Amblyopic Suppression: Passive Attenuation, Enhanced Dichoptic Masking by the Fellow Eye or Reduced Dichoptic Masking by the Amblyopic Eye?

Jiawei Zhou,1 Alexandre Reynaud,2 Zhimo Yao,1 Rong Liu,3 Lixia Feng,4 Yifeng Zhou,3 and Robert F. Hess2

1School of Ophthalmology and Optometry, Affiliated Eye Hospital, State Key Laboratory of Ophthalmology, Optometry and Vision Science, Wenzhou Medical University, Wenzhou, Zhejiang, People’s Republic of China
2McGill Vision Research, Department of Ophthalmology, McGill University, Montreal, Quebec, Canada
3Chinese Academy of Sciences Key Laboratory of Brain Function and Disease, School of Life Sciences, University of Science and Technology of China, Hefei, Anhui, People’s Republic of China
4Department of Ophthalmology, First Affiliated Hospital, Anhui Medical University, Hefei, Anhui, People’s Republic of China

Correspondence: Jiawei Zhou, School of Ophthalmology and Optometry, Affiliated Eye Hospital, State Key Laboratory of Ophthalmology, Optometry and Vision Science, Wenzhou Medical University, 270 Xueyuan Xi Road, Wenzhou, Zhejiang 325000, China; zhoujw@mail.eye.ac.cn.
Submitted: February 27, 2018
Accepted: July 24, 2018

PURPOSE. To test the amblyopic suppression at mid to low spatial frequencies when compensating for signal attenuation.

METHODS. Eight amblyopes with \((n = 5)\) or without \((n = 3)\) strabismus and 10 normal controls with normal or corrected to normal visual acuity (\(\geq 20/20\)) and normal stereopsis (\(< 5\) arcseconds) participated. Using a quick contrast sensitivity function approach, we measured individuals’ monocular contrast sensitivity functions when the untested eye saw a bandpass filtered noise whose peak spatial frequency was matched to that of the test grating. Interocular suppression was quantified by the difference in thresholds occurring between these two conditions for each eye. The contrast of the noise mask was set at five times the threshold of the untested eye.

RESULTS. Selected spatial frequencies (0.67–1.31 cyc/deg) were identified where neither ceiling (five times the mask contrast threshold in the amblyopic eye <100%) nor floor (threshold of the amblyopic eye when there was a noise mask in the fellow eye <100%) effects occurred for all observers. Within this frequency range, we found no interocular suppressive imbalance in normal observers. However, in amblyopes, the amblyopic eye exerted significantly less suppression than the fellow eye, while the suppression from the fellow eye to the amblyopic eye was similar to that found in the normal controls.

CONCLUSIONS. We conclude that the reduced dichoptic masking by the amblyopic eye, within the context of normally balanced interocular inhibition, produces the amblyopic suppression at mid to low frequencies.

Keywords: amblyopia, suppression, dichoptic masking, contrast sensitivity gain

For over a century,1 it has been known that people with amblyopia (incidence 4%) rely predominately on their fellow eye when both eyes are open. Originally, it was assumed that this was the result of an enhanced suppressive signal (e.g., dichoptic masking) emanating from the fellow eye.2,4 There are animal1,5–7 and human models1,4–10 of the underlying inhibitory network supporting this suppressive influence of the fellow eye. These models normally contain a reciprocal inhibitory pathway that modifies the contrast gain before binocular summation, for example, the two-stage model that contains a stage of monocular excitation and binocular suppression, the contrast gain control model that contains a stage of direct gain control from one eye to the other eye; and an indirect gain control that modifies the gain control power4 or with an additional gain enhancement stage5 before binocular summation.

