The Perceptual Consequences of Interocular Suppression in Amblyopia

Goro Maehara,[1,2] *Benjamin Thompson,*[3] *Behzad Mansouri,*[4] *Reza Farivar,*[5] *and Robert F. Hess*[6]

Purpose. It is known that information from an amblyopic eye can be strongly suppressed when both eyes are open. The authors investigated the way in which suppression influences the relative perception of suprathreshold contrast and luminance between a person's eyes under dichoptic viewing conditions.

Methods. Stimuli consisted of four patches of luminance or four patches containing gratings. Two patches were presented to each eye. Ten amblyopes with mild suppression (six strabismic, three anisometropic and strabismic, and one deprivation; mean age, 34.5 years) and three control observers with normal vision (mean age, 33.0 years) matched the appearance of the stimuli presented to each eye. The match involved manipulation of either luminance or contrast.

Results. Amblyopes with mild suppression decreased stimulus luminance in the fellow fixing eye or increased luminance in the amblyopic eye to achieve a match (mean matching luminance, 21.1 and 39.6 cd/m^2 for the fellow fixing eye and the amblyopic eye, respectively; standard luminance, 30 cd/m^2). This interocular mismatch was also observed when luminance was variable and contrast was kept constant (mean matching luminance, 22.8 cd/m^2 for the fellow fixing eye). On the other hand, the amblyopic eye showed no loss of perceived contrast. There was little or no mismatch between the two eyes of control participants with normal binocular vision.

Conclusions. Amblyopes have monocular deficits in contrast perception but dichoptic deficits in luminance perception, suggesting that suppression in its mild form involves luminance processing. (*Invest Ophthalmol Vis Sci.* 2011;52: 9011–9017) DOI:10.1167/iovs.11-7748

Amblyopia is a developmental disorder of vision associated with strabismus (misalignment of the eyes), anisometropia (unequal refractive power of the eyes), or deprivation (e.g., congenital cataract).[1] Various aspects of vision are impaired in amblyopia. It is well known that amblyopes show reductions in contrast sensitivity and spatial resolution in one eye (amblyopic eye), while the other eye (fellow fixing eye) is largely normal.[2–4] Moreover, spatial patterns may be perceived as distorted, and their spatial positions may be less certain when viewing through the amblyopic eye.[5–10] Impairments of temporal resolution have also been reported.[11] These dysfunctions cannot be corrected using lenses because amblyopia is a neural deficit. There is a growing consensus that amblyopia results from functional abnormalities in both the primary visual cortex and the extrastriate visual areas,[12–14] and there is recent evidence that the lateral geniculate nucleus may also be involved.[15] Although its exact cause is unclear, researchers have attributed amblyopia to strong binocular suppression,[16–18] an increase in neural noise,[9,19,20] undersampling of visual space,[21,22] and disorganization of neural connections.[10,23]

One might expect that perceived contrast is lower in the amblyopic eye than in the fellow fixing eye because of the poor contrast sensitivity. However, this is not the case when a stimulus is above threshold. Hess and Bradley[24] asked amblyopes to match the contrast of sinusoidal gratings between the amblyopic and fellow fixing eyes under monocular viewing and found that there was little mismatch in the high-contrast range. Rather, amblyopes slightly elevated the contrast of stimuli presented to the fellow fixing eye to achieve a match.[25,26] These findings suggest that perceived contrast in the amblyopic eye is near normal or overcompensated at suprathreshold contrast levels.

However, it is known that the information from the amblyopic eye is often strongly suppressed when both eyes are open. Suppression can be measured in amblyopia using clinical techniques such as the Worth four-dot test. In this test, dots presented to a suppressed eye cannot be perceived under dichoptic viewing conditions but can be clearly perceived under monocular viewing conditions.[2728] Tests such as this suggest that there must be a perceptual attenuation of suprathreshold signals processed by the amblyopic eye under dichoptic viewing at some site along the visual pathway. Dichoptic presentation is a useful tool with which to test amblyopes under conditions in which suppression is active. For example, Huang et al.[29,30] have measured the effects of suppression on interocular contrast matching in anisometric amblyopes and control observers with normal binocular vision using dichoptic stimuli. Their experiments replicated the previous findings that there was little interocular contrast mismatch.[24–26] On the other hand, they found that perceived contrast in one eye was significantly lowered when another grating was dichoptically presented at the same retinal position in the other eye (superimposed perceptually). This reduction in perceived contrast was much larger for anisometric amblyopes than control observers, indicating interocular inhibition in amblyopia. However, it should be noted that dichoptic presentation has one drawback in that suprathreshold perception cannot be ade-

From the [1]Graduate School of Arts and Sciences, University of Tokyo, Tokyo, Japan; [2]Japan Society for the Promotion of Science, Tokyo, Japan; [3]Department of Optometry and Vision Science, University of Auckland, Auckland, New Zealand; [4]Department of Internal Medicine, Section of Neurology, University of Manitoba, Winnipeg, Canada; [5]Harvard Medical School, Harvard University, Cambridge, Massachusetts; and [6]Department of Ophthalmology, McGill University, Montreal, Canada.

Supported by the Grant-in-Aid for JSPS Fellows from the Japan Society for Promotion of Science (GM), the Faculty Research Development Fund from University of Auckland (BT), and Canadian Institutes of Health Research Grants MOP53346 and MT108-18 (RFH).

