Interocular suppression in amblyopia for global orientation processing

Jiawei Zhou
McGill Vision Research, Department of Ophthalmology, McGill University, Montreal, Québec, Canada

Pi-Chun Huang
McGill Vision Research, Department of Ophthalmology, McGill University, Montreal, Québec, Canada

Robert F. Hess
McGill Vision Research, Department of Ophthalmology, McGill University, Montreal, Québec, Canada

We developed a dichoptic global orientation coherence paradigm to quantify interocular suppression in amblyopia. This task is biased towards ventral processing and allows comparison with two other techniques—global motion processing, which is more dorsally biased, and binocular phase combination, which most likely reflects striate function. We found a similar pattern for the relationship between coherence threshold and interocular contrast curves (thresholds vs. interocular contrast ratios or TvRs) in our new paradigm compared with those of the previous dichoptic global motion coherence paradigm. The effective contrast ratios at balance point (where the signals from the two eyes have equal weighting) in our new paradigm were larger than those of the dichoptic global motion coherence paradigm but less than those of the binocular phase combination paradigm. The measured effective contrast ratios in the three paradigms were also positively correlated with each other, with the two global coherence paradigms having the highest correlation. We concluded that: (a) The dichoptic global orientation coherence paradigm is effective in quantifying interocular suppression in amblyopia; and (b) Interocular suppression, while sharing a common suppression mechanism at the early stage in the pathway (e.g., striate cortex), may have additional extra-striate contributions that affect both dorsal and ventral streams differentially.

Introduction

Amblyopia is a developmental condition resulting from disrupted visual development in which visibility is impaired in one eye even after optical correction (McKee, Levi, & Movshon, 2003; Simmers, Bex, & Hess, 2003; Woodruff, 1991). Recently, researchers have changed their focus from the monocular loss in amblyopia (Bedell & Flom, 1981; Fronius & Sireteanu, 1989; Hess & Holliday, 1992; Hess & Howell, 1977; Levi & Harwerth, 1977; McKee et al., 2003) to binocular interactions (Baker, Meese, & Hess, 2008; Baker, Meese, Mansouri, & Hess, 2007; Huang, Zhou, Lu, Feng, & Zhou, 2009; Huang, Zhou, Lu, & Zhou, 2011; Maehara, Thompson, Mansouri, Farivar, & Hess, 2011; Mansouri, Thompson, & Hess, 2008), especially interocular suppression. Several studies have shown that amblyopes tend to show normal binocular combination when the input in the fellow eye is artificially attenuated (Baker et al., 2007; Huang et al., 2009; Huang et al., 2011; Mansouri et al., 2008), revealing the potential importance of interocular suppression as a cause of amblyopia. Furthermore, there is evidence suggesting that antisuppression training recovers binocular function and, to some extent, monocular visual function in strabismic amblyopia (Hess, Mansouri, & Thompson, 2010a, 2010b; Hess, Mansouri, & Thompson, 2011; To et al., 2011), highlighting the importance of suppression in the deficit of amblyopia. It has also been shown that the application of 10-min repetitive transcranial magnetic stimulation (rTMS) of the visual cortex can improve the contrast sensitivity of the amblyopic eye, indicating that the reduced function may have been suppressed, not lost (Thompson, Mansouri, Koski, & Hess, 2008). Recently, Li et al. (2011) compared the strength of suppression with the degree of amblyopia and found that stronger suppression was associated with a greater difference in interocular acuity and poorer stereo acuity. Their results suggested that suppression may...
cause the amblyopia. The importance of suppression in amblyopia or (and) strabismus has also been supported in physiological studies (Sengpiel, Blakemore, Kind, & Harrad, 1994; Sengpiel, Freeman, & Blakemore, 1995; Sengpiel, Jirmann, Vorobyov, & Eysel, 2006). For example, it has also been shown that the application of bicuculline (a blocker of GABA<sub>A</sub> receptors) significantly improves the response of binocular cortical neurons in strabismic cats (Mower, Christen, Burchfiel, & Duffy, 1984; Sengpiel et al., 2006), indicating that at least part of the visual loss is not lost, but inhibited. Also in human functional imaging (fMRI), Farivar, Thompson, Mansouri, and Hess (2011) found that the cortical response to stimulation of the amblyopic eye was attenuated and delayed relative to that of the dominant eye when the dominant eye had a visual input, suggesting that interocular suppression underlies both of these effects.

On the other hand, interocular suppression in amblyopes has also been shown to be weak or absent when the fellow fixing eye sees only mean luminance. For instance, Barrett, Panesar, Scally, and Pacey (2012) found that the sensitivity of amblyopic eye to blue light stimulus on a yellow background didn’t change much no matter whether the fellow eye saw the full field background or not. This is consistent with a recent study by Huang, Baker, & Hess (2012), in which they found quite a weak masking effect caused by a dichoptic full field luminance modulation. However, a stronger masking effect was revealed when they used dichoptic contrast modulation of a noise texture, illustrating the contrast-dependent nature of suppression.