More recently, another explanation has been advanced that suggests that the passive attenuation that results from the monocular acuity deficit is the reason for the predominance of the good eye when amblyopes are binocular viewing.11 The presence of standing contrast attenuation in the amblyopic eye (i.e., raised contrast thresholds) means that at any fixed contrast the dichoptic masking from the fellow eye will always dominate because the strength of dichoptic masking depends on the relative contrast of the mask to the threshold. Here, using a dichoptic-masking paradigm, we studied the masking effect of visibility-matched visual stimuli from one eye to the other eye so to factor out any influence from the raised contrast thresholds of the amblyopic eye (i.e., the attenuator explanation). Using this approach, we show that the fellow eye does not exert abnormally strong dichoptic masking over the amblyopic eye. However, the effect that the amblyopic eye has on the fellow eye is much reduced, and it is the imbalance that this produces within the context of reciprocal interocular inhibition, rather than an abnormally higher inhibition from the fellow to the amblyopic eye per se, that lies at the heart of the suppression that reduces binocular sensitivity in lazy eye syndrome.
Amblyopic Suppression at Mid to Low Spatial Frequencies

TABLE Clinical Details of the Participants

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age/Sex</th>
<th>Cycloplegic Refractive Errors, OD/OS</th>
<th>LogMAR Visual Acuity, OD/OS</th>
<th>Strabismus, OD/OS</th>
<th>History</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>24/F</td>
<td>−0.75 DS/+0.75 DC × 102°</td>
<td>0.5</td>
<td>XT 15°</td>
<td>Detected at 3 years old, patched occasionally until 7 years old, then received surgery on right eye, no stereopsis</td>
</tr>
<tr>
<td>S2</td>
<td>34/M</td>
<td>+0.50 DC × 150°</td>
<td>−0.1</td>
<td>Ø</td>
<td>Diagnosed at 5 years old, patching and glasses until 7 years old, no surgery, no stereopsis</td>
</tr>
<tr>
<td>S3</td>
<td>37/F</td>
<td>+2.00 DS</td>
<td>0.8</td>
<td>XT 15°, HT 1°</td>
<td>Detected at 5 years old, patched when 5 years old for 2 months, no surgery, no stereopsis</td>
</tr>
<tr>
<td>S4</td>
<td>26/M</td>
<td>+6.00 DS/+1.00 DC × 25°</td>
<td>−0.1</td>
<td>Ø</td>
<td>ET 5°</td>
</tr>
<tr>
<td>S5</td>
<td>26/M</td>
<td>+1.50 DS/+1.50 DC × 60°</td>
<td>0.22</td>
<td>Ø</td>
<td>Detected at 18 years old, no surgery, no treatment, stereo vision 100'</td>
</tr>
<tr>
<td>S6</td>
<td>22/M</td>
<td>+4.00 DS/+1.00 DC × 85°</td>
<td>0.7</td>
<td>Ø</td>
<td>Detected at 23 years old, no surgery, no treatment, stereo vision 400'</td>
</tr>
<tr>
<td>S7</td>
<td>7/F</td>
<td>+2.00 DS</td>
<td>−0.08</td>
<td>Ø</td>
<td>Detected at 17 years old, no patching, no surgery, no stereopsis</td>
</tr>
<tr>
<td>S8</td>
<td>25/M</td>
<td>+2.50 DS/+1.50 DC × 100°</td>
<td>0.22</td>
<td>Ø</td>
<td>Detected at 23 years old, no patching, no surgery, stereo vision 400'</td>
</tr>
</tbody>
</table>

DS, diopeter sphere; DC, diopeter cylinder; XT, exotropia; Ø, straight; HT, hypertropia; ET, esotropia.

MATERIALS AND METHODS

Participants

Eight amblyopes with \((n = 5)\) or without \((n = 3)\) constant strabismus and 10 adults with normal eyes (mean age: 25.3 ± 2.0 years old; four females) with normal or corrected to normal visual acuity \((20/20\) or better) and normal stereopsis \((40\) arcseconds or better) participated in our experiment. All amblyopes had no obvious structural anomalies or ocular disease; their clinical details are provided in the Table. Observers’ cycloplegic refractive errors, if existing, were fully corrected in the data collection. Two patients (S2 and S7), one with mild hyperopic anisometropia and the other with mild bilateral hyperopia, were not chronic spectacle wearers but were corrected during testing. The eye dominances of normal adults were defined by the hole-in-the-card test. All participants were naive to the purpose of the study. Written informed consent was obtained from all participants or from the parents or legal guardian of participants aged less than 18 years old after explanation of the nature and possible consequences of the study. This study followed the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of Wenzhou Medical University. The methods were carried out in accordance with the approved guidelines.

