Visual Neuroscience

Is Suppression Just Normal Dichoptic Masking? Suprathreshold Considerations

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Purpose. Amblyopic patients have a deficit in visual acuity and contrast sensitivity in their amblyopic eye as well as suppression of the amblyopic eye input under binocular viewing conditions. In this study we wanted to assess the origin of the amblyopic suppression by studying the contrast perception of the amblyopic eye at suprathreshold levels under binocular and monocular viewing.

Methods. Using a suprathreshold contrast matching task in which the reference and target stimuli were presented to different eyes either simultaneously or successively, we measured interocular contrast matching in 10 controls and 11 amblyopes (mean age 35 ± 15; 5 strabismics; 3 anisometropes; 3 mixed). This was then used as an index of the binocular balance across spatial frequency and compared against the contrast sensitivity ratio measured with the same stimuli.

Results. We observed that binocular matching becomes more imbalanced at high spatial frequency for amblyopes, compared with controls; that this imbalance did not depend in either group on whether the stimuli were presented simultaneously or successively; and that for both modes of presentation the matching balance correlates well with the interocular contrast sensitivity ratio (mean correlation coefficient of the slopes $R = 0.7125$).

Conclusions. The results from our amblyopes show comparable losses of contrast perception at and above threshold under these binocular viewing conditions across a wide spatial frequency range, much stronger than that observed for our controls. This occurs under conditions in which there should be no dichoptic masking. Furthermore, the matching contrast could be well predicted by the monocular contrast sensitivity. Altogether, this suggests that amblyopic suppression cannot be explained by normal dichoptic masking but rather an attenuation of the input.

Keywords: interocular matching, amblyopia, qCSF, contrast constancy, suppression

Amblyopia involves a loss of monocular vision and a suppression of the amblyopic eye's function under binocular viewing. There is debate about the causal relationship between these two factors. One possibility is that the suppression seen in amblyopia is a consequence of combining normal dichoptic masking with elevated contrast threshold in the amblyopic eye. Dichoptic masking depends on the level of suprathreshold contrast, so an elevated threshold in one eye (e.g., the amblyopic eye) would automatically result in imbalanced masking at all contrast levels, such that one eye (e.g., the fellow fixing eye) will always dominate over the other. We refer to this as the threshold hypothesis, as implemented by the offset subtraction model (see Appendix) where the primary deficit is the amblyopia and the secondary consequence is the binocular dysfunction.[1,2] An alternate explanation is that the suppression results from anomalously large dichoptic inhibition of the amblyopic eye's input by the fellow fixing eye's input that in the long term results in a contrast threshold elevation in the amblyopic eye. We refer to this as the inhibition hypothesis, where the primary deficit is the binocular dysfunction and the secondary deficit, the amblyopia.[2–4]

One of the key features of amblyopia is a characteristic increase of contrast detection thresholds (which is more severe at higher spatial frequencies[5,6]) but virtually normal contrast perception for monocularly viewed stimuli shown at contrasts above their detection threshold.[7–9] That is to say that amblyopes do not perceive their world to be simply reduced in contrast when viewing with their amblyopic eye.[10] Under binocular viewing conditions there is thought to be little or no contribution from the amblyopic eye due to a strong dominance of the fixing eye, a condition known clinically as suppression. It has recently been suggested that therapies that reduce suppression hold the key to restoring normal binocular function in amblyopes,[11,12] something often sought after but rarely attained using the traditional patching therapy. Methods designed to reduce suppression and subsequently strengthen fusion have been shown to be effective in restoring binocular vision, improving stereopsis and improving the monocular vision of the amblyopic eye.[11,12] The mechanism underlying the amblyopic suppression is therefore important to understand, the key issue being whether the binocular dysfunction causes the amblyopia or vice versa.

Studies of binocular interactions in the normal visual system have identified not only excitatory combination of signal from the two eyes but also inhibitory interactions between the signals from the two eyes.[13,14] Normally these inhibitory interactions from each eye are in balance, and as a consequence, downstream excitatory combination is not disrupted.

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TABLE 1. Clinical Details of Amblyopic Subjects; Suppression Was Measured With the Bagolini Striated Glasses Test; Their Measured Cutoff Frequency f_c Is Reported in the Last Column