The inconsistency of interocular suppression in different paradigms gives rise to a fundamental question concerning amblyopia, namely, how to quantitatively determine and compare suppression in different individuals and involving different types of visual processing. Quantitative determination of suppression in amblyopia is also critical in clinical diagnosis, treatment and our understanding of amblyopia syndrome. Several paradigms have attempted to quantify the suppression in amblyopia. For example, the dichoptic global motion coherence paradigm, which was first developed by Hess, Hutchinson, Ledgeway, & Mansouri (2007), and then applied to the study of amblyopia by Mansouri et al. (2008). In this measure, signal dots with a coherent motion direction that is either to the left or to the right are presented to one eye, while noise dots having random motion directions are presented to the other eye. The contrast of the dots is kept constant for the amblyopic eye but varied for the fellow eye. The coherence threshold is measured when the amblyopic eye sees signal dots and fellow eye sees noise dots, and vice versa, at different interocular contrast ratios. This procedure results in two thresholds versus interocular contrast ratios (TvR) curves, one for when the fixing eye sees the signal dots and one for when the amblyopic eye sees the signal dots. The crossover point of these two TvRs represents a balance point, the contrast ratio where the two eyes are balanced in performance (i.e., the threshold is the same no matter which eye sees signal dots and which eye sees noise dots). They found that the effective contrast ratios at balance point were much less than 1, indicating suppression from the fellow eye to the amblyopic eye. Recently, this method has been adapted to the Z800 dual pro head-mounted display (eMagin, Bellevue, WA) to facilitate its use in the clinic (Black, Thompson, Maehara, & Hess, 2011). It has also been successfully adapted to measure suppression in children with amblyopia (Narasimhan, Harrison, & Giaschi, 2012).

The dichoptic global motion coherence paradigm provides a way to quantify suppression in the motion domain. Even though the underlying mechanisms are not fully understood (Hedges et al., 2011), the global motion task has been demonstrated to involve the dorsal extrastriate pathway, especially areas middle temporal area/medial superior temporal area (Baker Jr, Hess, & Zihl, 1991; Newsome & Pare, 1988), where neurons have large receptive fields enabling them to integrate local motion signals (Morrone, Burr, & Vaina, 1995). Mansouri et al. (2008) also showed that suppression could be measured using a global spatial task that possibly reflects activity in the ventral pathway (Braddick, O’Brien, Wattam-Bell, Atkinson, & Turner, 2000). However this global spatial task was different in nature (involving a pure integration process) from their global motion task (involving both integration and segregation processes) and required a different type of analysis (equivalent noise analysis) that did not lend itself to direct comparison between dorsal and ventral function.

Another method for accessing suppression is based on a local spatial phase task likely to be accomplished in a low-level cortical area, possibly the striate area, where neurons have smaller receptive fields and sensitive to the local phase properties of a stimulus (Hubel & Wiesel, 1968). The phase combination paradigm was first proposed by Ding & Sperling (2006) and subsequently applied to measure suppression in amblyopia by Huang et al. (2009). In this paradigm, two horizontal sine-wave gratings of the same spatial frequency and size are dichoptically presented. These stimuli have their spatial phase shifted in equal but opposite directions in two eyes at the same retinal location. The perceived binocular phase of the fused dichoptic pair is measured for a range of different interocular contrast ratios when the contrast in the amblyopic eye is fixed. The resultant perceived phase
versus interocular contrast ratios (PvR) curve displays a zero-crossing point, representing the interocular contrast ratio where the two eyes are balanced in their contribution (i.e., perceived phase is 0). Similar to previously reported results using the dichoptic global motion coherence paradigm, they also found that this was displaced to a lower contrast in the fellow eyes of amblyopes, suggesting suppression from the fellow to amblyopic eye.

These two different tasks, one involving a global orientation measure, possibly reflecting dorsal extra-striate function (Newsome & Pare, 1988; Simmers, Ledgeway, Hess, & McGraw, 2003) and the other involving a local spatial measure that may reflect low-level striate function (Huang, Zhou, Zhou, & Lu, 2010; Hubel & Wiesel, 1968), provide an easy and precise way to probe interocular suppression in two different parts of the cortex. What is needed is a global spatial task that could provide an assessment of ventral function to compare with the assessments of dorsal function that is provided by the global motion task. For the reasons previously discussed, the global integration task previously used by Mansouri et al. (2008) does not lend itself to such a comparison. To rectify this, in the present study, we therefore set out to develop a new global form-based paradigm, i.e., dichoptic global orientation coherence paradigm, to access suppression in amblyopia using the same coherence metric to that which has already been in use for global motion (Mansouri et al., 2008). The parallel designs of the global motion and form tests will facilitate their comparison to better understand suppression in the two different streams of extrastriate cortex. In this measure, signal Gabors with a coherent orientation, either vertical or horizontal, were presented to one eye, while noise Gabors having random orientations were presented to the other eye. The contrast of Gabors was fixed for the amblyopic eye but varied for the fellow fixing eye. The relationship between the orientation coherence threshold and the interocular contrast ratios was measured when the amblyopic eye sees the signal Gabors and the fellow eye sees noise Gabors, and vice versa. The degree of suppression was then assessed by calculating the effective contrast ratio corresponding to the balance point in performance (i.e., the crossover point of the two TvR functions).