Apparatus

All stimuli were generated and controlled by a PC computer running Matlab (MathWorks, Natick, MA, USA) with psychophysics, Palamedes, and quick contrast sensitivity function \(qCSF\) toolboxes. Stimuli were displayed on a gamma-corrected CRT monitor (Iiyama Vision Master Pro 513; Iiyama Corp., Hoofddorp, The Netherlands) (width 40 cm; spatial resolution: 1280 pixels × 960 pixels; refresh rate: 100 Hz) for patients S1 to S3 and on a gamma-corrected CRT monitor (Sony G220; Sony Corp., Tokyo, Japan) (width 32.5 cm; spatial resolution: 1024 pixels × 768 pixels; refresh rate: 100 Hz) for the other patients and all the normal controls. Mean luminance of the screen was 54 candela per square meter \(\text{(cd/m}^2\) for the first monitor and 40 \text{cd/m}^2 for the second monitor. All experiments were conducted in a dark room. During the measurement, observers viewed the stimuli dichoptically via a custom-built eight-mirror stereoscope at an equivalent viewing distance of 60 cm.

Design

By using the \(qCSF\) approach, we measured individual’s monocular contrast sensitivity function \(\text{(CSF)}\) when the untested eye viewed a mean luminance background and when the untested eye viewed a bandpass filtered noise stimulus whose peak spatial frequency matched that of the test Gabor presented to the tested eye. Interocular suppression was quantified by the difference in thresholds occurring between these two conditions for each eye. To factor out any signal attenuation by the amblyopic eye, the contrast of the noise mask was set to five times the threshold (or 100% if the ceiling was reached) of the untested eye. The \(qCSF\) approach has already been validated for its use on amblyopic populations. It was used to ascertain the threshold attenuation of the amblyopic eye under monocular viewing conditions. The \(qCSF\) approach has also been validated in our previous study for using a noise stimulus.

In total, we measured six CSFs for each observer: three conditions \(\text{(Gabor CSF, noise CSF, and Gabor plus noise-masking CSF)}\) for two eyes. Each CSF was measured in 150 trials, preceded by a five-trial practice with high contrast \(\text{(100%) stimuli presented. Normally, observers could finish one CSF measurement in 5 minutes. A 2-minute break was provided before the start of the next session. The six CSFs were measured twice in 2 days, and the results were averaged based on these two repetitions.}\

Stimuli

Stimuli included oriented Gabors for measuring the tested eye’s Gabor CSF (Fig. 1A), oriented bandpass filtered white noise patterns for measuring the monocular contrast threshold in discriminating the noise pattern (Fig. 1B), and isotropic bandpass filtered noise that served as a mask in the Gabor plus noise-masking condition (Fig. 1C). The orientation of the Gabors or the bandpass filtered white noise patterns was horizontal or vertical in different trials. Oriented noise patterns were created by convolving a white noise in the space domain by a Gabor filter with a half-
the two lines were then used to present the stimuli in the two eyes in the following measures.

In a CSF trial, a fixation point (radius 0.1°), signaled by a brief tone to begin, was presented in the middle of the screen seen by each eye for 200 milliseconds; this was followed by a 1-second presentation of a tested stimulus (oriented Gabor or oriented noise) in the tested eye and an isotropic noise or mean luminance background in the untested eye. Subjects were asked to identify the orientation of the test stimulus (horizontal or vertical) by pressing the appropriate key on the keyboard. Auditory feedback was provided to indicate the correctness of the response. The next trial started immediately after the response.