Subject	Age	Sex	Type	Eye	Refraction	VA	Squint	Suppression	History	f_c, cyc/deg
A1	25	F	Strab	NAE	Plano	20/20	R exo 15°	Strong	Detected at 2 y; patched for 5 y; 2 strabismic surgeries at 2 y	4.08
				AE	−0.75/−0.50×60°	20/63				
A2	43	M	Strab	NAE	−1.25/−0.25×103°	20/12.5	R exo 10°	Central	Detected around 10 y; patched for around 1.5 y	11.27
				AE	+0.5/−1.25×90°	20/80				
A3	54	M	Mixed	NAE	+2.00	20/12.5	L eso 8°	Strong	Detected at 3 y; microtropia	3.20
				AE	+2.00	20/125				
A4	23	M	Aniso	NAE	Plano	20/16		Central	Strabismus detected at 1 y; surgeries to correct; patched from 4 to 6 y	12.98
				AE	+0.50/−1.00×15°	20/32				
A5	21	M	Mixed	NAE	−2.75	20/10	L exo 5°	No	Detected at 11 y; patched for 5 y	6.47
				AE	+1.75/−1.00×30°	20/32				
A6	61	F	Strab	NAE	+3/−1×73°	20/12.5	R exo 5°	Strong	Detected at 12 y; patched for 6 mo	0.82
				AE	+6/+2.5×0°	20/63				
A7	53	M	Strab	NAE	−1.25/−0.50×30°	20/20	L exo 6°	No	Detected at 11 y; exercises for 1–2 y	7.76
				AE	+2.50/−1.50×75°	20/50				
A8	23	M	Aniso	NAE	−0.50	20/16		Central	Detected around 15 y	4.24
				AE	+2.00	20/63				
A9	25	M	Mixed	NAE	+3.50	20/16	L exo 4°	Central	Detected at 5 y; patched for 3 mo all day long	15.20
				AE	+5.25/2.25×30	20/100				
A10	35	M	Strab	NAE	Plano/−0.25×80°	20/20	R eso 10°	Strong	Patched for 1 y	2.54
				AE	+4.00/−0.50×160°	20/50				
A11	25	F	Aniso	NAE	−1.50	20/12.5		No	Detected around 12 y	5.85
				AE	+1.50	20/63				

VA, visual acuity; Strab, strabismus; Aniso, anisometropia; NAE, nonamblyopic eye; AE, amblyopic eye; R, right; L, left; exo, exotropia; eso, esotropia.

In amblyopia, it has been proposed that dichoptic masking that is normally balanced between the two eyes is imbalanced owing to the loss of threshold sensitivity of the amblyopic eye, and that this in turn results in a disruption to the excitatory combination resulting in a loss of binocularity.[15]

This suggestion was first made by Harrad and Hess[2] and is consistent with studies involving threshold detection tasks and pedestal detection tasks.[15–17] It represents a special case of the attenuation model of Baker et al.,[15] where only threshold attenuation is considered (see Appendix for detailed discussion). However, can this explanation also explain the contrast perception of suprathreshold stimuli? Here, we used an interocular contrast matching task in which stimuli were presented to the two eyes in different visual field positions either simultaneously or successively. Our assumption, based on the findings of Meese and Hess[14] and Maehara et al.,[18] was that in the simultaneous case, the fellow eye should suppress the amblyopic eye. However, in the successive case, the stimuli in one eye are paired with only mean luminance stimulation in the other eye. This ensures that there is no contrast-dependent stimulation of the amblyopic eye and hence there should be no dichoptic masking. This provides a clear testbed to assess the dichoptic masking explanation of suppression.

The threshold hypothesis would predict an interocular matching ratio around 1 for the successive stimulation condition (veridical perception of suprathreshold contrast) but a smaller ratio for the simultaneous stimulation (suppression of the amblyopic eye by the fellow eye). However, the inhibition hypothesis would predict a ratio less than 1 in both the successive and simultaneous conditions. Furthermore, the difference in perceived contrast between these two predictions may depend on the spatial frequency of the stimuli used.

We measured the perceived suprathreshold contrast, using a contrast matching adjustment task with both simultaneous binocular presentation and successive binocular presentation, and compared it to contrast sensitivity. These experiments were both performed across different spatial frequencies.

METHODS

Apparatus

Stimuli and experimental procedures were programmed with Matlab R2010a (The MathWorks, Natick, MA, USA) using the Psychophysics Toolbox[19–21] and the qCSF[22] toolboxes, running on an Apple iMac11.1 (MacOSX; Cupertino, CA, USA) computer. The stimuli were displayed on the CRT monitor Mitsubishi DiamondPro 2070SB (Ø49 cm, 1280*1024 px, 85 Hz; Minato, Tokyo, Japan) and presented dichoptically with an eight-mirror custom Wheatstone stereoscope so that the left image was seen only by the left eye and the right image by the right eye, resulting in a viewing distance of 57 cm. The monitor was gamma@ corrected, with a measured mean luminance of 55 cd.m^{-2}, and the experiments were run in a dark room.

Subjects

Eleven amblyopic subjects (5 strabismic, 3 anisometropes, and 3 mixed; 3 females; mean age 35 ± 15) and 10 control subjects (1 author, 5 females; mean age 28 ± 7) participated in this study. The clinical details of the amblyopic subjects are reported in Table 1. The eye dominance of the control subjects was assessed with the Porta test. This research was approved by the Ethics Review Board of the McGill University Health Center and adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from the subjects after explanation of the nature and possible consequences of the study.

Stimuli and Procedures

The full study consisted of three experiments: the simultaneous matching, the successive matching, and the contrast sensitivity measure. Two runs of each of the matching experiments were performed. The sequences of the runs were pseudorandomly ordered and balanced between all subjects.