Submitted for publication April 16, 2011; revised September 20 and October 1, 2011; accepted October 11, 2011.

Disclosure: **G. Maehara**, None; **B. Thompson**, None; **B. Mansouri**, None; **R. Farivar**, None; **R.F. Hess**, None

Corresponding author: Goro Maehara, Graduate School of Arts and Sciences, University of Tokyo, 3–8-1 Komaba, Meguro-ku, Tokyo 153-8902, Japan; goro@fechner.c.u-tokyo.ac.jp.

quately tested in amblyopes with strong suppression because they cannot perceive the stimulus presented to the amblyopic eye and a perceptual match cannot be obtained. In the present study, we therefore limited our selection of subjects to those who were able to perceive the dichoptic stimuli with both eyes simultaneously. To maximize the possibility that this could be done, we used parafoveal nonoverlapping stimuli. A similar approach is taken by the Worth four-dot test. We asked observers with amblyopia to match the luminance or contrast of stimuli under dichoptic viewing conditions to determine the extent to which either of these two image attributes is susceptible to the perceptual effects of suppression.

Materials and Methods

We conducted four matching experiments. In all the experiments, stimuli consisted of four square patches (Fig. 1). Patches were uniform gray squares in experiments 1 and 4, whereas a sinusoidal grating was presented within each patch in experiments 2 and 3. Gratings had an orientation of 45° and were counterphased at 4 Hz. Their spatial frequencies were 0.5 or 4 cyc/deg for experiment 2, and 1, 5, or 10 cyc/deg for experiment 3. Patch size was 3.5° of visual angle in the first two experiments and 2° in the latter experiments. Stimuli were presented for 2 seconds in experiment 3 and for 1.25 seconds in the other experiments. A square frame subtending 8.2° of visual angle was always presented to each eye throughout testing to support binocular fusion. The frames had 60 cd/m^2 of luminance. The stimulus background was black (0 cd/m^2) in all experiments with the exception of experiment 4.

Under dichoptic presentation conditions, one eye viewed the top-left and bottom-right patches and the other eye viewed the top-right and bottom-left patches. The observers' task was to manipulate a pair of patches seen by one eye (target) so that they had the same appearance as the pair of patches seen by the other eye (standard). In experiment 1, observers adjusted the luminance of the target patches. Luminance changed in log steps of a factor of 1.25. Standard patches had a luminance of 30 cd/m^2. In experiment 2, observers adjusted the contrast of target gratings with a step size of a factor of 1.6. Standard gratings had contrasts of 10%, 25%, or 50%. Mean luminance of the gratings was fixed to be 30 cd/m^2 both for the target and the standard stimuli. In experiment 3, the mean luminance of the target gratings was adjustable, with a step size of a factor of 1.4. Both target and standard gratings had a fixed contrast of 25%. In other words, if an observer decreased (or increased) mean luminance, peak-to-peak amplitude of sinusoidal gratings also decreased (or increased) to keep the contrast constant. Mean luminance of the standard gratings was 30 cd/m^2. In experiment 4, observers adjusted patch luminance and background luminance with a step size of a factor of 1.4. The standard stimulus had 30 cd/m^2 of patch luminance and 5 cd/m^2 of background luminance. The contrast between the patches and the background was kept constant at 71%; for example, $(30 - 5)/(30 + 5) = 0.71$ for both the target and the standard stimuli. Low-pass-filtered stimuli were also used in experiment 4. The cutoff frequency of the filter was 0.5 cyc/deg.

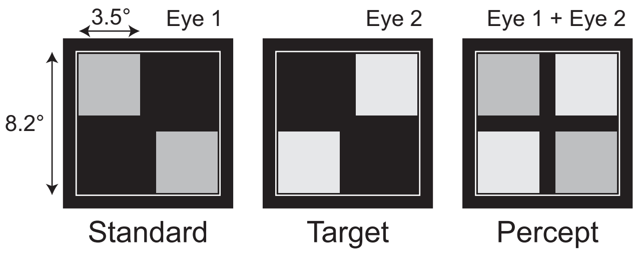

Figure 1. Stimuli presented in experiment 1. The patch size was 2° of visual angle for experiments 3 and 4. Gratings were presented within the patches in experiments 2 and 3.

Target stimuli were presented either to the amblyopic/nondominant eye or the fellow fixing/dominant eye in experiments 1 and 2, whereas only the fellow fixing/dominant eye saw the target stimuli in experiments 3 and 4. Observers completed four or eight trials for each condition. We report mean matching values over trials for individual observers.

In addition to the main experiments described, we conducted additional experiments to test the effects of sequential presentation of the target and standard stimuli on luminance matching (experiment 1), high spatial frequencies on contrast matching (experiment 2), the difference between the nasal versus temporal visual fields in luminance matching (experiment 3), and dilated pupils on luminance matching (experiment 4). A subset of our observers with amblyopia participated in these additional experiments.