The monocular and masked CSFs were measured using the qCSF function approach.16,17 This method is a Bayesian adaptive procedure that estimates the contrast sensitivity as a function of spatial frequency with the truncated log-parabola model.21 For each trial, it tests the stimulus with optimal frequency and contrast in order to maximize the expected information gain about the CSF.16 The frequency range for the contrast sensitivity measurement was set from 0.25 to 9.57 cyc/deg.

**Statistical Analysis**
Contrast sensitivities at selected spatial frequencies were obtained from the qCSF for statistical analysis. We choose spatial frequencies in which there was no limitation to the masking strength from either ceiling or floor effects owing to the reduced contrast sensitivity of the amblyopic eye. A ceiling effect would have limited the highest spatial frequency for which we could achieve a constant suprathreshold mask of five times the threshold in the amblyopic eye. Its consequence would be to reduce the effective masking from the amblyopic to the fellow eye. A floor effect would have limited the highest spatial frequency where the contrast sensitivity of the amblyopic eye was too low to reflect the full extent of masking by the fellow eye. Its effect would be to restrict the effective masking from fellow to amblyopic eye. Selected spatial frequencies (0.67 cyc/deg, 0.94 cyc/deg, and 1.31 cyc/deg) were identified where neither ceiling (five times the mask contrast threshold in the amblyopic eye <100% contrast) nor floor (threshold of the amblyopic eye when there was a noise mask in the fellow eye <100%) effects occurred for all observers. Data are presented as mean ± SEM unless otherwise indicated. Sample number (n) indicates the number of observers in each group, which is indicated in the figure. Repeated measures ANOVA, based on the selected frequencies, was used to compare the degree of interocular suppression between eyes and between groups. Differences in means were considered statistically significant at P < 0.05. Analyses were performed using software (SPSS 24.0; IBM Corp., Armonk, NY, USA).

**RESULTS**
To test the assumption of an abnormally strong suppressive signal emanating from the fellow eye responses, we used a dichoptic-masking approach in which we measured the suppressive effect of bandpass visual noise presented to one eye on the contrast detectability of a Gabor stimulus presented to the other eye. The noise mask was shown at five times the mask contrast threshold in the amblyopic eye to the fellow eye. A floor effect would have limited the highest spatial frequency where the contrast sensitivity of the amblyopic eye was too low to reflect the full extent of masking by the fellow eye. Its effect would be to restrict the effective masking from fellow to amblyopic eye. Selected spatial frequencies (0.67 cyc/deg, 0.94 cyc/deg, and 1.31 cyc/deg) were identified where neither ceiling (five times the mask contrast threshold in the amblyopic eye <100% contrast) nor floor (threshold of the amblyopic eye when there was a noise mask in the fellow eye <100%) effects occurred for all observers. Data are presented as mean ± SEM unless otherwise indicated. Sample number (n) indicates the number of observers in each group, which is indicated in the figure. Repeated measures ANOVA, based on the selected frequencies, was used to compare the degree of interocular suppression between eyes and between groups. Differences in means were considered statistically significant at P < 0.05. Analyses were performed using software (SPSS 24.0; IBM Corp., Armonk, NY, USA).

**Figure 1.** Dichoptic stimuli in the dichoptic-masking test. CSFs were tested when the tested eye viewed a Gabor and the untested eye viewed a mean luminance background, that is, Gabor (A); when the tested eye viewed a bandpass filtered noise and the untested eye viewed a mean luminance background, that is, noise (B); and when the tested eye viewed a Gabor and the untested eye viewed a noise mask whose peak spatial frequency matched that of the test Gabor presented to the tested eye and whose contrast was five times that of the untested eye's contrast threshold for discriminating the said oriented noise pattern in (B), that is, masking (C). An orientation-discrimination task (horizontal versus vertical) was used for all of these measures, which is why we used isotropic noise pattern as the mask (C). The oriented noise condition (B) was used to determine the contrast threshold of the relevant information in the isotropic noise (C). According to our previous study,19 the contrast threshold of the oriented noise is same as that of the isotropic noise. All contrasts in this study are expressed as Michelson's contrast. Threshold elevation was calculated by subtracting the decibel values of the masking CSF (C) from the grating CSF (A) for each eye, respectively.