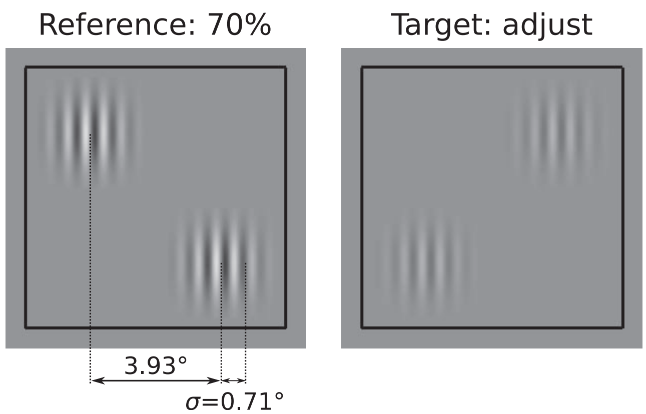

Figure 1. Stimuli. Four Gabor patches of 0.71° sigma@ diameter were dichoptically presented in a square arrangement with distance of 3.93° from center to center. The top-left and bottom-right patches consisted of the reference and were presented in one eye; the top-right and bottom-left patches, the target, were presented in the other eye. The reference patches were presented at 70% contrast. The subjects' task was to adjust their perceived contrast of the target patches to match the one of the reference by pressing the up and down arrow keys of a keypad.

An alignment task was performed at the beginning of each session: Subjects had to align two vertical line segments, a green one seen by the left eye and a red one seen by the right eye on top of each other in the middle of the viewing area. The coordinates of the two segments were then used to present the stimuli in the following experiments.

Simultaneous Matching Experiment. For the matching experiments, we used a design close to the one used by Maehara and collaborators.[18] In the simultaneous matching experiment, four Gabor patches with Gaussian envelopes of 0.71° sigma@ and a 0° sine phase were dichoptically presented in a square arrangement with distance of 3.93° from center to center. A black frame was presented around them in both eyes to help fusion. The top-left and bottom-right patches constituted the reference and were presented to one eye, and the top-right and bottom-left patches constituted the target and were presented to the other eye (Fig. 1). The reference patches were presented at 70% contrast, and the subjects' task was to then adjust the perceived contrast of the target patches to match that of the reference patches by pressing the up and down arrow keys of a keypad. Ten different frequencies were tested: 0.35, 0.49, 0.68, 0.94, 1.31, 1.83, 2.54, 3.54, 4.93, and 6.87 cyc/deg.

Successive Matching Experiment. The successive matching experiment procedure was the same as for the simultaneous matching except that the reference and target were never displayed together at the same time. Only one was displayed at a time, so the presentation was monocular, the other eye seeing the mean luminance. The subjects still had to adjust the contrast of the target, and they could switch between the presentation of the reference or the target as many times as they wished before making their decision.

Contrast Sensitivity Measure. The monocular sensitivity functions were measured using the same arrangement of stimuli with the quick contrast sensitivity function (qCSF) method.[22] The use of this method for amblyopic populations has previously been validated.[23,24] The frequency range was truncated from 0.35 to 6.87 cyc/deg. The initial gain prior was set to 100, the peak frequency prior set to 2 cyc/deg, the bandwidth prior set to 3 octaves, and the truncation prior set to 0.5. The two monocular measures, with 100 trials each, were performed together, with the trials between the two conditions randomly interleaved so that the subject did not know in which eye the stimulus was presented.

In a trial, a pair of Gabor patches appeared in one eye in the same spatial layout as for the matching experiments: either at the top-left and bottom-right or the top-right and bottom-left positions. The other eye saw the mean luminance in corresponding visual field positions. They were presented along with an audio beep for 400 ms at a contrast and spatial frequency chosen by the qCSF algorithm. The subjects' task was then to identify the position of the Gabor patches that appeared.

Data Analysis

Fitting Functions. In order to reduce the dimensionality of the data, we computed the contrast sensitivity ratios between the contrast sensitivity functions of the two eyes. These ratios and the matching functions r were subsequently fitted by a logarithmic function of the spatial frequency f (Equation 1) on the full tested spatial frequency range for the control subjects, and on the valid interval from the minimal frequency 0.35 cyc/deg to the cutoff frequency f_c of the amblyopic eye sensitivity function for the amblyopes.

$$r = a \log_{10}(f) + b \qquad (1)$$

where a and b are the estimated slope and intercepts.

For the amblyopic subjects, the cutoff frequency f_c of the amblyopic eye's contrast sensitivity functions was calculated from the output parameters of the qCSF: the peak gain $\gamma_{\max}$, the peak frequency, $f_{\max}$, and the bandwidth β as in Equation 2 (see Ref. 24):

$$f_c = f_{\max} \cdot 10^{\frac{\beta'}{2}\sqrt{\frac{\log_{10}(\gamma_{\max})}{\kappa}}} \qquad (2)$$

with $\kappa = \log_{10}(2)$ and $\beta' = \log_{10}(2\beta)$.

The average coefficient of determination R^2 of the fits was 0.72 for the controls and 0.77 for the amblyopes, thus proving their accuracy.

Statistics. In order to compare the different conditions within subjects, we performed paired 2-tailed Wilcoxon's signed rank tests on the estimated slopes and intercept to assess the significance at $\alpha = 0.05$ of the difference between the conditions two by two.