Moreover, to verify that measurements made with the method of adjustment were accurate, we also measured points of subjective equality (PSE) in perceived luminance between the eyes using the method of constant stimuli in the context of experiment 3. For these measurements, there were six levels of target luminance (7.8, 11, 16, 22, 30, and 42 cd/m^2 for amblyopes; 18, 21, 25, 30, 36, and 42 cd/m^2 for controls) and three levels of spatial frequency (1, 5, and 10 cyc/deg). The standard luminance was fixed at 30 cd/m^2. Observers judged which grating pair was brighter and performed 40 trials at each target luminance. These measurements therefore consisted of $6 \times 3 \times 40 = 720$ trials in total, with a test duration of approximately 90 minutes. We used Palamedes, a set of MatLab (MathWorks, Natick, MA) functions, to fit logistic functions to the data and to estimate standard errors.[31] The PSE was calculated as the target luminance at which the probability of choosing the target was 50%.

Before starting a session, observers adjusted the perceived positions of stimuli for precise binocular alignment. For this purpose, a black nonius line was presented dichoptically. One vertical line appeared at the top center of a uniform gray square subtending 8.2° of visual angle; another appeared at the bottom center. We instructed observers to move the positions of the lines horizontally so that they were aligned. Observers were preadapted in a dimly lit room for 5 minutes so that their sensitivity was constant across sessions. The adaptation period was set at 10 minutes in the PSE experiment using the method of constant stimuli.

Stimuli were generated using a visual stimulating graphics card (VSG 2/5; Cambridge Research System Ltd., Kent, UK), which produces 15-bit gray-level resolution, and were presented on a video monitor (P1210; Compaq, Houston, TX). The display resolution was set to 1024×768 pixels. The refresh rate of the monitor was set to 120 Hz. The highest luminance of the display was 60 cd/m^2. The image on half the screen was directed to one eye and the image on the other half was directed to the other eye by means of an eight-mirror stereoscope. Presentation regions on the monitor subtended a visual angle of $10° \times 8.5°$ for each eye. The viewing distance was 57 cm.

Fourteen observers with amblyopia were recruited for this study. Four participants were excluded at the initial screening stage because they could not perceive stimuli presented to the amblyopic eye under dichoptic viewing due to strong suppression. Clinical details of the remaining 10 patients (age range, 20–49 years; mean age, 34.5 years) are provided in Table 1. All participants took part in experiment 1, and a subset took part in experiments 2 to 4 (Table 1). All participants, except for SP, had strabismus. Three participants (AS, KS, MA) had both strabismus and anisometropia (mixed deficits). Participant SP had deprivation amblyopia. Three control observers with normal stereovision and visual acuities of 20/20 also took part in the experiments (age range, 31–34 years; mean age, 33.0 years). One control observer (GM) was an author, and the other two were naive as to the aim of the experiment. All observers provided full informed consent to participate in this study, and the study followed protocols approved by the institutional ethics committee that were in accordance with the Declaration of Helsinki.

TABLE 1. Clinical Data of Patients with Amblyopia

Patient	Age (y)	Type	Eye	Refraction	Acuity	Age Detected (y)	Patching	Surgery	Experiment
AA	46	LE Strab	R	∅	20/20	4	None	None	1, 2, 3, 4
		ET 23°	L	∅	20/80				
ADS	25	RE Strab	R	∅	20/80	4	1 y	Age 7	1, 2, 3, 4
		ET 15°	L	∅	20/20		Age 4		
AM	33	RE Strab	R	∅	20/80	8	None	None	1, 2, 3, 4
		XT 1°	L	∅	20/20				
AR	49	RE Strab	R	+1.00 × 180	20/25	6	None	None	1, 3, 4
		ET 2°	L	+1.00 × 130	20/80				
MaS	36	LE Strab	R	∅	20/20	1	1 y	None	1, 2
		ET 2°	L	∅	20/70				
MoS	39	LE Strab	R	∅	20/20	8	None	None	1, 2, 3, 4
		ET 10°	L	∅	20/60				
AS	32	RE Mixed	R	+4.00	20/125	3	None	None	1, 3, 4
		ET 20°	L	∅	20/25				
KS	43	RE Mixed	R	+5.00/−1.00 × 180	20/100	10	1 mo	None	1, 2, 3, 4
		XT 4°	L	+0.50	20/25		Age 10		
MA	20	RE Mixed	R	+2.25/−0.5 × 110	20/50	Unknown	None	None	1, 2
		ET 2°	L	0.75 × 90	20/25				
SP	22	LE Dprv	R	∅	20/32	1	1 mo	None	1, 3, 4
			L	∅	20/80				

Visual acuity was measured using a Snellen chart. The Experiment column shows in which main experiments each observer participated. RE, right eye; LE, left eye; Strab, strabismus; Mixed, mixed deficits; Dprv, deprivation; ET, esotropia; XT, exotropia.

Statistical Analysis

Results from the four main experiments were analyzed using mixed ANOVAs. These ANOVAs included a between-subjects factor of amblyopia (amblyopes vs. controls) and within-subjects factors appropriate for the specific experiment. Except for comparison between the nasal and the temporal visual fields in luminance matching, ANOVAs were not conducted on data from the additional experiments because of the small sample size.