**Procedure**
Before beginning each CSF measure, subjects completed an alignment task to facilitate fusion of their two eyes. In this task, they were instructed to align a vertical red line in the middle of the screen seen by one eye with a vertical green line in the middle of the screen seen by the other eye. The coordinates of...
sensitivities of the amblyopic eye (Fig. 2A, left panel) for both the Gabor (red curves) and the noise patterns (green curves) were lower than those of the fellow eye (Fig. 2A, right panel). However, no clear difference was found between the nondominant and dominant eyes of normal controls (Fig. 2B) or between normal control eyes and the fellow eyes of amblyopes. Contrast sensitivities dramatically reduced when the untested eye was presented with a noise mask (Figs. 2A, 2B, blue curves) compared to when the untested eye viewed only a mean luminance background (Figs. 2A, 2B, red curves) for both groups, indicating significant interocular suppressive effects across a range of spatial frequencies. The threshold elevations (our measure of interocular suppression) were similar in the two eyes for normal controls (Fig. 2D) but different in the two eyes for amblyopes (Fig. 2C).

Although it was our intention to use masks that were all five times the threshold, the fact that amblyopes have raised thresholds at high spatial frequencies makes this impossible at high spatial frequencies due to both ceiling (less than five times threshold suprathreshold mask in the amblyopic eye due to its raised threshold) and floor (the test in the amblyopic eye would have reduced effective masking due to its restricted range) effects. For these reasons we make no conclusions for stimuli above 1.5 cyc/deg because in this high spatial-frequency range one or more amblyopes exhibited either ceiling or floor effects. Thus, to better reveal the influence of suppression in amblyopia, we analyzed the data only at the spatial frequencies at which the matched visibilities for our noise stimuli were achieved without any ceiling effect and where the thresholds were sufficiently low to avoid any floor effect for all patients, namely 0.67 to 1.31 cyc/deg.

Figure 3A–C shows interocular suppression for three low spatial frequencies (0.67, 0.94, 1.31 cyc/deg) for all eight amblyopes (Fig. 3, filled symbols) and 10 normal controls (Fig. 3, unfilled symbols) for the Gabor noise-masking condition. The large square symbols represent the mean interocular masking for the amblyopes (filled) and controls (unfilled). As expected from the results graphed in Figure 2, for normal controls masking suppression from dominant eye to nondominant eye was similar to that from the nondominant eye to the dominant eye (unfilled symbols cluster around the line of equality, i.e., the dashed line). A within-subject repeated measures ANOVA with eye (two levels) and spatial frequency (three levels) as within-subject factors showed that the interocular suppression strengths were not significantly different between eyes: $F(1,9) = 1.22, P = 0.298$. The results for amblyopes are quite different in that the masking suppression from the amblyopic eye to the fellow eye was much less than that from the fellow eye to the amblyopic eye (the filled symbols fall below the unity line). A within-subject repeated measures ANOVA with eye (two levels) and spatial frequency (three levels) as within-subject factors showed that interocular suppression was significantly different between eyes: $F(1,7) = 16.11, P = 0.005$. We also performed between-

**FIGURE 2.** Lack of suppression from the amblyopic eye to the fellow eye in amblyopes. CSFs for the three test conditions, that is, Gabor alone, noise alone, and Gabor plus noise masking. (A) CSFs of the amblyopes ($n = 8$). (B) CSFs of the normal controls ($n = 10$). (C) Threshold elevation functions of the amblyopes. (D) Threshold elevation functions of the normal controls. In all panels, the areas show the range of $\pm$SEM.
subjects repeated measures ANOVA tests with spatial frequency (three levels) as a within-subject factor to compare suppression between groups. We found that the suppression strength from the amblyopic eye to the fellow eye in amblyopes was significantly less than that from the nondominant eye to the dominant eye in normal controls: \( F(1,16) = 46.06, P < 0.001 \). The suppression strength from the fellow eye to the amblyopic eye in amblyopes was not significantly different than from the dominant eye to the nondominant eye in normal controls: \( F(1,16) = 0.71, P = 0.41 \). There is also evidence for a facilitatory effect; S6 and S7 exhibited negative masking or facilitation of the fellow eye when a mask was present in the amblyopic eye.