To test if the amblyopic group performed worse than the control group in the different conditions, we used a left-tailed Wilcoxon rank sum test on the absolute estimates of the intercept and negative absolute estimates of the slope to assess the significance at $\alpha = 0.05$. We tested the absolute value of the estimates in order to account for the fact that for some controls the nondominant eye was not necessarily the less sensitive one, resulting in a positive rather than a negative slope.

Results

Controls

We first measured the monocular contrast sensitivity functions of the control subjects in their two eyes (Fig. 2). Their sensitivities show a normal pattern with an average peak sensitivity of approximately 50 at 2 cyc/deg. Furthermore, there were no consistent differences in the sensitivity for the two eyes of our control subjects, consistent with our observations on a larger normative dataset.[25]

From these monocular contrast sensitivities, we calculated the ratio between the sensitivities of the nondominant and dominant eyes. These ratios are reported as a function of the spatial frequency in Figure 3a. Most of them deviate from the

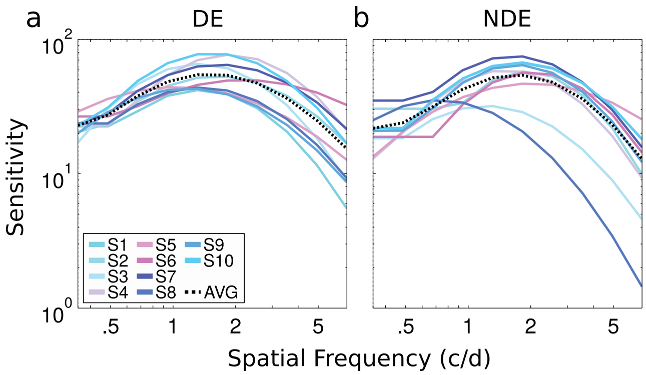

Figure 2. Contrast sensitivity in the dominant and nondominant eye of the control subjects as a function of the spatial frequency. (**a**) Sensitivity of the dominant eye of each subject (*colored lines*) and average (*dotted black line*). (**b**) Sensitivity of the nondominant eyes, same color code.

unity line at high spatial frequency. However, on average this ratio is flat, very close to 1, confirming that the sensitivity is not different between the two eyes (black dotted curve).

We then computed this ratio for the interocular contrast matching task in which stimuli for the two eyes were presented either simultaneously (Fig. 3b) or successively in time (Fig. 3c), with the variable target presented to the dominant eye (see Methods). In these conditions, the balance varies monotonically, either decreasing or increasing away from 1, as a function of the spatial frequency. These variations in perceived contrast are also consistent with the contrast sensitivity ratios between the two eyes. However, on average they decrease only slightly as a function of the spatial frequency (black solid and dashed curve).

To better quantify these comparisons, we fitted each subject's data with a logarithmic function (see Methods) and then extracted two parameters: the offset and the slope in log-space. These individual fits are reported as dashed lines in Figure 3. They reasonably describe the data ($R^2 = 0.72$) and then the average estimated parameters are reported in Figures 3d and 3e. Every subject shows the same trend for the three conditions. The correlation coefficients of the intercepts and slopes for all subjects between the three conditions are good and are reported in Table 2. Only the slope between the contrast sensitivity ratio and the simultaneous matching are significantly different (Wilcoxon signed rank test, 2-tailed, $\alpha =$

Table 2. Correlation Coefficients of the Intercepts and Slopes for All Control and Amblyopic Subjects Between the Three Conditions

	Sim./Succ.	Sim./Det.	Succ./Det.
Controls			
Intercepts	0.88	0.32	0.44
Slopes	0.88	0.84	0.84
Amblyopes			
Intercepts	0.78	0.74	0.59
Slopes	0.63	0.78	0.39

Sim, simultaneous matching; succ, successive matching; Det, sensitivity ratio.

0.05); overall these fits confirm that although the sensitivity ratio between the eyes is flat on average, the slope decreases, but only slightly, for the matching tasks.

We tested the importance of the laterality (i.e., which eye saw the target and which eye saw the reference) of the adjustment method in a subset of six subjects by switching the presentation of the variable target and the fixed reference between the two eyes (Fig. 4). The individual subject's data, when the target is presented in the dominant eye (Figs. 4a, 4d), are replotted from Figure 3. The functions look very comparable for each subject, whether the target is presented to one eye or the other, for both simultaneous (compare Figs. 4a, 4b) and successive (compare Figs. 4d, 4e) presentation conditions. They are fitted by the same logarithmic function for best comparison. The estimated parameters, whether the target is placed in one eye or the other for the simultaneous matching experiment, are reported in Figure 4c and the estimated parameters for the successive matching experiment in Figure 4f. These parameters are not significantly different in the two configurations, showing that the matching balance is symmetrical (Wilcoxon signed rank test, 2-tailed, $\alpha = 0.05$).

