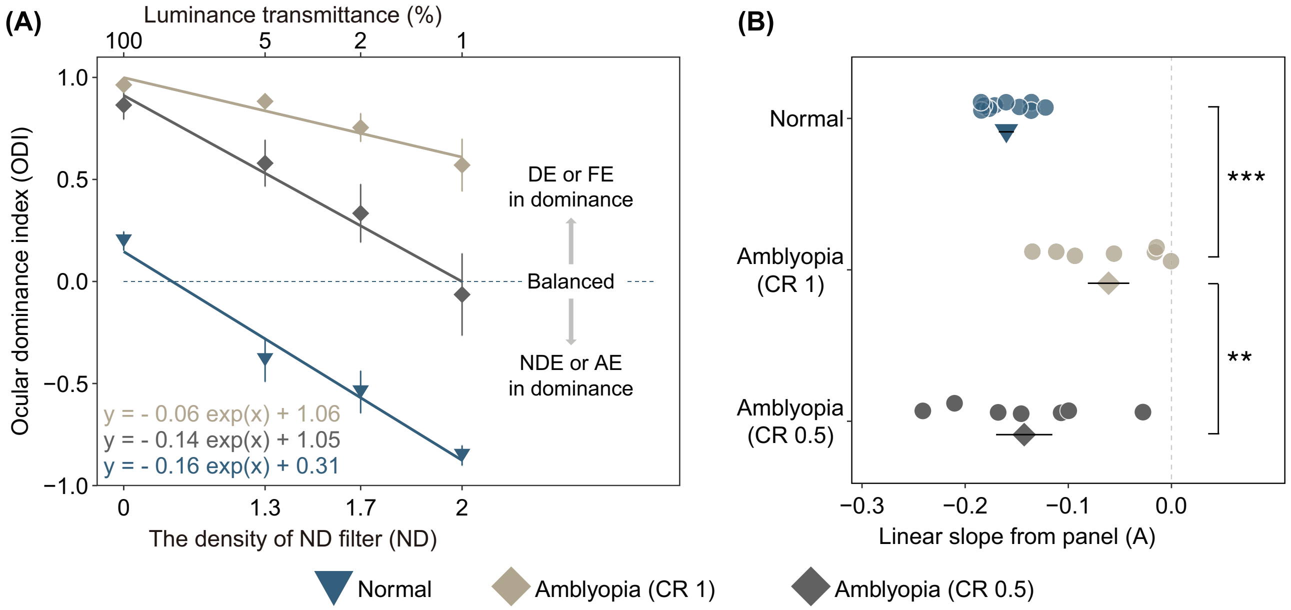

Figure 5. Changes in ODI after monocular luminance reduction in normal ($n = 10$) and amblyopic ($n = 7$) observers. (**A**) ODIs as a function of the density of ND filter in exponential scale. The secondary x-axis above represents the proportion of luminance transmittance. The *linear solid lines* indicate the best fit from linear regression (equations for each group are provided) and the *horizontal dashed line* represents binocular balance (ODI = 0). (**B**) Forest plot showing linear slopes from panel **A**. Each *circle point* represents the result of one subject. Each *diamond point* represents the mean slope of amblyope's data. The *triangle point* represents the mean slope of control's data. Each shape of the mean represents one sample pool. Error bars denote standard errors. ** $P < 0.00333$, *** $P < 0.00033$ after the Bonferroni correction for the P value. CR, contrast ratio.