Figure 3D shows how the interocular imbalance in suppression varies across the spatial frequency for amblyopes and normal controls within this low spatial-frequency range where all the masks were of the same suprathreshold strength. It is apparent that normal observers exhibit no interocular suppressive imbalance within this frequency range, while amblyopes exhibit an imbalance that favors the fellow eye. An ANOVA test, with spatial frequency as within-subjects factor (three levels), showed that there was a significant group

![Figure 3](image-url)
Amblyopic Suppression at Mid to Low Spatial Frequencies

**Figure 4.** Averaged threshold elevations at the three low spatial frequencies. Threshold elevations are plotted in the same manner as that in Figure 3. The results are shown for the averaged results across the three low spatial frequencies in Figure 3A–C. *Error bars* denote the range of ±SEM.

The difference in the interocular imbalance in suppression: \( F(1,16) = 14.53, P = 0.002 \).

One potential limitation of the above-mentioned statistical analysis is that the contrast sensitivities of the three low spatial frequencies might not be independent, as they were derived from the qCSF approach. We thus also provide the averaged results across these three low spatial frequencies in Figure 4. *t*-tests based on the averaged data showed similar results: the suppression from the fellow eye to the amblyopic eye in amblyopes was not significantly different from that of the dominant eye to the nondominant eye in normal controls \( (P = 0.45, \text{2-tailed independent samples } t\text{-test}) \); the suppression from the amblyopic eye to the fellow eye was significantly different from that of the fellow eye to the amblyopic eye \( (P = 0.005, \text{2-tailed paired-samples } t\text{-test}) \).

**DISCUSSION**

In the low to mid spatial-frequency range where we were able to use masks of equal suprathreshold strength for both the fellow and amblyopic eyes, we were able to demonstrate clear suppressive effects. This argues against the pure attenuator explanation for suppression for two reasons: first the equal suprathreshold strength masks factored out any contrast threshold deficit in the amblyopic eye, and second, at low spatial frequencies suppression is evident where contrast thresholds are least affected. These results also rule out another popular explanation based on an abnormally high suppressive signal from the fellow good eye because we show that the suppression from the fellow eye to the amblyopic eye is of a normal form. However, the suppression from the amblyopic to the fellow eye is much reduced, and it is the imbalance that results within the context of reciprocal inhibition\(^{10,22,56} \) that lies at the heart of the dominance of the fellow eye under binocular viewing. At high spatial frequencies, monocular signals are reduced in the amblyopic eye, and our strategy of maintaining the noise mask at five times the threshold contrast was no longer possible. Here, an explanation based on passive attenuation alone might be sufficient to account for the binocular imbalance in amblyopes under normal viewing conditions\(^{23} \), as the strength of masking depends on the suprathreshold and not the physical contrast\(^{24} \).

What is of greater interest is what happens at low spatial frequencies. They are seen almost normally by the amblyopic eye and could therefore make a contribution to binocular perception. We show that vision in this frequency band is suppressed under dichoptic viewing as the result of an imbalance in dichoptic masking between the fellow and amblyopic eyes when compensating for signal attenuation. Under conditions of normal binocular viewing (same stimuli in both eyes), this increased masking would result in a suppression of low spatial-frequency information seen through the amblyopic eye. This conclusion in humans with amblyopia gains support from a recent nonhuman primate model of amblyopia in which it has also been shown that there is reduced dichoptic masking by cells driven by the amblyopic eye\(^7 \); this, in principle, could be due to attenuation (a threshold offset) or reduced contrast gain per se. Shooner et al.\(^{25} \) didn’t present their stimuli at a constant suprathreshold contrast as we were able to do psychophysically. Therefore, their result supports the reduced amblyopic-to-fellow eye interaction but is not definitive about its cause. We also observed the facilitatory effect that Shooner et al.\(^{25} \) report for the interactions between single cells driven by the amblyopic and fellow eyes in their primate animal model of amblyopia. Subject S6 and S7’s masking from the amblyopic eye was so reduced that it provided negative masking (i.e., facilitation) of the fellow eye.