Subjects With Amblyopia

Subsequently, we characterized the interocular interactions in subjects with amblyopia using the same protocol. First, we measured the monocular contrast sensitivity functions of the amblyopic subjects for their two eyes (Fig. 5). The accuracy of the qCSF method for amblyopes has already been validated.[23,24] The sensitivities for the fellow eye show a normal pattern with an average peak sensitivity of approximately 40 at

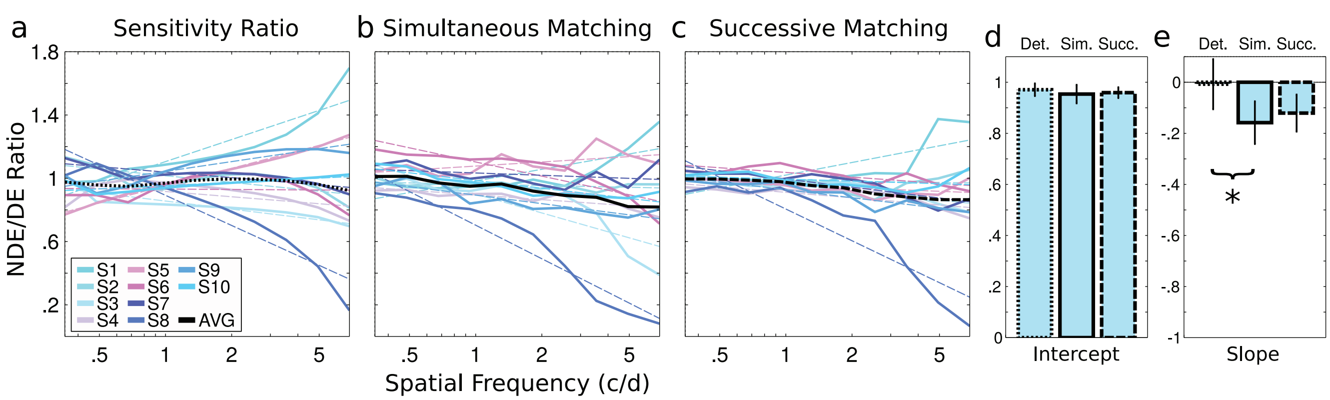

Figure 3. (**a**) Ratio between the monocular sensitivities of the two eyes as a function of the spatial frequency for control subjects. *Color continuous lines* represent individual subjects' data and respective *dotted lines* represent fits by a logarithmic function (see Methods). *Black line* represents average. (**b**) Matching balance ratio between the two eyes in the simultaneous matching condition with the target presented in the dominant eye. Same color code. (**c**) Same for the successive matching condition. (**d**) Average estimated intercept of the fitted logarithmic function for the sensitivity ratio, the simultaneous matching balance, and the successive matching balance for the control group. (**e**) Slope of the logarithmic function. The *asterisk* indicates significance at 5% (2-tailed Wilcoxon signed rank test). *Error bars* ± standard deviation.

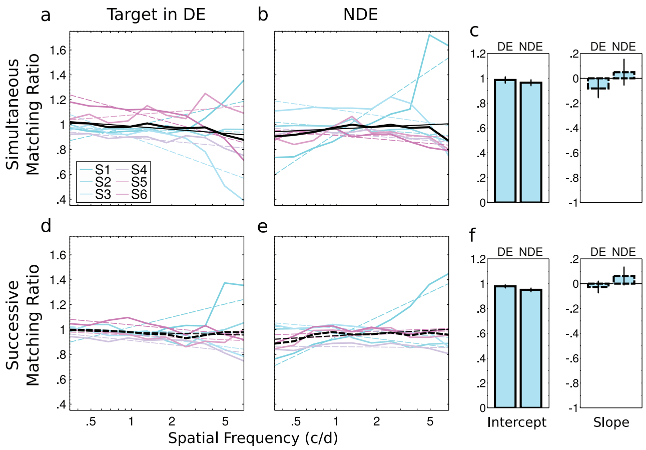

Figure 4. Control experiment. (**a**, **b**) Matching balance ratio between the two eyes in the simultaneous matching condition when the target is presented in the dominant eye (**a**) or the nondominant eye (**b**). *Color continuous lines* represent data and respective *dotted lines* represent fits by a logarithmic function. *Black lines* represent averages. (**c**) Parameters of the fitted logarithmic function for the simultaneous matching condition. *Left*: intercept; *right*: slope. (**d**, **e**) Matching balance ratio between the two eyes in the successive matching condition when the target is presented in the dominant eye (**d**) or the nondominant eye (**e**). *Color continuous lines* represent data and respective *dotted lines* represent fits by a logarithmic function. *Black dashed lines* represent averages. (**f**) Parameters of the fitted power function for the successive matching condition. *Left*: intercept; *right*: slope.

2 cyc/deg (Fig. 5a). However, the sensitivities for the amblyopic eyes are greatly reduced compared to their fellow eyes and controls, with an average peak sensitivity of approximately 20 at 1.2 cyc/deg (Fig. 5b), slightly lower than reported under purely monocular conditions.[24] The cutoff frequency f_c of their amblyopic eye (see calculation in Methods and Table 1) is, in general, much lower than that of their fellow eye, as expected.[5,6] This can be observed in Figure 5b.

Then, we computed the ratio between the sensitivities of the amblyopic/fellow eye. These ratios are reported as a function of the spatial frequency in Figure 6a. We can see that for 9 of the 11 amblyopic participants, this ratio is significantly below 1 and decreases as spatial frequency increases.[26] On average, it decreases from 0.7 at 0.3 cyc/deg to 0.5 at 7 cyc/deg.