RESULTS

Observers matched the luminance of gray uniform patches in experiment 1. The results, displayed in Figure 2, show that under dichoptic viewing conditions, observers with amblyopia and mild suppression tended to decrease the luminance of the target patches presented to the fellow fixing eye (white bar; mean, 21.1 cd/m^2), whereas they tended to increase the luminance of target patches presented to the amblyopic eye (gray bar; mean, 39.6 cd/m^2). As expected, there was little interocular mismatch within the control group. Two-way ANOVA with factors of eye (amblyopic/nondominant eye vs. fellow fixing/dominant eye) and Amblyopia (amblyopes vs. controls) revealed a significant interaction ($F_{(1,11)} = 5.37$, $P = 0.041$), indicating that only amblyopes showed a mismatch in matching luminance. These results suggest that patches appeared darker when seen by the amblyopic eye compared with the fellow fixing eye under dichoptic viewing conditions. This is interesting because previous reports have indicated that there is little mismatch in perceived contrast between the amblyopic and fellow fixing eyes when stimuli are presented sequentially.[24–26]

To address this difference from previous studies, we examined whether dichoptic viewing is important for the interocular mismatch. Two observers with strabismic amblyopia (ADS, AM) and one observer with mixed amblyopia (KS) participated in an additional experiment in which target and standard stimuli were sequentially presented to each eye. Under these monocular viewing conditions there was almost no mismatch between the fellow fixing and amblyopic eyes for the strabismic amblyopes (ADS: 30.5 cd/m^2 and 31.2 cd/m^2 for the fellow-fixing-eye target and the amblyopic-eye target, respectively; AM: 30.5 cd/m^2 for both targets). However, the observer with mixed amblyopia showed a mismatch between the two eyes (27.8 and 39.6 cd/m^2 for the fellow-fixing-eye target and the amblyopic-eye target, respectively). Interestingly, this mismatch was smaller than that found under dichoptic presentation conditions for this observer. These results suggest that the perceptual mismatch found in experiment 1 was due to suppression that was triggered by the dichoptic nature of the stimulus.

In experiment 2, we examined whether there was a mismatch in perceived contrast above threshold. This experiment was similar to previous matching experiments[24–26] but differ-

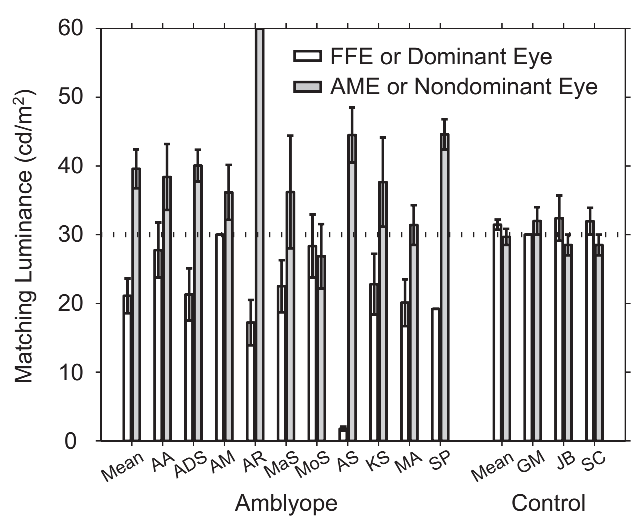

FIGURE 2. Mismatch between the fellow fixing eye (FFE) and the amblyopic eye (AME) in luminance matching of patches. Amblyopes adjusted a stimulus presented to either the fellow fixing eye or the amblyopic eye. Observer AR reported that the luminance of the target stimulus presented to the amblyopic eye would have to be higher than 60 cd/m^2 (outside the luminance range of the display) to make a match. Error bars show SE. The absence of an error bar indicates an error of 0.

ent because observers matched the target and standard gratings under dichoptic viewing. Figure 3 shows matching contrast as a function of standard contrast. The results fell into two categories. Four amblyopes (ADS, AM, MaS, MoS) were able to match the contrasts for all the conditions (Fig. 3a, left). On the other hand, for three other amblyopes (AA, KS, MA), matching contrast was out of the range (higher than 100%) for the standard contrast of 50% when the fellow fixing eye saw a target (Fig. 3a, middle, missing data point). We subjected the data to three-way ANOVA with factors of eye (amblyopic/nondominant eye vs. fellow fixing/dominant eye), standard contrast (10%, 25%, or 50%), and amblyopia (amblyopes vs. controls). Data for the standard contrast of 50% was excluded from this ANOVA because not all observers with amblyopia could perform a match at this standard contrast level as described. The main effect of eye was significant ($F_{(1,7)} = 7.75$, $P = 0.027$), indicating that matching contrast was higher when the fellow fixing eye viewed the target stimulus (Fig. 3a, open circle) than when the amblyopic eye did (Fig. 3a, gray diamond). This suggests overcompensation for the amblyopic eye. In other words, perceived contrast was higher for the amblyopic eye than for the fellow fixing eye. Although the eye × amblyopia interaction was only marginal ($F_{(1,7)} = 4.62$, $P = 0.069$), this was driven by the fact that the interocular mismatch was larger for amblyopes than for the control group (Fig. 3a). Because the spatial frequency of gratings was low (0.5 cyc/deg), three amblyopes repeated the matching task using gratings with a higher spatial frequency (4 cyc/deg). As can be seen in Figure 3b, there was little mismatch between the two eyes for these three participants. However, one observer (KS) was not able to perceive the gratings presented to the amblyopic eye at the lowest contrast (10%). As a whole, these results indicate that the amblyopic eye has no loss of perceived contrast for dichoptic stimuli above threshold, extending previous findings obtained under monocular viewing conditions.[24–26]