The advantage of our new paradigm is that it quantifies the interocular suppression using the same metric as that previously used in the dichoptic global motion coherence task and the binocular phase combination task (i.e., the effective contrast ratios corresponding to the balance point), thus ensuring a more valid comparison between different tasks and types of visual processing. Based on this new paradigm, we addressed two questions: Can suppression be demonstrated for global orientation processing in amblyopia, reflecting ventral extrastriate function? What is the relationship between the suppression in global orientation processing, global motion processing, and local spatial phase processing? The answers to these questions could facilitate our understanding of the cortical site of suppression in amblyopia and how best to diagnose and treat it clinically.

Materials and methods

Participants

Eleven adult amblyopes (six females), between ages 21 and 58 years (mean age: 34.4 years) were recruited for this study. Three observers, A1, A2, and A3, had only strabismus (‘Stra’ type). One observer, A4, had only anisometropia (‘Anis’ type). All other observers had both strabismus and anisometropia (‘Mix’ type). Clinical details of these amblyopes are provided in Table 1.

This study complied with the Declaration of Helsinki and was approved by the institutional ethics committee of McGill University. All observers were naive to the purpose of the experiment; informed consent was obtained from each observer.

Apparatus

All experiments were conducted at a constant room luminance environment. Stimuli were generated by a Mac computer (Apple, Cupertino, CA) running Matlab with PsychTool Box 3.0.9 extension (Brainard, 1997; Pelli, 1997) and dichoptically presented with OLED goggles (Z800 pro, eMagin Corp., Washington, DC). The goggles simulated to a viewing distance of 3.6 m. The two OLED microdisplays are linear in luminance response, thus no gamma correction was needed (Black et al., 2011). The resolution was 800 × 600 in each eye. The refresh rate of goggles was 60 Hz. The mean luminance was 190 cd/m².

Design

We accessed the suprathreshold interocular suppression using a dichoptic global orientation coherence task and compared it with two other paradigms, a dichoptic global motion coherence task (Black et al., 2011; Mansouri et al., 2008) and a binocular phase combination task (Ding & Sperling, 2006; Huang et al., 2009).

The suppression measurements for the dichoptic global orientation coherence task and for the dichoptic
global motion coherence task are based on the same principle: The coherence signal and random noise are always dichoptically presented. The coherence threshold is measured when the amblyopic eye sees the signal elements and the fellow eye sees the noise elements, and vice versa, at different interocular contrast ratios. The interocular suppression is then quantified by the interocular contrast difference that is needed to obtain the same coherence thresholds when the signal elements are presented in different eyes. In our measure, the contrast of the grating in the amblyopic eye was fixed at 100%, and five interocular contrast ratios between 0.05 and 1 were chosen based on each individual’s performance in the practice trials.

The binocular phase combination paradigm was different from the two other methods previously described. In this paradigm, two monocular sine-wave gratings with different contrast and phase-shifted in opposite directions by the same magnitude are dichoptically presented. The perceived phase of the cyclopean grating depends on the internal representations of the two inputs. Interocular suppression is quantified by the interocular contrast difference that is needed to achieve 0° of perceived phase. In our measure, the contrast of the grating in the amblyopic eye was fixed at 100%, and the following interocular contrast ratios were used: 0, 0.1, 0.2, 0.4, 0.8, and 1.

These three measures were conducted in randomized orders between observers. Except observer A11, who only participated in the measures of dichoptic global orientation coherence task and binocular phase combination task, all other observers participated in all three measures. Demonstrations of the task and practice trials were provided prior to data collection.