We then compared this ratio with the interocular suprathreshold contrast matching balance measured in the simultaneous (Fig. 6b) and successive (Fig. 6c) presentation conditions, with the target presented to the amblyopic eye. The threshold contrast ratio and the matching balance data for each amblyopic subject were also fitted with the same logarithmic function as previously described for the data obtained from controls. However, here, for each subject the fit was performed only on the valid interval, from 0.35 cyc/deg to the individual subject cutoff frequency f_c (see Table 1 and Methods). Here again, the quality of the fits is good ($R^2 = 0.77$), and the average estimated parameters are reported in Figures 6d and 6e.

Here, we did not observe any consistent difference between the different forms of amblyopia that our subjects suffer. For most subjects except A7, the two matching conditions are very similar, with a consistent drop-off at high spatial frequencies.[27] The correlation coefficients of the estimated intercepts and slopes of the logarithmic function are high (Table 2), and their statistical analysis did not show any significant difference (Wilcoxon signed rank test, 2-tailed, $\alpha = 0.05$). For subject A7, his balance progressively decreased from 0.8 to 0.2 over the spatial frequency range in the successive matching condition

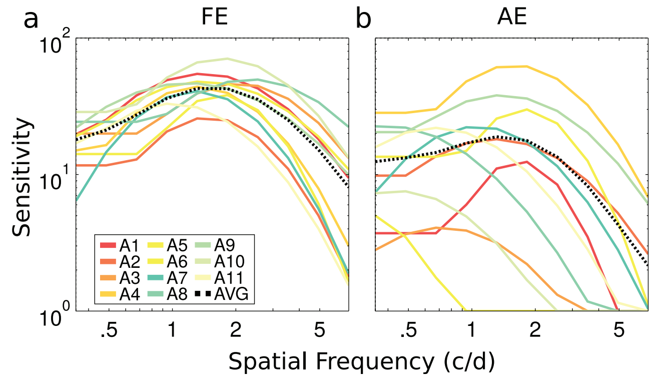

Figure 5. Contrast sensitivity in the fellow eye and the amblyopic eye of the amblyopic subjects as a function of the spatial frequency. (**a**) Sensitivity of the fellow eye of each subject (*colored lines*) and average (*dotted black line*). (**b**) Sensitivity of the amblyopic eyes; same color code.

(Fig. 6c), whereas it remained constant around 1 over a large range of spatial frequency and dropped only at frequencies above 3 cyc/deg in the simultaneous matching condition (Fig. 6b).

On the other hand, the intercepts for the two matching conditions were substantially different compared to the contrast sensitivity ratio (Fig. 6d). In the matching conditions the subjects required less contrast in their amblyopic eye than what would be predicted by their contrast sensitivity, which is slightly different from what has been reported in a binocular fusion task.[28] This difference seemed quite consistent between subjects because the correlation coefficients of the estimated intercepts and slopes of the logarithmic function were still high (Table 2), but not significant (Wilcoxon signed rank test, 2-tailed, $\alpha = 0.05$, Figs. 6d, 6e).

Figure 7 summarizes our results. The averages of the different measures are reported in orange for the amblyopic group and in blue for the control group. The superimposed, thin darker straight lines represent the logarithmic model estimates replotted using the average slope and intercept estimates for each condition (Fig. 7a).

It is apparent from this graph that the matching balances closely follow the contrast sensitivity ratio between the eyes for both groups and that they depart from the unity balance as the spatial frequency increases. This effect is more marked for amblyopes than for controls. However, it is noticeable that for controls, the slope is partly reduced because the balance is above 1 at high spatial frequencies for some participants (see Fig. 3), which results in an increased standard deviation (shaded blue area).

For clarity, we replotted the logarithmic model by using the absolute value of the estimated intercept and the negative absolute of the estimated slope (Fig. 7b). It is now clear that the fall-off of the balance at high spatial frequencies is much more pronounced for the amblyopes than for the controls. To better quantify this comparison, these absolute values are reported in Figures 7c and 7d. They are significantly lower for the amblyopic group compared to controls in all conditions except for the intercept of the simultaneous matching task (left-tailed Wilcoxon rank sum test, $\alpha = 0.05$). For the control group, the sensitivity ratio and the simultaneous matching condition are not significantly negative (left-tailed sign test, $\alpha = 0.05$). This observation confirms that the matching balance of the amblyopes, unlike that of controls, exhibits a strong deterioration as spatial frequency increases. In other words, as spatial frequency is increased, perceived contrast is reduced for the amblyopic eye under these viewing conditions.