The results of experiments 1 and 2 demonstrate opposite effects for luminance and contrast. When viewed through the amblyopic eye, patch luminance was perceived to be reduced relative to the fellow eye, whereas grating contrast was perceived to be higher. These results are consistent with a decrement in perceived luminance for the amblyopic eye. In experiment 3, we asked observers to match the mean luminance of target gratings presented to the fellow fixing eye with that of standard gratings presented to the amblyopic eye. Here, only the mean luminance of the target gratings was variable because the contrast was kept constant for both target and standard gratings. Figure 4 shows the mean and individual matching luminance for different spatial frequencies. Two-way ANOVA with factors of spatial frequency (1, 5, or 10 cyc/deg) and amblyopia (amblyopes vs. controls) produced a significant main effect of amblyopia ($F_{(1,9)} = 10.7$, $P = 0.010$), indicating that amblyopes decreased the mean luminance but controls did not. This is consistent with our findings from experiment 1. There was no significant main effect of spatial frequency and no significant spatial frequency × amblyopia interaction ($P > 0.05$), indicating that spatial frequency was not an effective factor for the interocular mismatch. These results support the notion that luminance is perceived to be lower when viewing through the amblyopic eye. In addition to the measurements made using the method of adjustment, the open circles in Figure 4 indicate the PSE measured using the method of constant stimuli for a subset of participants. These PSE results also indicated a luminance mismatch for amblyopes but not for controls. This confirms that our observers were accurate when using the method of adjustment.

It has been reported that strabismic amblyopes exhibit an asymmetry in visual acuity between the nasal and temporal sides of visual field[32]; therefore, we conducted an additional experiment in which each eye viewed a grating presented to either the nasal or the temporal visual hemifield. Three observ-

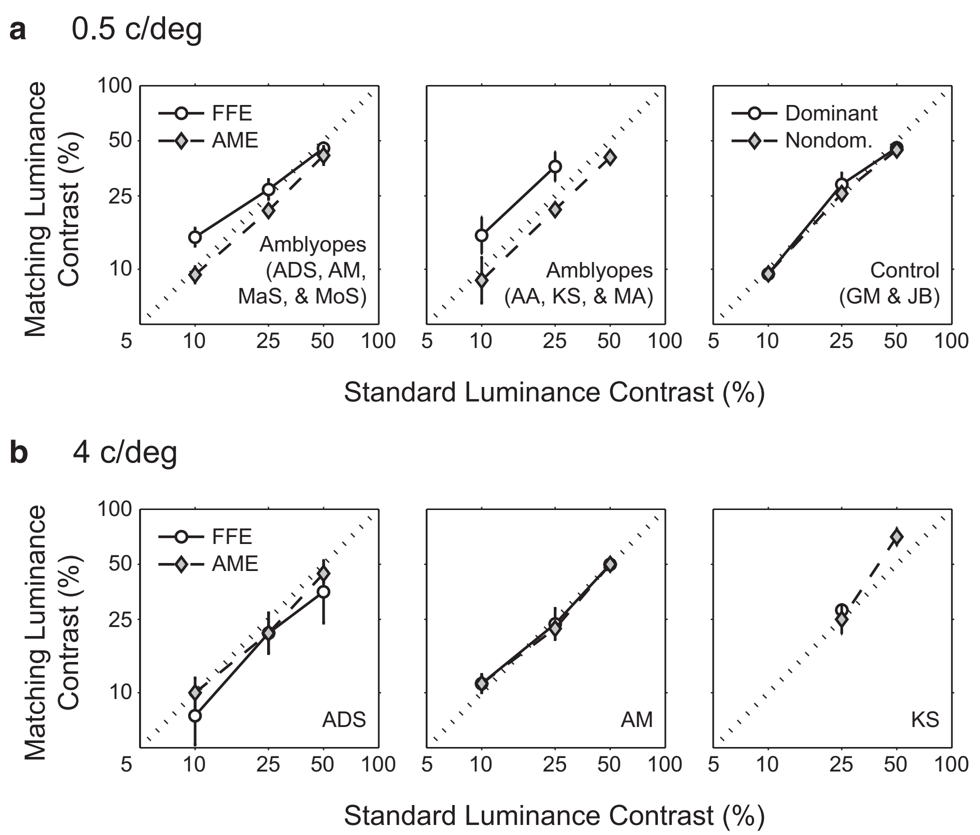

FIGURE 3. Matching luminance contrast of 0.5 cyc/deg gratings as a function of standard luminance contrast. Amblyopes adjusted a stimulus presented to either the fellow fixing eye (FFE, *open circle*) or the amblyopic eye (AME, *gray diamond*). Axes are in log scale. (**a**) The results suggest that the perceived contrast was higher for the amblyopic eye than for the fellow fixing eye (overcompensation). (**b**) Individual participant results for the same experiment but with 4 cyc/deg gratings. Error bars show SE (some error bars are smaller than the symbols).