<table>
<thead>
<tr>
<th>Subject#</th>
<th>Age/Sex</th>
<th>Type</th>
<th>Refractive Error (OD/OS)</th>
<th>Visual Acuity (OD/OS)</th>
<th>Strabismus (distance)</th>
<th>History, stereo</th>
</tr>
</thead>
<tbody>
<tr>
<td>◼ A1</td>
<td>51/M</td>
<td>RE</td>
<td>+4.50+0.75X135</td>
<td>0.1</td>
<td>Alternating XT2°*</td>
<td>Detected at 2 years old, surgery at 2 years old, patched for 3 years, no stereopsis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LE</td>
<td>+4.50+0.75X135</td>
<td>0.1</td>
<td>Alternating XT2°*</td>
<td>Detected at 2 years old, surgery at 2 years old, patched for 3 years, no stereopsis</td>
</tr>
<tr>
<td>□ A2</td>
<td>23/F</td>
<td>RE</td>
<td>-1.00-0.75X30</td>
<td>0.5</td>
<td>XT4°, HT2.5°*</td>
<td>Detected at 11 years old, no surgery and patching, eye exercise 1-2 years, glasses since 12 years old, no stereopsis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LE</td>
<td>-1.00-0.75X30</td>
<td>0.5</td>
<td>XT4°, HT2.5°*</td>
<td>Detected at 11 years old, no surgery and patching, eye exercise 1-2 years, glasses since 12 years old, no stereopsis</td>
</tr>
<tr>
<td>◼ A3</td>
<td>29/F</td>
<td>RE</td>
<td>+2.50+1.25X20</td>
<td>0.6</td>
<td>ET4.5°*</td>
<td>Detected at age 11 years old, patched for 2 months at age 11 years, tried again at age 22 for 2 months. Stereo vision 200°*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LE</td>
<td>+2.50+1.25X20</td>
<td>0.6</td>
<td>ET4.5°*</td>
<td>Detected at age 11 years old, patched for 2 months at age 11 years, tried again at age 22 for 2 months. Stereo vision 200°*</td>
</tr>
<tr>
<td>▲ A8</td>
<td>22/M</td>
<td>RE</td>
<td>+5.00</td>
<td>0.46</td>
<td>ET4°*</td>
<td>No surgery, had a combination of patching and drops at 5 years old for 4 months, no stereopsis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LE</td>
<td>+5.00</td>
<td>0.46</td>
<td>ET4°*</td>
<td>No surgery, had a combination of patching and drops at 5 years old for 4 months, no stereopsis</td>
</tr>
<tr>
<td>▲ A9</td>
<td>32/F</td>
<td>RE</td>
<td>+4.00</td>
<td>1.3</td>
<td>ET8°*</td>
<td>Detected at 3 years old, no surgery, patched for 2 years, no stereopsis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LE</td>
<td>+4.00</td>
<td>1.3</td>
<td>ET8°*</td>
<td>Detected at 3 years old, no surgery, patched for 2 years, no stereopsis</td>
</tr>
<tr>
<td>▼ A10</td>
<td>21/F</td>
<td>RE</td>
<td>-0.75X192</td>
<td>0.5</td>
<td>XT15°*</td>
<td>Detected at 3 years old, patched occasionally until 7 years old then received surgery, no stereopsis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>LE</td>
<td>-0.75X192</td>
<td>0.5</td>
<td>XT15°*</td>
<td>Detected at 3 years old, patched occasionally until 7 years old then received surgery, no stereopsis</td>
</tr>
<tr>
<td>▼ A11</td>
<td>28/M</td>
<td>RE</td>
<td>+0.50+1.50X180</td>
<td>0.3</td>
<td>ET7°*</td>
<td>Detected at 5 years old, then patched 1 hour per day for 6 months, no surgery, no stereopsis</td>
</tr>
</tbody>
</table>

Table 1. Clinical details of the participants. Strabismus angle was measured using the prism cover test; stereopsis was measured by random dot stereo test (preschool version). Notes: RE = right eye; LE = left eye; Stra = strabismus; Anis = anisometropia; Mix = mixed (strabismus + anisometropia); XT = exotropia; ET = esotropia; HT = hypertropia.
Stimuli

The dichoptic global orientation coherence stimulus consisted of an array of 100 small Gabor patches, arranged in a $10 \times 10$ square grid (grid length $= 19.67^\circ$ of visual angle). A binocular black rectangular frame (visual angles: length $= 21.14^\circ$, width $= 0.19^\circ$) with four extensional monocular short fixation lines at the edges (visual angles: length $= 0.76^\circ$, width $= 0.19^\circ$), of which two were in the left eye and two in the right eye, were presented surrounding the grating to aid binocular fusion. A binocular center dark fixation dot ($0.26\cdot 0.26$ visual angles: length $= 21.14^\circ$, width $= 0.19^\circ$) was always presented in the measurement. The individual Gabor patches were sampled by $1.97\cdot 1.97$ of visual angle, and defined by the equation:

$$g(x, y) = c \sin\{2 \pi f[x \sin(\theta) + y \cos(\theta)]\} \times \exp\left[-\frac{(x^2 + y^2)}{(2\sigma^2)}\right]$$

(1)

In which, $c$ is the contrast of the grating, $f$ is the spatial frequency of the grating, $\theta$ is the orientation of the grating, and $\sigma$ is the bandwidth of Gaussian envelope.

For each Gabor patch, the spatial frequency was $1.02 c/\circ$, the bandwidth of Gaussian envelope was $0.37^\circ$. Within the array, the spatial positions of signal and noise elements were randomly assigned prior to their presentation. The orientation of signal elements was sampled from a narrow uniform distribution, i.e., a “$\pm 5^\circ$” jitter around vertical or horizontal, while the orientation of noise elements was sampled from a uniform distribution between $1^\circ$ and $360^\circ$. The spatial position and orientation of all elements were varied on different trials (each trial lasted 200 ms). An illustration of the stimulus is shown in Figure 1A.

The dichoptic global motion coherence stimulus was similar to that previously described (Black et al., 2011): 100 moving dots (each diameter $0.40^\circ$ of visual angle) with randomized positions were presented in a circular display window (diameter, $8.40^\circ$ of visual angle). Some of them were assigned as signal dots and had a coherent motion direction (either leftward or rightward), while others were assigned as noise dots and had a random motion direction (sampled from a uniform distribution between $1^\circ$ and $360^\circ$). The dots were moved at $3.36^\circ$/s. To lessen tracking of individual dots, a $5\%$ probability of limited lifetime was assigned on each dot in each presentation frame. When a dot reached to its limited lifetime, a new dot was born at a random location.