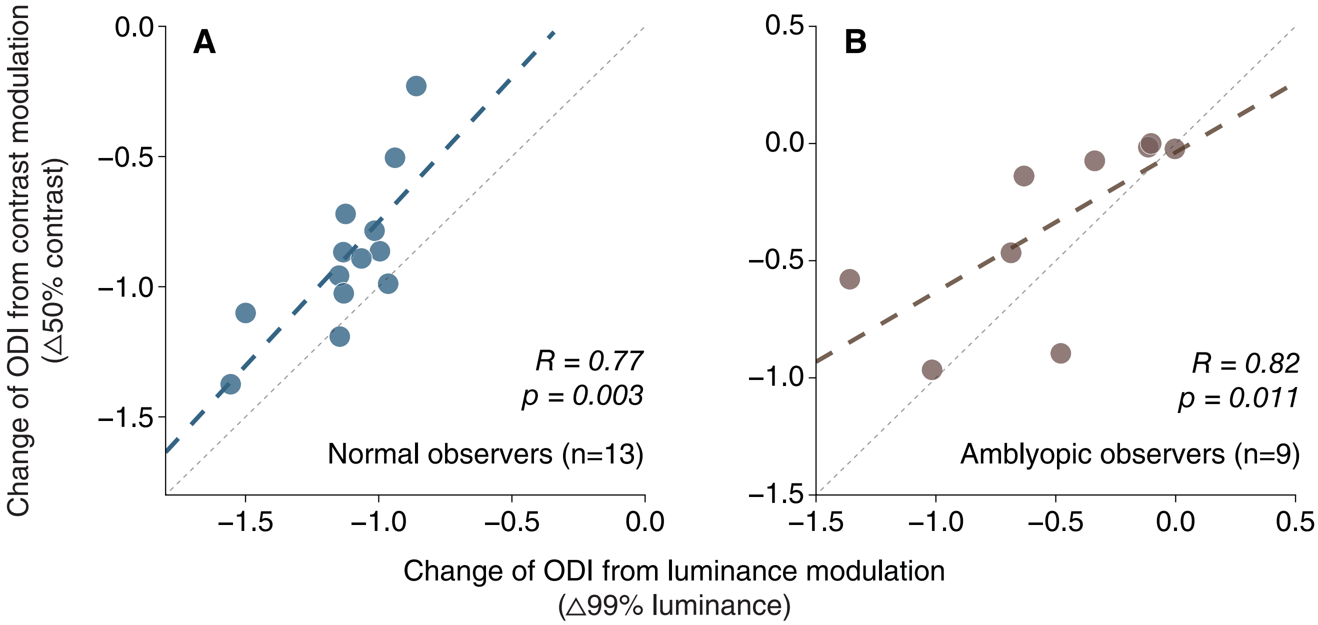

Figure 6. Correlation between changes in ODIs after contrast and luminance modulation in normal (panel **A**) and amblyopic observers (panel **B**). The amount of monocular contrast modulation was 50% whereas the amount of monocular luminance modulation was 99%. The *gray dashed line* represents the slope of unity. Each point represents the result of one subject.

Experiment 2A: How Does Ocular Dominance Respond to Luminance Reduction in One Eye?

Earlier in experiment 1, we observed that percept durations responded differently to monocular luminance reduction between normal and amblyopic observers. This difference could be due to the fact that controls have no net imbalance, whereas patients with amblyopia have a net imbalance due to the stronger suppression from the fellow eye to the amblyopic eye.[16] The ratio of 0.5 represents a moderate suppression from the FE and the ratio of 1 represents its severe suppression. The responsiveness of ocular dominance to monocular luminance reduction in these two suppression states of amblyopia was then compared to that of healthy controls (contrast ratio = 1).

An index of binocular balance, ODI was computed from proportions of phase durations (see Methods) and then plotted as a function of ND filters (Fig. 5A). For optimal fitting of linear regression, the x-axis was set to the exponential scale (i.e. exp(strength of ND)). The lower (or steeper) the linear slope, the more readily ocular dominance responds to changes in monocular luminance. The averaged slopes across all groups are shown in Figure 5B, which illustrates that the slopes of patients with amblyopia with moderate suppression state (contrast ratio = 0.5) and those of controls are similar ($W = 42$, P value = 0.536). On the other hand, the slopes were significantly different between the two contrast ratios in amblyopes ($t(6) = 4.71$, $P = 0.00328$), demonstrating that the suppression state determines how ocular dominance responds to changes in luminance within amblyopia.

Experiment 2B: Are Changes in Ocular Dominance From Contrast- and Luminance-Modulation Related?