As we pointed out above, current theories of binocular interactions normally contain a reciprocal inhibitory pathway that modifies the contrast gain before binocular summation, for example, the two-stage model\(^{10} \), the double contrast gain control model\(^8 \), and contrast gain control and gain enhancement model\(^9 \). This inhibitory interocular pathway interacts to determine the effective strength of input from each eye. There are balanced interocular weights before binocular summation in normal adults, while in amblyopes there is an asymmetry that results in suppression of amblyopic eye information in amblyopes, as we reported in this study.

In a range of low spatial frequencies similar to ours (i.e., 0.67–1.31 cyc/deg), Huang et al.\(^8 \) evaluated the binocular interactions using the binocular phase and contrast compensation paradigm at 1 cyc/deg in four anisometropic amblyopes. They showed that the abnormal binocular vision could be explained by a multichannel contrast gain control model: a combination of attenuated monocular signals in the amblyopic eye, stronger suppression from the fellow eye to the amblyopic eye’s signal (direct suppression), and stronger suppression from the fellow eye to the amblyopic eye’s suppression power (indirect suppression). Recently, Ding et al.\(^{26} \) studied the binocular phase and contrast combination at 0.68, 1.36, and 2.72 cyc/deg in two subjects with amblyopia and four subjects with nonamblyopic strabismus. They proposed a nondoni- dominant-to-dominant eye enhancement explanation to account for the larger interocular imbalance when higher contrast was presented to the nondominant eye. In the current study, we adopted the dichoptic-masking paradigm to measure the interocular interactions. We narrowed our analysis to low spatial frequencies, where the attenuation effects due to raised contrast thresholds of the amblyopic eye could be ruled out. We found that there was less suppression from the amblyopic to the fellow eye, while the suppression from the fellow eye to the amblyopic eye was normal.
Consistent with the above-mentioned two reports, we also showed a clear binocular imbalance in amblyopes. Nevertheless, there are several differences between our study and these two previous reports. First, there are different numbers of subjects. There were four amblyopes in the study of Huang et al.,8 two amblyopes in the study of Ding et al.,26 and eight amblyopes in the current study. The interocular interactions could be different in different patients, as is illustrated in Figure 3 (also see Ref. 27). For example, for amblyopic subjects S3 and S7, the two interocular suppression magnitudes (good to weak eye, weak to good eye) were similar and small. On the other hand, amblyopic subjects S1 and S8 showed relatively larger suppression from the good to weak eye, even more so than all the normal controls. Nevertheless, we didn’t find meaningful differences between the amblyopes with and without strabismus. Larger samples in future studies would be necessary to clarify the differences between different types of amblyopia.

Second, different paradigms are used. In the studies of Huang et al.8 and Ding et al.,26 suprathreshold binocular interactions were investigated when the contrasts in both eyes were well above the contrast thresholds. In contrast, when we tested the suppression from the mask (in the untested eye) to the grating (in the tested eye), only the mask was suprathreshold (five times the contrast threshold), while the grating was at threshold. The advantage of using this dichoptic-masking approach is that the suppression from the tested eye (seeing the threshold grating) to the untested eye (seeing the suprathreshold mask) is quite minimal, thus enabling one to directly quantify the suppression from the eye seeing the mask in terms of the threshold of the other eye. Third, different contrast levels are used. In both the studies of Huang et al.,8 and Ding et al.,26 the contrast in the amblyopic eye was fixed at one particular level (i.e., base contrast), and the binocular perceived phase and contrast was measured by varying the contrast in the fellow eye to find the interocular contrast ratio when the two eyes were balanced in binocular combination. We would argue that a fixed visibility criterion (i.e., five times the contrast threshold) is better than a fixed absolute contrast criterion (as used in the above-mentioned two studies) in the current study. It enables a better comparison across individuals or spatial frequencies where contrast thresholds under these conditions could be very different. Also, previous studies have shown that different base contrast could produce different extents of binocular imbalance, even in the same observer.2,8