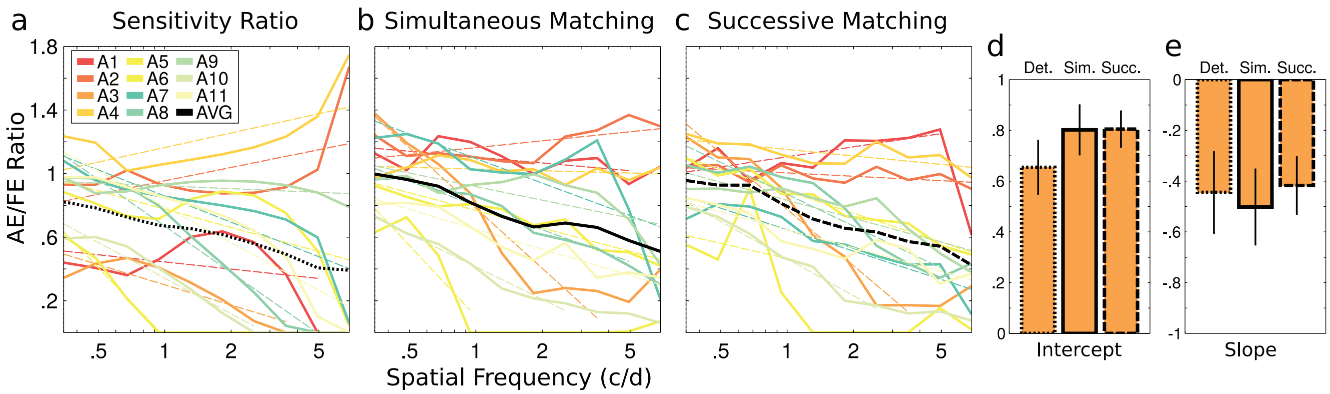

Figure 6. (**a**) Ratio between the monocular sensitivities of the two eyes as a function of the spatial frequency for amblyopic subjects. *Color continuous lines* represent individual subjects' data and respective *dotted lines* represent fits by a logarithmic function on the valid interval (see Methods). *Black line* represents average. (**b**) Matching balance ratio between the two eyes in the simultaneous matching condition. Same color code. (**c**) Matching balance ratio between the two eyes in the successive matching condition. (**d**) Average estimated intercept of the fitted logarithmic function for the sensitivity ratio, the simultaneous matching balance, and the successive matching balance for the amblyope group. (**e**) Slope of the logarithmic function. *Error bars* ± standard deviation.

Discussion

Suprathreshold Contrast Constancy

The simplest explanation for amblyopic suppression is one based on our knowledge of masking data showing that the effectiveness of interocular masking depends on the suprathreshold contrast of the stimuli in the two eyes.[1] In other words, the amount the stimulus is above threshold will determine its effective masking power. If one eye, as in the case of amblyopia, has an elevated threshold, then at all contrast levels, masking from the fixing eye will be stronger than the masking from the amblyopic eye. This imbalance in interocular masking will operate at all suprathreshold contrasts for stimuli seen by the two eyes and can provide, in principle, a complete understanding of amblyopic suppression. Results from a number of studies are compatible with this simple model.[2,29,30]

In the present study, we measured the binocular balance across spatial frequency using a matching paradigm, utilizing either simultaneous or successive presentation between the two eyes. We compared this with the contrast sensitivity ratio measured with the same stimuli in amblyopic and control subjects. For controls, we observed only a slight imbalance between the two eyes at high spatial frequencies for either contrast thresholds or matching.

For amblyopes, we observed a much more pronounced imbalance as a function of the spatial frequency.[27,28] When the fellow fixing eye is occluded, the amblyopic eye perceives contrast veridically (i.e., approaching contrast constancy).[7,9] However, here we report a different result concerning the interocular balance as the function of spatial frequency. We observe a breakdown in contrast constancy at high spatial frequencies for suprathreshold stimuli for both simultaneous and successive presentations. This suggests that in our paradigm, the fellow eye viewing a mean luminance causes