Changes in ocular dominance could result from modulating contrast or luminance in one eye (see Fig. 5A). To examine whether contrast- and luminance-modulation shift ocular dominance through a common substrate, we measured the correlation between changes in ODIs from these two, separate experimental manipulations (Fig. 6). ODIs were measured at two contrast levels and two luminance levels. At one contrast level, 2 eyes were shown with 50% contrast; in another, one eye's contrast was increased to 100% contrast (see Methods for details). The differences in ODIs from 50% difference in contrast in one eye were computed and plotted along the y-axis of Figure 6. Similarly, at one luminance level, two eyes were shown at 100% light transmittance; in another, one eye's light transmittance was reduced to 1% (see Methods). The changes in ODIs from the difference of 99% light transmittance in one eye were then calculated and plotted along the x-axis of Figure 6. A Spearman correlation test was separately conducted in normal ($R = 0.77$, $P = 0.003$; see Fig. 6A) and amblyopic groups ($R = 0.82$, $P = 0.011$; see Fig. 6B). The strong correlation in both groups provides evidence that contrast and luminance might regulate ocular dominance through a common pathway.

Discussion

Reduced luminance in one eye decreases its perceptual gain in binocular vision[17–19] and its physiological response[53] from the visual cortex, thereby shifting the balance in favor of the brighter eye.[54] For example, amblyopic binocular imbalance can be alleviated if the FE's luminance is reduced[17–19,55] across spatial frequency. However, the perceptual consequences of reducing imbalance in amblyopia can vary depending on how the human visual system processes information from both the AE, which supposedly has increased internal noise,[25,26] and the FE with its reduced weight. One possibility is the failure of the two eyes to fuse information in situations where perceptual states of suppression, fusion, and mixed perception can co-exist, thereby diminishing visual experience and inducing mixed perception. Another possibility is that improved binocular balance from luminance modulation facilitates fusion. To resolve this issue, we used a novel binocular rivalry task to measure the effect of reduced monocular luminance on interocular dynamics in normal and amblyopic vision. In addition, we examined whether changes in ODI from contrast modulation were correlated with those from luminance modulation to see whether luminance regulates binocular balance in the human visual system by directly modulating the contrast-gain of the filtered eye.

In the first experiment, we examined the effect of monocular luminance reduction on the proportion of total duration from the four perceptual responses in normal and amblyopic observers. The effect was notably more significant in normal observers presumably because their state of interocular suppression was balanced; the proportion of the brighter NDE's phase duration significantly increased after dimming DE, whereas the proportion of the dimmer DE, fusion, and mixed perception's phase durations decreased dramatically (see Fig. 2). Conversely, in amblyopic observers (contrast ratio = 0.5; see Fig. 3A), the imbalance was reduced because the dimmer FE's phase duration decreased and the brighter AE's duration increased. In addition, the relative proportion of fusion increased while that of mixed response remained similar after luminance reduction. In addition, the total duration (sum of all keypresses) for fusion was the highest in patients with amblyopia when a 2-ND filter was applied (proportion of 0.23; see panel iv in Fig. 3A); this is similar to the proportion of fusion in controls when their stimuli were individually optimized (proportion of 0.28; see Fig. 2A). However, the median phase duration per key press of all fusion responses was the longest in patients with amblyopia when a 1.7-ND filter was introduced (see Fig. 4C). This was unexpected because the ocular dominance index was closer to 0 (i.e. perfect balance) when patients with amblyopia were viewing stimuli at contrast ratio of 0.5 with a 2-ND filter than with a 1.7-ND filter (see the dark brown line in Fig. 5A). Therefore, the high proportion of fusion at 2-ND in amblyopia could be due to the summation of short pulses of fusion rather than that of long, steady states of fusion. These findings show that the increased proportion of fusion in amblyopia after the ND filter has been applied does not equate to the increased stability of each fusion percept during binocular rivalry.

Results from experiment 2A revealed that ocular dominance was more susceptible to change from interocular luminance difference when the net suppression state was more moderate in amblyopia (i.e. when patients with amblyopia were tested at a contrast ratio of 0.5 rather than at 1; see Fig. 5A). Previous studies have shown that ocular dominance of controls responds more readily to monocular changes in luminance or contrast,[17–19] but whether this response can be different in amblyopes depending on their net suppression state has not been reported. Contrast sensitivity of the amblyopic eye shows deficits at intermediate and high ranges of spatial frequency.[56,57] However, we set the contrast of the amblyopic eye at 50% (contrast ratio = 1) and 100% (contrast ratio = 0.5) in the 2 contrast conditions, all of which were above the detection threshold, and at a low spatial frequency (0.75 c/deg). For these reasons, we believe that suppression from the AE to the FE, rather than the reported contrast sensitivity deficit of the amblyopic eye,[56,57] was responsible for the ODI that responded more to interocular luminance difference when the contrast ratio was set at 0.5 than at 1. In addition, according to the prediction from the model of Georgeson and Wallis,[36] mixed perception, but not fusion, would be induced when there was a failure of interocular suppression. However, patients with amblyopia from experiment 1 did not perceive mixed perception more frequently after wearing ND filters, demonstrating that suppression between the two eyes was still functional. Together, our findings from the two experiments both support that, in patients with amblyopia, suppression from the AE to the FE is functionally significant and that it determines the responsiveness of their ocular dominance to monocular luminance reduction.