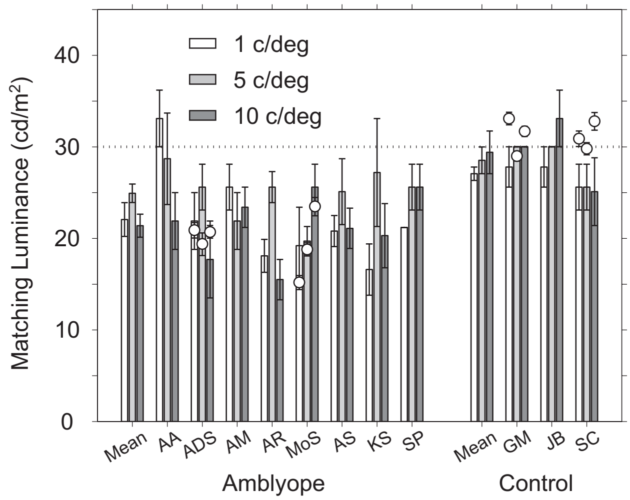

FIGURE 4. Matching the luminance of gratings while the luminance contrast of the gratings was kept constant between two eyes. Gratings had a spatial frequency of 1, 5, or 10 cyc/deg. Amblyopes adjusted the mean luminance of gratings presented to the fellow fixing eye. Error bars show SE. The absence of an error bar indicates a SE of 0. *Open circles*: PSE in luminance between two eyes. The PSE was measured using the method of constant stimuli.

ers with strabismic amblyopia (ADS, AR, MoS) and two observers with mixed amblyopia (AS, KS) repeated the task under these conditions. All observers had esotropia with the exception of KS, who had an exotropia. Two-way ANOVA with factors of spatial frequency (1, 5, or 10 cyc/deg) and Hemifield (nasal vs. temporal) produced no significant main effects or interactions ($P > 0.05$), suggesting that for the group data there was no difference in perceived luminance between the nasal and temporal visual fields. However, examination of the individual data indicated that observer KS, who had an exotropia, showed a large difference in matching luminance between the nasal (15.8 cd/m^2) and the temporal (25.8 cd/m^2) hemifields. This is consistent with a previous study that reported asymmetric suppression in amblyopes with exotropia.[28]

When amblyopes decreased patch luminance, the contrast between the patches and background was also lowered in experiments 1 and 3 because background luminance was fixed at 0 cd/m^2. We wondered whether the patch-background contrast was important for the interocular mismatch we observed. Experiment 4 examined this possibility by setting patch luminance and background luminance to be variable in the fellow fixing eye while their contrast was kept constant in both the amblyopic and the fellow fixing eyes. In addition, we tested low-pass-filtered stimuli with a cutoff spatial frequency of 0.5 cyc/deg in case the sharp edges of our stimulus patches were important in determining the interocular mismatch. The data shown in Figure 5 was subjected to two-way ANOVA with factors of filter (nonfiltered vs. low-pass-filtered) and amblyopia (amblyopes vs. controls). Observer AS was excluded from the ANOVA because her results were too variable; she showed a decreased matching luminance on 4 of 8 trials and an increased matching luminance on remaining trials. This result is addressed further in the Discussion. The main effect of amblyopia was significant ($F_{(1,8)} = 7.29$, $P = 0.027$), suggesting that amblyopes decreased the matching luminance even when the patch-background contrast was kept constant. The low-pass filtering did not significantly influence matching luminance ($P > 0.05$), and the interaction was also not significant ($P > 0.05$). Sharp edges were not a critical factor for the interocular mismatch.

We considered the possibility that the interocular mismatch in perceived luminance was due to the amblyopic eye having a smaller pupil size than the fellow fixing eye. A previous study[33] reported that the pupil size in the amblyopic eye under binocular viewing was not significantly different from that for the fixing eye. Furthermore, observer ADS decreased stimulus luminance in the fellow fixing eye for matching (patch luminance of 22.6 cd/m^2 in experiment 4), when her pupils were fixed and dilated (although her pupil size was not measured). It therefore seems reasonable to assume that the mismatch in perceived luminance was not due to the pupil size difference.

Eight amblyopes participated in both experiment 1 and experiment 4. Five showed consistent results between the two experiments. The mean difference in their matching luminance between the two experiments was only 3.6 cd/m^2. On the other hand, observers AA, AS, and KS showed substantial differences. For observers AS and KS, the substantial intraindividual differences were possibly due to alternating fixation and the difference between the nasal and the temporal hemifields. This will be considered in the Discussion. However, it is unclear why observer AA showed a lower matching luminance in experiment 4 than in experiment 1.

DISCUSSION

The present study investigated the nature of the perceptual mismatch between amblyopic and fellow fixing eyes when both eyes are open. For this purpose, observers with amblyopia matched the appearance of spatially separated stimuli presented to the two eyes under dichoptic viewing conditions. We were restricted to using amblyopes with mild suppression; subjects with strong suppression cannot perform this task because the stimuli presented to one eye are totally suppressed. We found that amblyopes with mild suppression decreased stimulus luminance in the fellow fixing eye or increased it in the amblyopic eye to obtain a match. This interocular mismatch was also observed when luminance was variable but contrast was kept constant. These results suggest that interocular suppression associated with amblyopia causes