When a dot moved to the edge of the display window, it disappeared and immediately reappeared at the opposite edge. An illustration of the stimulus is shown in Figure 1B. Detailed information can be found in Black et al. (2011; their Method 1).

The stimulus in the binocular phase combination task was similar to that previously described (Huang et al., 2009): two monocular sine-wave gratings of different contrast and phase-shifted in opposite directions with same magnitude were dichoptically presented. A high-contrast frame (visual angles: width $= 0.378^\circ$, length $= 20.43^\circ$) with four white diagonal bars (visual angles: width $= 0.378^\circ$, length $= 9.63^\circ$) was presented surrounding the grating to help observers in maintaining vergence. A 1-pixel black reference line was provided to help observers to indicate the perceived phase after combination. Perceived phase was calculated by the difference of the two configurations to cancel possible positional bias. An illustration of the stimulus is shown in Figure 1C (for details, see Huang et al.’s [2009] methods and figure 1). In the measure, the two monocular sine-wave gratings had a phase difference of $45^\circ$. To match the same accuracy with that in Huang et al. (2009), we also used 180-pixel two-cycle gratings, which subtended $6.8^\circ$ of visual angle (i.e., $0.29 c/\circ$).

Procedure

We used the same procedure as used by Black et al. (2011) for measuring coherence thresholds. In one typical trial of the dichoptic global orientation coherence task, the grating array was presented for 200 ms, and subjects were instructed to answer whether the coherent orientation was vertical or horizontal by pressing a keyboard. In one typical trial of the dichoptic global motion coherence task, the moving dots were presented for $1\ s$, and subjects needed to answer whether the coherent motion direction was left or right by pressing a keyboard. The number of signal elements was controlled by a three-down one-up staircase procedure with step size of $50\%$ in the first trial and $25\%$ thereafter. The coherence thresholds were measured when the amblyopic eye saw signal elements and the fellow eye saw noise elements (configuration 1), and vice versa (configuration 2), at five interocular contrast ratios. In all, there were 10 staircases for one measure (2 configurations $\times$ 5 interocular contrast ratios). Different staircases were randomly interleaved, and terminated at the sixth reversal point. The coherence threshold and its standard error were then calculated based on the last five reversals. Before the measure, subjects also completed a line alignment task to fuse their two eyes. In the line alignment task, they were instructed to move the stimuli in the amblyopic eye to align with the stimuli in the fellow eye. The corresponding coordinate between two eyes was then used in the following measurement. Thus measurements were done at the subjective angle that may or may not have coincided.
with the objective angle of strabismus (i.e., anomalous retinal correspondence).

We used the same adjustment procedure as that used by Huang et al. (2009) in measuring perceived phase after binocular combination. In each trial, subjects first completed an alignment task by changing the coordinate of images in the amblyopic eye to make sure their two eyes were perfectly fused. This followed the second task, i.e., phase adjustment task, where observers were asked to adjust the position of a sided reference line to indicate the perceived phase of the cyclopean sine-wave grating after binocular combination, defined as the location of the center of the dark stripe of the grating. The reference line was presented binocularly, with its initial position randomly (−9 to 10 pixels) assigned relative to the center of the frame in each trial. The reference line was moved with a fixed step size of 1 pixel, corresponding to a 4° phase angle of the sine-wave grating. During one trial, the stimuli were presented continually until subjects finished the phase adjustment task. The perceived phases were measured when the phase-shift of the grating was 22.5° in amblyopic eye and −22.5° in fellow eye (configuration 1), and vice versa (configuration 2), at six interocular contrast ratios. Each configuration was measured eight times using constant stimuli. The perceived phase and its standard error were then calculated based on the eight repetitions. In all, there were 96 trials in one measure (2 configurations × 6 interocular contrast ratios × 8 repetitions).

Figure 1. An illustration of the stimulus in the three paradigms for measuring interocular suppression. (A) Dichoptic global orientation coherence paradigm. (B) Dichoptic global motion coherence paradigm. (C) Binocular phase combination paradigm.
Data fitting

Unlike the empirical linear fitting in Black et al.’s study (2011), we fitted the coherence thresholds (% of signal elements) versus interocular contrast ratio curves (TvRs) using cumulative distribution functions. For the diverse interocular contrast ratios that were measured in our observers, the empirical cumulative distribution functions fitted better than the linear functions. We fitted TvRs in Matlab by the following equations:

\[
Th_{AE} = 1 + \eta_{AE} \frac{1}{\sigma_{AE}\sqrt{2\pi}} \int_{-\infty}^{\delta} e^{-\frac{-(l-\mu_{AE})^2}{2\sigma_{AE}^2}} dt,
\]

\[
Th_{FE} = 1 + \eta_{FE} \left(1 - \frac{1}{\sigma_{FE}\sqrt{2\pi}} \int_{-\infty}^{\delta} e^{-\frac{-(l-\mu_{FE})^2}{2\sigma_{FE}^2}} dt \right).
\]

In which, \(Th_{AE}\) is the threshold (in %) when signal was presented in the amblyopic eye, range from 1 to 1+\(\eta_{AE}\) (in which, 1 ≤ \(\eta_{AE}\) ≤ 99); \(\delta\) is the interocular contrast ratio, range: 0–1; \(\mu_{AE}\) and \(\sigma_{AE}\) represent the mean and standard deviation of a normal cumulative distribution function \((cdf)\) for the amblyopic eye condition. Similarly, \(Th_{FE}\) is the threshold (in %) when the signal elements were presented in fellow eye, range from 1 to 1+\(\eta_{FE}\) (in which, 1 ≤ \(\eta_{FE}\) ≤ 99); \(\delta\) is the interocular contrast ratio, range: 0–1; \(\mu_{FE}\) and \(\sigma_{FE}\) represent the mean and standard deviation of a normal cdf for the fellow eye condition.