This difference might account for the different spatial-frequency dependency of the binocular imbalance in different studies: for example, Ding et al.26 found more binocular imbalance at higher spatial frequencies (0.68 vs. 1.36 cyc/deg), while we didn’t find this phenomenon within the range of 0.67 to 1.31 cyc/deg.

We measured responses under dichoptic conditions where the detectability of threshold stimuli were affected by suprathreshold masks shown to the other eye. What can we conclude from these results about suppressive effects in amblyopes under natural viewing? Since we know from the work of Legge24 and others that the degree of interocular masking is a function of the suprathreshold contrast, we can make a number of simple predictions. First, at high spatial frequencies where contrast thresholds are raised, there will always be higher masking of the amblyopic eye by the fellow eye because the suprathreshold contrast of the fellow eye will be higher at all physical contrasts. This is the attenuator model of suppression (see Refs. 11 and 27). At low spatial frequencies where amblyopes either don’t have a threshold deficit for contrast or it is very minimal, the present results suggest there is another explanation. In this frequency region, the contrast gains of the inhibitory interactions are reduced from the amblyopic to the fellow eye, and this produces a net suppression of amblyopic eye function owing to reciprocal interocular inhibition.

To summarize, to determine the underlying mechanism of binocular imbalance in amblyopes, we calculated the average strength of interocular suppression in decibel units across observers in the low spatial-frequency range where we ensured all our dichoptic masks were set to five times their detectability in both the fellow and amblyopic eyes of all our amblyopes. It is apparent that normal observers exhibit no interocular suppressive imbalance within this frequency range, while amblyopes exhibit an imbalance that favors the fellow eye. Furthermore, this reduction in the influence that the amblyopic eye exerts over the fellow eye is not simply a consequence of the contrast deficit of the amblyopic eye; our use of stimuli of constant suprathreshold contrast factors out the effects of any contrast detection deficit, suggesting that the binocular deficit involves imbalanced contrast gain control rather than low-level attenuation. This conclusion covers most but not all of the visible spatial-frequency range over which amblyopes can see. At the highest spatial frequencies where the thresholds are greatly elevated, the resultant monocular attenuation ensures that any dichoptic masking of the fellow eye by the amblyopic eye will be necessarily weak because of the correspondingly reduced suprathreshold contrast range. This would be consistent with the attenuation hypothesis. Thus, the mechanism by which high and low frequencies are suppressed in amblyopes when using binocular viewing is likely to be different.

Acknowledgments

Supported by the National Natural Science Foundation of China Grant NSFC 81500754, the Qianjiang Talent Project Grant QTD1702021, the Wenzhou Medical University Grant QTIJ16005, and a grant from the Ministry of Human Resources and Social Security, China (JZ), the National Natural Science Foundation of China Grant NSFC 81300796 (LF), Canadian Institutes of Health Research Grants CI1-125686 and 228103, and ERA-NET Neuron Grant JTC2015 (RHF). The authors alone are responsible for the writing and content of the paper.

Disclosure: J. Zhou, None; A. Reynaud, None; Z. Yao, None; R. Liu, None; L. Feng, None; Y. Zhou, None; R.F. Hess, None

References

15. Prins N, Kingdom FAA. Applying the model-comparison approach to test specific research hypotheses in psychophysical research using the Palamedes toolbox. Front Psychol. 2018;9:1250.