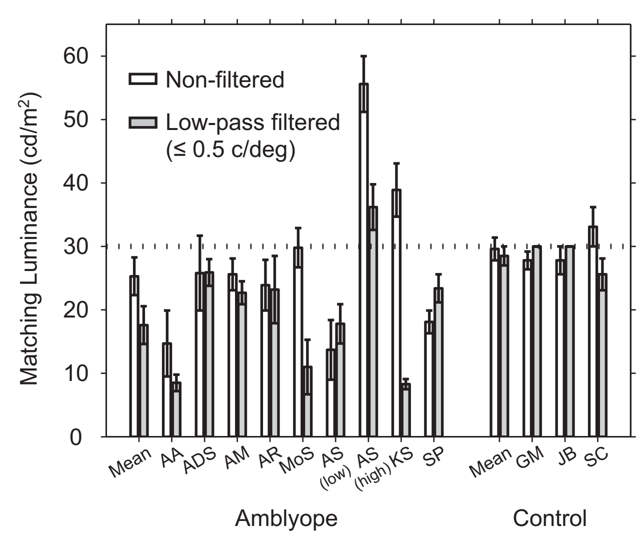

FIGURE 5. Matching luminance of patches. The contrast between the patch and the background was kept constant between the two eyes. Amblyopes adjusted the luminance of the patches presented to the fellow fixing eye. There were two types of stimuli, nonfiltered (*white bar*) and low-pass-filtered (*gray bar*). Data of observer AS were excluded from the mean calculation because of variable response. Error bars show SE. The absence of an error bar indicates an SE of 0.

a decrement in the perceived luminance of stimuli presented to the amblyopic eye.

It is difficult to attribute this interocular mismatch to anomalous contrast perception. Previous studies have shown that contrast perception in the amblyopic eye is near normal or overcompensated at suprathreshold contrast levels, in agreement with the results reported here.[24–26,30] In addition, the loss of contrast sensitivity in the amblyopic eye is known to be more pronounced for high spatial frequencies than low spatial frequencies.[2–4] However, we found that the interocular mismatch did not increase with spatial frequency. Amblyopes showed the mismatch even for the low-pass-filtered stimuli, for which the monocular contrast sensitivity would be only minimally different between the two eyes. One might argue that a perceived lower patch-background contrast in the amblyopic eye than in the fellow fixing eye might have resulted in the observed matching luminance decrement for the fellow fixing eye. However, most of the amblyopic observers showed the interocular mismatch even under conditions in which the patch-background contrast was kept constant between the two eyes. Thus, it is reasonable to conclude that suppression for some amblyopes (i.e., those with mild suppression) influences not only contrast perception but also luminance perception under dichoptic viewing conditions.

The process of dark adaptation can influence perceived luminance, and it has previously been shown that dark adaption is slower for amblyopic eyes than for the fellow fixing eyes.[34] However, because our stimuli were presented with 60 cd/m^2 of luminance and therefore engaged photopic vision, we are confident that interocular differences in dark adaptation processes cannot account for the results we report.

Two amblyopes (AS, KS) showed substantial intraindividual differences in matching luminance when the patch-background contrast was kept constant (Fig. 5). Their matches also differed substantially between experiment 1 and experiment 4. Given that observer AS had strabismus with alternating fixation, we speculate that she switched the eye with which she fixated during the experiment, resulting in an alternation of suppression between the test and standard stimulus during each experiment. This would explain the variability in her responses. Observer KS generally had larger variability in his responses than the other observers (Figs. 2, 4, 5). It is possible that his unstable responses resulted from the difference between the nasal and temporal hemifields that were identified in experiment 3. It would be difficult to make a match if the two stimuli seen by one eye differed from one another, depending on which hemifield they were imaged on.

We have previously shown that suppression can be quantified and treated by adjusting the contrast of the signal viewed by the fellow fixing eye.[35–37] This cannot be done by adjusting the mean luminance of the signal viewed by the fellow fixing eye (data unpublished, 2011), presumably because of monocular light adaptation mechanisms. It is interesting that, for subjects with mild suppression, there is a difference between the contrast dependence of the signal from the fixing eye that initiates suppression and the resultant perceptual consequence that involves luminance.

We conclude from the present results that the world appears darker when viewed through the amblyopic eye when both eyes are open. This is the first experimental suggestion that the perceptual consequences of suppression affect luminance. It is important to note that suppression varies according to the type of stimuli used to measure it and their relative positions within the visual field.[28] Our stimuli not only stimulated noncorresponding retinal points in the two eyes but also involved comparisons between stimuli imaged in very different regions of the two retinas. That an image in one part of the visual field of one eye can suppress a remote region in the visual field seen by the other eye attests to the long-range nature of the underlying interactions. It remains a possibility that the luminance dependence we found is unique to the long-range nature of such interactions.