In experiment 2B, we found that the changes in ODIs from contrast modulation were correlated with those from luminance modulation in normal and amblyopic observers. This indicates that both manipulations may influence the contribution of two eyes in binocular vision in a similar fashion. The process of binocular combination has been modeled and studied.[22,58–60] For example, a contrast-gain control model predicts how the two eyes combine spatial information at a suprathreshold contrast.[18,24,61] According to the model, reduction of luminance or contrast in one eye decreases the degree of suppression (i.e. gain-control) from said eye to the other eye.[18,24] The model describes how both mean luminance and contrast levels directly influence the strength of gain-control. Previous neurophysiological studies have provided evidence that in the primary visual cortex, there are a large number of neurons that can be modulated by both luminance and contrast change (i.e. luminance-contrast cells).[62,63] Ding and Levi,[18] who developed the said model, speculated that these neurons that process both luminance and contrast might modulate the depth of gain-control energy and determine how two eyes get combined into one binocular percept. Our findings that the effects of monocular luminance- and contrast-modulation on ocular dominance were correlated (see Fig. 6) also support their neurophysiological prediction.

In amblyopia, suppression from the FE to the AE is greater than its opposing counterpart.[5,21,22,64–66] In the past century, there have been a number of attempts on rebalancing interocular suppression in amblyopia, including the application of optical defocus[67,68] and atropine.[69] A modern approach involves controlling the contrast or luminance level of one eye's image using digital headsets or goggles.[22,70–72] However, adjusting the contrast level must occur in real-time under the natural viewing condition because the immediate visual environment can contain a wide and different range of spatial frequencies over time, requiring the real-time contrast adjustment to be differential across spatial frequency. Besides, reducing contrast compromises stereopsis.[73,74] Therefore, modulating mean luminance, which does not perturb contrast,[19] might be a promising approach to relieving the imbalance in amblyopia. However, adjusting luminance can bring about different changes under natural viewing conditions depending on the mean luminance level of the immediate environment. Therefore, it should be applied in a controlled viewing environment, where the mean luminance level remains fixed. Adjusting the luminance alone, however, might not be enough for patients with amblyopia to reach a normal balance because some amblyopes needed to have both contrast and luminance reduced (see Fig. 5 from experiment 2A). In the future, both contrast and luminance adjustments can be incorporated in a personalized fashion to dichoptic viewing therapies,[75–77] which have already been shown to improve the visual acuity of the AE and binocular balance.[76,78,79]

In this study, we measured the four perceptual responses at a low spatial frequency because the orientation tuning for fusion gets significantly narrowed as a function of spatial frequency.[45] Nevertheless, whether our findings can be generalized at higher spatial frequencies remains to be studied in the future. In addition, the age of some recruited patients with amblyopia was much older than their detected age. Although we had confirmed that they still had amblyopia before their enrollment, their age gap between the time of detection and the period of recruitment could have affected our results. Future studies should examine whether the tendency of changes in fusion and mixed perception is similar in patients with amblyopia who had just been diagnosed. Finally, only patients with anisometropic amblyopia were recruited in our study, limiting the potential applicability of our results to individuals with other types of amblyopia.

Our results show that the application of ND filters is promising both for reducing binocular imbalance and promoting fusion. Future studies should investigate the clinical utility of an ND filter for those with abnormal binocular vision. As we observed, the preferred strength of the ND filter could vary depending on the balance of each observer and their immediate visual surroundings.[18] Some might even require a combination of luminance and contrast reduction to achieve a normal balance. Finally, it will be worthwhile to investigate how the immediate benefit in binocular balance and increased occurrence of fusion upon wearing an ND filter can persist after its removal.

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