The perceived phases versus interocular contrast ratio (PvR) curves in the binocular phase combination paradigm were fitted by the previously described modified contrast gain control model for amblyopia (Huang et al., 2009):

\[
\varphi = 2 \tan^{-1}\left[\frac{1 - a\delta^{1+\gamma}}{1 + a\delta^{1+\gamma}}\right] \tan\left(\frac{\theta}{2}\right).
\]

In which, \(\varphi\) is the measured perceived phase when the interocular contrast ratio is \(\delta\), \(\theta\) is the interocular phase difference (i.e., 45° in our study), and the two free parameters, \(a\) and \(\gamma\), represent inhibition factor and nonlinear factor in the binocular combination, respectively.

Fittings were conducted in Matlab using nonlinear least squares method to minimized \(\sum (Th_{theory} - Th_{observed})^2\). The goodness-of-fit was statistically tested by computing the \(R\)-square value:

\[
r^2 = 1 - \frac{\sum (Th_{theory} - Th_{observed})^2}{\sum [Th_{observed} - mean(Th_{observed})]^2},
\]

Results

The TvR functions in the dichoptic global orientation coherence paradigm for all 11 observers (A1 – A11) and that in the dichoptic global motion coherence paradigm for 10 observers (A1 – A10) are shown in Figures 2 and 3, respectively. In each figure, different panels are organized by the subject IDs. Each panel consists of two sets of TvR functions. The coherence thresholds that were measured when the amblyopic eye saw the signal elements (\(Th_{AE}\)) and when the fellow eye saw the signal elements (\(Th_{FE}\)) are plotted as functions of the interocular contrast ratios (fellow eye / amblyopic eye). Interestingly, while the threshold varied across participants and paradigms, similar patterns of TvRs were apparent. As the interocular contrast ratio increased, the thresholds, when the signal elements were presented to the amblyopic eye (\(Th_{AE}\)), monotonically increased. However, when the signal elements were presented to the fellow eye (\(Th_{FE}\)), thresholds monotonically decreased. The contrast ratio at the crossover point of these two TvRs (i.e., balance point) is much less than 1 (i.e., range, 0–0.614), indicating suppression from fellow eye to amblyopic eye in all observers (Black et al., 2011).

The TvR functions are fitted well by our empirical cumulative distribution functions (see Methods). The average goodness-of-fit is 0.873 ± 0.114 (mean ± SD) in the dichoptic global orientation coherence paradigm and 0.970 ± 0.046 (mean ± SD) in the dichoptic global motion coherence paradigm, respectively. The average contrast ratio at balance point, which was derived from the crossover point of the two fitted TvR functions, is 0.228 ± 0.192 (mean ± SD) in the dichoptic global orientation coherence task, and 0.137 ± 0.102 (mean ± SD) in the dichoptic global motion coherence task. They are much less than the previously reported results using the dichoptic global motion coherence task in normal adults, which is 0.88 ± 0.18 (mean ± SD); Zhang, Bobier, Thompson, & Hess, 2011), indicating more suppression exists in the amblyopic visual system than the normal visual system. The different techniques for quantifying suppression that were used in our dichoptic global orientation coherence paradigm (i.e., interocular contrast ratio) and the global form based task in Mansouri et al. (2008; i.e., interocular contrast ratio and elements ratio), make it hard to directly compare these results. However, these two are consistent in showing suppression from the fellow eye.

The PvR curves in the binocular phase combination paradigm for all 11 observers (A1 – A11) are shown in Figure 4, with its panels organized in the same manner as Figure 2. All subjects shown a pattern consistent with previous findings in amblyopia (Huang et al., 2009): As the interocular contrast ratio increased from 0 (0 contrast in the fellow eye) to 1 (when two eyes have equal...
Figure 2. The coherence threshold versus interocular contrast ratio curves of the dichoptic global orientation coherence paradigm. Data of different observers are shown in separate panels. In each panel, the vertical axis represents coherence threshold (in %), the horizontal axis represents interocular contrast ratio (fellow eye / amblyopic eye). The ID and amblyopia type of each observer is shown on the right top corner. The coherence thresholds that were measured when the amblyopic eye saw signal Gabors ($T_{AE}$) are shown in ‘□’ points, and the coherence thresholds that were measured when fellow eye saw signal Gabors ($T_{FE}$) are shown in ‘○’ points. Solid lines represent predictions of the best fitting cumulative distribution functions. Error bars represent standard errors.