References

1. Noorden GK. Factors involved in the production of amblyopia. *Br J Ophthalmol.* 1974;58:158–164.
2. Levi DM, Harwerth RS. Spatio-temporal interactions in anisometropic and strabismic amblyopia. *Invest Ophthalmol Vis Sci.* 1977;16:90–95.
3. Hess RF, Howell ER. The threshold contrast sensitivity function in strabismic amblyopia: evidence for a two type classification. *Vision Res.* 1977;17:1049–1055.
4. Hilz R, Rentschler I, Brettel H. Myopic and strabismic amblyopia: substantial differences in human visual development. *Exp Brain Res.* 1977;30:445–446.
5. Bedell HD, Flom MC. Monocular spatial distortion in strabismic amblyopia. *Invest Ophthalmol Vis Sci.* 1981;20:263–268.
6. Fronius M, Sireteanu R. Monocular geometry is selectively distorted in the central visual field of strabismic amblyopes. *Invest Ophthalmol Vis Sci.* 1989;30:2034–2044.
7. Hess RF, Holliday IE. The spatial localization deficit in amblyopia. *Vision Res.* 1992;32:1319–1339.
8. Demanins R, Hess RF. Effect of exposure duration on spatial uncertainty in normal and amblyopic eyes. *Vision Res.* 1996;36:1189–1193.
9. Levi DM, Klein SA. Noise provides some new signals about the spatial vision of amblyopes. *J Neurosci.* 2003;23:2522–2526.
10. Hess RF, Wang YZ, Demanins R, Wilkinson F, Wilson HR. A deficit in strabismic amblyopia for global shape detection. *Vision Res.* 1999;39:901–914.
11. Spang K, Fahle M. Impaired temporal, not just spatial, resolution in amblyopia. *Invest Ophthalmol Vis Sci.* 2009;50:5207–5212.
12. Kiorpes L, McKee SP. Neural mechanisms underlying amblyopia. *Curr Opin Neurobiol.* 1999;9:480–486.
13. Imamura K, Richter H, Fischer H, et al. Reduced activity in the extrastriate visual cortex of individuals with strabismic amblyopia. *Neurosci Lett.* 1997;225:173–176.
14. Barnes GR, Hess RF, Dumoulin SO, Achtman RL, Pike GB. The cortical deficit in humans with strabismic amblyopia. *J Physiol.* 2001;533:281–297.
15. Hess RF, Thompson B, Gole G, Mullen KT. Deficient responses from the lateral geniculate nucleus in humans with amblyopia. *Eur J Neurosci.* 2009;29:1064–1070.
16. Sengpiel F, Blakemore C. The neural basis of suppression and amblyopia in strabismus. *Eye.* 1996;10(pt 2):250–258.
17. Fahle M. Non-fusable stimuli and the role of binocular inhibition in normal and pathologic vision, especially strabismus. *Doc Ophthalmol.* 1983;55:323–340.
18. Pardhan S, Gilchrist J. Binocular contrast summation and inhibition in amblyopia: the influence of the interocular difference on binocular contrast sensitivity. *Doc Ophthalmol.* 1992;82:239–248.
19. Huang C, Tao L, Zhou Y, Lu ZL. Treated amblyopes remain deficient in spatial vision: a contrast sensitivity and external noise study. *Vision Res.* 2007;47:22–34.
20. Baker DH, Meese TS, Hess RF. Contrast masking in strabismic amblyopia: attenuation, noise, interocular suppression and binocular summation. *Vision Res.* 2008;48:1625–1640.
21. Levi DM, Klein SA. Vernier acuity, crowding and amblyopia. *Vision Res.* 1985;25:979–991.
22. Levi DM, Klein SA. Limitations on position coding imposed by undersampling and univariance. *Vision Res.* 1996;36:2111–2120.
23. Hess RF, Field DJ. Is the spatial deficit in strabismic amblyopia due to loss of cells or an uncalibrated disarray of cells? *Vision Res.* 1994;34:3397–3406.
24. Hess RF, Bradley A. Contrast perception above threshold is only minimally impaired in human amblyopia. *Nature.* 1980;287:463–464.

25. Hess RF, Bradley A, Piotrowski L. Contrast-coding in amblyopia, I: differences in the neural basis of human amblyopia. *Proc R Soc Lond B Biol Sci.* 1983;217:309–330.
26. Loshin DS, Levi DM. Suprathreshold contrast perception in functional amblyopia. *Doc Ophthalmol.* 1983;55:213–236.
27. Jampolsky A. Characteristics of suppression in strabismus. *AMA Arch Ophthalmol.* 1955;54:683–696.
28. Travers TA. Suppression of vision in squint and its association with retinal correspondence and amblyopia. *Br J Ophthalmol.* 1938;22:577–604.
29. Huang CB, Zhou J, Zhou Y, Lu ZL. Contrast and phase combination in binocular vision. *PLoS One.* 2010;5:e15075.
30. Huang CB, Zhou J, Lu ZL, Zhou Y. Deficient binocular combination reveals mechanisms of anisometropic amblyopia: signal attenuation and interocular inhibition. *J Vis.* 2011;11.
31. Kingdom FA, Prins N. *Psychophysics: A Practical Introduction*. London: Academic Press; 2010.
32. Sireteanu R, Fronius M. Naso-temporal asymmetries in human amblyopia consequence of long-term interocular suppression. *Vision Res.* 1981;21:1055–1063.
33. Barbur JL, Hess RF, Pinney HD. Pupillary function in human amblyopia. *Ophthalmic Physiol Opt.* 1994;14:139–149.
34. Flynn JT. Dark adaptation in amblyopia. *Arch Ophthalmol.* 1968;79:697–704.
35. Mansouri B, Thompson B, Hess RF. Measurement of suprathreshold binocular interactions in amblyopia. *Vision Res.* 2008;48:2775–2784.
36. Hess RF, Mansouri B, Thompson B. A new binocular approach to the treatment of amblyopia in adults well beyond the critical period of visual development. *Restorative Neurol Neurosci.* 2010;28:1–10.
37. Hess RF, Mansouri B, Thompson B. A binocular approach to treating amblyopia: anti-suppression therapy. *Optom Vision Sci.* 2010;87:697–704.