Figure 3. The coherence threshold versus interocular contrast ratio curves of the dichoptic global motion coherence paradigm. Data of different subjects are shown in separate panels. In each panel, the vertical axis represents coherence threshold (in %), the horizontal axis represents interocular contrast ratio. The ID and amblyopia type of each observer is shown on the right top corner. The coherence thresholds that were measured when the amblyopic eye saw signal dots ($T_{AE}$) are shown in ‘□’ points, and the coherence thresholds that were measured when the fellow eye saw signal dots ($T_{FE}$) are shown in ‘○’ points. Solid lines represent predictions of the best fitting cumulative distribution functions. Error bars represent standard errors.
contrast), the perceived phase of the cyclopean grating monotonically shifted from +45 (represent totally dominant of amblyopic eye), to zero (represent when two eyes are balanced), and to less than zero (represent the dominance of the fellow eye). The PvR curves are fitted well by the modified contrast gain control model for amblyopia (Huang et al., 2009), with an average goodness-of-fit of 0.951 ± 0.022 (mean ± SD). Averaged across all 11 observers, the contrast ratio at the zero crossing point of the PvR curves is 0.338 ± 0.180 (mean ± SD). Our results are consistent with a previous report (Huang et al., 2009), which used the same paradigm and showed that the effective contrast ratios were in the range of 0.11–0.28 for five anisometropic amblyopes, and much less than that found in normals (i.e., approximately 1), indicating, in the case of amblyopes, a much lower effectiveness of the amblyopic eye relative to fellow eye in the binocular phase combination.

Comparisons of the effective ratios at the balance point (our measure of “suppression”) between these three paradigms are shown in Figure 5. Because subject A11 didn’t finish the measurements using the dichoptic global motion coherence paradigm, any comparisons between the dichoptic global motion coherence paradigm and other paradigms are based on the results from subjects A1 to A10, while other comparisons are based on the results from A1 to A11. (Removing the data of subject A11 slightly changed the statistical results but did not change the conclusions). The measured effective contrast ratios in the dichoptic global orientation coherence paradigm are plotted as a function of that found in the dichoptic global motion coherence paradigm in Figure 5A. Paired samples t test shows that the effective contrast ratios corresponding to the balance point are significant different in these two paradigms: $t(9) = 2.379$, $p = 0.041$, two-tailed. While paired samples correlation test shows that there is a significant positive correlation between the results in these two paradigms: $r = 0.783$, $p = 0.007$, two-tailed. Similarly, the measured effective contrast ratios in the dichoptic global orientation coherence paradigm are plotted against that found in the binocular phase combination paradigm in Figure 5B. Paired samples $t$ test shows that the effective contrast ratios are significantly different in these two paradigms: $t(10) = 1.995$, $p = 0.074$, two-tailed. While paired samples correlation test shows that there is a significant positive correlation between the effective ratios in these two paradigms: $r = 0.523$, $p = 0.098$, two-tailed. Comparisons between the results in the dichoptic global motion coherence paradigm and the binocular phase combination paradigm are shown in Figure 5C. The measured effective contrast ratios in the dichoptic global motion coherence paradigm are significantly less than that found in the binocular phase combination paradigm: $t(9) = 4.403$, $p = 0.002$, paired samples $t$ test, two-tailed. The correlation between results in these two paradigms is also significant: $r = 0.660$, $p = 0.038$, two-tailed. Furthermore, a repeated measures ANOVA based on the results from subjects A1 to A10 also
shows that the effective contrast ratios are significantly different in these three paradigms (within-subjects factor): $F(2, 18) = 8.055, p = 0.003$.

Since a previous report has shown that the degree of amblyopia is directly related to the magnitude of suppression (Li et al., 2011), it is interesting to see the extent to which they are related in our participants. We address this question in Figure 6 (subject A3 was not included in this analysis as she had an alternating strabismus, unlike all other subjects who had constant strabismus). There was a trend toward decreasing contrast ratios (i.e., increasing suppression) being associated with increasing interocular visual acuity differences (i.e., increasing depth of amblyopia) for all three paradigms. However, none of them reached significance, due to the small sample size: orientation coherence task, $n = 10, r = -0.348, p = 0.323$; motion coherence task, $n = 9, r = -0.469, p = 0.203$; Phase combination task, $n = 10, r = -0.441, p = 0.202$ (paired samples $t$ test, two-tailed).

**Discussion**

A new method for measuring interocular suppression—the dichoptic global orientation coherence paradigm—is described here. The rationale of this method is that it provides a comparable approach for ventral-based function, using a dichoptic global orientation coherence paradigm to that already in use for dorsal-based function using a dichoptic global motion coherence paradigm (Black et al., 2011; Mansouri et al., 2008). Unlike the random dot kinematograms used in the dichoptic global motion coherence paradigm, the dichoptic global orientation coherence paradigm uses an array of static orientation Gabor patches as the stimulus. We found similar patterns of TVRs in the dichoptic global motion coherence paradigm, the dichoptic global orientation coherence paradigm uses an array of static orientation Gabor patches as the stimulus. We found similar patterns of TVRs in the dichoptic global motion coherence paradigm to that found in the dichoptic global motion coherence paradigm: as the interocular contrast ratio (fellow eye / amblyopic eye) increased, the coherence threshold, measured when the amblyopic eye saw the signal elements and the fellow eye saw the noise elements, monotonically increased; while measured in the reverse condition, it monotonically decreased. This provides an
answer to the first question we raised by demonstrating suppressive influences using a global spatial paradigm, suggesting involvement of the ventral extrastriate cortex. To address the second question raised in the Introduction, we also compared the difference and correlation of the effective ratios among the dichoptic global orientation coherence paradigm, dichoptic global motion coherence paradigm and binocular phase combination paradigm. The measured effective contrast ratios at balance point were all less than 1 in these three paradigms, confirming their efficiencies in quantifying interocular suppression in amblyopia. However, the two eyes were balanced at different interocular contrast ratios in these three paradigms, suggesting different degrees of suppression associated with each task. Averaged across subjects, the relationship of the magnitude of the effective contrast ratios in these three paradigms is: binocular phase combination paradigm > dichoptic global orientation coherence paradigm > dichoptic global motion coherence paradigm. The effective contrast ratios were also positively correlated with each other in these three paradigms, and the highest correlation occurred between the dichoptic global orientation coherence paradigm and the dichoptic global motion coherence paradigm.

The similar pattern of TVRs and high correlation between the dichoptic global orientation coherence paradigm and the dichoptic global motion coherence paradigm is not surprising, since they both reflect extrastriate function although along different pathways (Braddick et al., 2000). In addition, previous evidence has also suggested that the monocular global processing deficit may be similar for both the orientation sensitive (ventral) and the motion sensitive (dorsal) pathways (Simmers et al., 2003; Simmers, Ledgeway, & Hess, 2005). In turn, the present study provides further support for the similarity of suppressive deficit in global orientation and global motion processing.

The three paradigms that were used in the current study involve stimuli of different spatial frequency, field size, and noise level. However, we do not believe that the difference we find in strength of suppression is due to stimulus differences. The only candidate parameter is spatial frequency because it displays a similar rank order to that of the strength of suppression (0.29 c/° – phase; 1.02 c/° – orientation; 2.50 c/° – motion). However, we have unpublished data suggesting suppression is independent of spatial frequency (Babu, Thompson, & Hess, 2013). It is therefore more likely that the differences we find in the strength of suppression for these three different tasks is because they probe different cortical sites; there are a number of predictions for how the results from these tasks could relate to one another. If all the results are highly correlated and produced equivalent estimate of suppression then the most parsimonious explanation is a common underlying site, early in the pathway. If the results are uncorrelated and produce different estimates of suppression then independent sites have to be considered. The results are somewhere in-between these two extreme cases. The finding that there is a strong positive correlation of effective ratios in two eyes’ balance point between tasks is consistent with a common mechanism at an early site in the cortical pathway. This is consistent with several animal neurophysiological investigations, which have shown that the interocular suppression occurs in V1 cells (Harrad, Sengpiel, & Blakemore, 1996; Sengpiel & Blakemore, 1996; Sengpiel et al., 2006; Wong, Burkhalter, & Tychsen, 2005) and V2 (Bi et al., 2011). There are also studies using event-related potentials
that have found suppression at a very early stage of visual cortical process in adults with amblyopia. The finding that the estimates of suppression from different tasks are statistically different suggests that additional deficits at different parts along the ventral and dorsal pathway need to be considered. This general conclusion is consistent with two recent studies which showed that different aspects of dichoptic stimuli are computed in different pathways, but share an early common cross-eye gain control in normals (Huang et al., 2010) and amblyopes (Huang et al., 2011).

The finding that greater suppression occurred in extrastriate cortex and that motion-based processing is more affected than comparable spatial-based estimates, is consistent with the finding that global-motion processing is more affected than global-orientation processing in developmental disorders (Braddick, Atkinson, & Wattam-Bell, 2003).

The differences reported between the effective ratios measured for the three paradigms in the current study suggest that there is no one test that can provide a full description of suppression; different tests must be used to assess different functions and cortical regions affected.

**Conclusion**

The present study provides a novel method to quantify interocular suppression for global orientation processing relevant to ventral extrastriate function, thus extending our understanding of the binocular deficit in amblyopia. By comparing suppression using three different tasks, each targeting a different cortical function and location, we obtain a better understanding of the extent to which cortical functions and cortical locations are affected. Suppression is ubiquitous in the visual cortex and is greater in extrastriate cortex, particularly the dorsal pathway.

**Keywords:** suppression, amblyopia, global orientation, extra-striate

**Acknowledgments**

This work was supported by the Canadian Institutes of Health Research Grants MOP53346 (RFH). The authors would like to thank Dr. Anthony Norcia and two anonymous reviewers for their helpful comments and thoughtful suggestions.

Commercial relationships: none.

Corresponding author: Jiawei Zhou.

Email: jiawei.zhou@mcgill.ca.

Address: McGill Vision Research, Department of Ophthalmology, McGill University, Montreal, Québec, Canada.

**References**