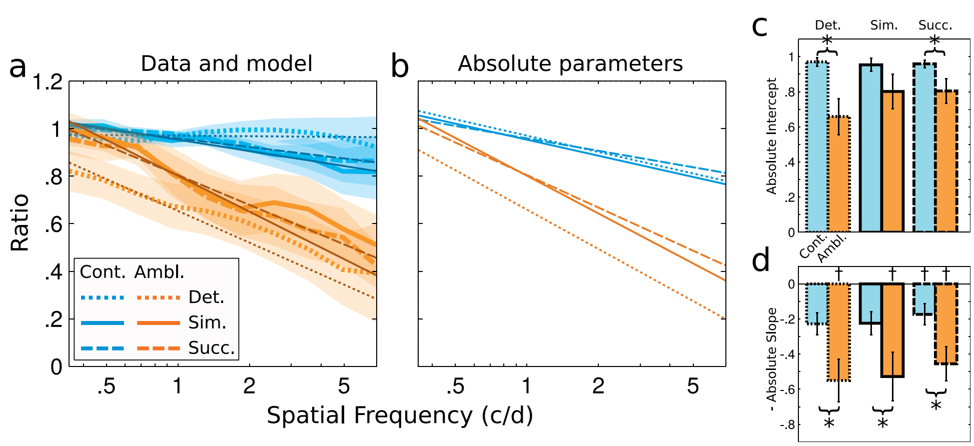

Figure 7. Summary. (**a**) Average monocular sensitivity ratio (*dotted*), simultaneous matching balance (*continuous*), and successive matching balance (*dashed*) as a function of the spatial frequency for amblyopic (*orange*) and control (*blue*) groups, replotted from Figures 3 and 7. *Shaded areas* represent ±standard deviation. Respective *straight darker lines* represent the logarithmic function model computed with the average estimated parameters for each condition, for the two groups from Figures 4 and 8. (**b**) Same logarithmic function model but this time computed with the average of the absolute estimated intercepts and the negative absolute estimated slopes for each condition, for the two groups. Same code. (**c**) Average absolute estimated intercept of the fitted logarithmic function for the sensitivity ratio, the simultaneous matching balance, and the successive matching balance for the control group (*blue*) and amblyopic group (*orange*). (**d**) Negative absolute slope for the controls and amblyopes. The *dagger symbols* indicate that the absolute slopes are significantly negative (left-tailed sign test, $\alpha = 0.05$) and the *asterisks* indicates significance at 5% between the amblyopic and control groups (left-tailed Wilcoxon rank sum test, $\alpha = 0.05$). *Error bars* ± standard deviation.

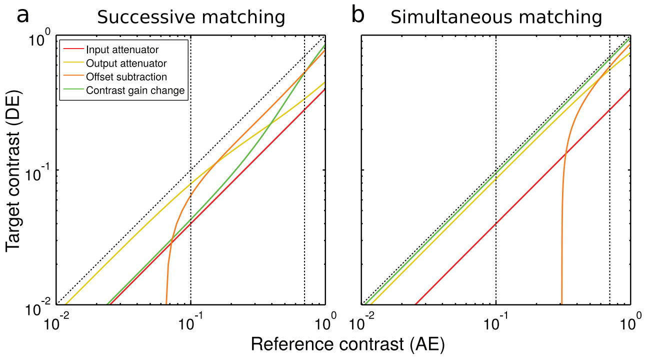

Figure 8. Simulations of a simple version of the interocular normalization model for the successive (**a**) and simultaneous (**b**) matching conditions. For a range of contrasts in the fellow eye, the simulated matching contrast in the amblyopic eye is reported according to four possible mechanisms: the input attenuator (*red*), the output attenuator (*yellow*), the offset subtraction (*orange*), and the contrast gain change (*green*). The full model equations are provided in the Appendix. The *oblique dotted line* represents the identity, and the *vertical dotted line* represents matching contrast of 10% and 70%.

the suppression to operate. However, this is not the case for normal dichoptic masking[31] or for monocular viewing.[7,9]

Potential Role of Suppression

We report that the monocular contrast sensitivity predicts the matching data in both groups. More precisely, we show a strong correlation between the spatial frequency dependence of perceived contrast and that of the threshold deficit in individual amblyopes, which could, in principle, be due to either a monocular or a binocular deficit.

If one accepts the argument that it is suppression that is causing a breakdown in contrast constancy at high spatial frequencies in amblyopia, then this directly bears on the role of inhibitory processes in suppression. Normal dichoptic masking does not occur when the unstimulated eye views a mean luminance,[18,32] so cannot provide an explanation for the successive matching results reported here. This in turn suggests that while dichoptic masking may play a role in suppression when the fixing eye is stimulated with contrast information, it cannot provide a complete explanation.

The reason one should consider this loss in suprathreshold contrast at high spatial frequencies the result of a binocular suppressive interaction[23] is the existence of evidence that there is significant suppression of the amblyopic eye when the fellow eye is open and views a mean luminance.[33] This was the case for successive matching tasks, consistent with the inhibition hypothesis.

Models Involving Attenuation as an Explanation for Suppression

The suppression observed here can take many forms[15] depending on whether it affects just the input, the contrast gain, or the normalized response.

To better understand these mechanisms, we implemented a simple version of the interocular normalization model[13,15,34] accounting for four possible mechanisms for amblyopia: (1) the input attenuator, where the input contrast of the amblyopic eye would be attenuated; (2) the output attenuator, where the output response of the amblyopic eye would be attenuated; (3) the offset subtraction, where the output of the amblyopic eye would be reduced by a constant amount; and (4) the contrast gain change, where the contrast gain of the normalization would be increased. The full model equations are provided in the Appendix; and the model simulations of the matching contrast in the amblyopic eye as a function of the contrast in the dominant eye in the successive and simultaneous matching conditions are, respectively, presented in Figures 8a and 8b.

Table 3. Model Predictions; Table Summarizes Which of Our Observations Each Model Accurately Predicts (o) or Fails to Predict (x)

Model	Threshold Data	Successive Matching	Simultaneous Matching
Input attenuator	x	o	o
Output attenuator	x	x	o
Offset subtraction	o	o	x
Contrast gain change	o	o	x

As suggested by the inhibition hypothesis, we can note that the input attenuator model is the only one that can account for the similar results we observe with the successive or simultaneous matching tasks (see Table 3 linking data to model predictions and the red curve in Figs. 8a, 8b). However, the fact that we also observe a difference, though it is small, in the contrast threshold ratio compared to the matching in amblyopes would be more consistent with a curve being farther from identity at low contrast and getting closer to the identity at high contrast, such as predicted by either the offset subtraction or the contrast gain change models (Table 3; see the dashed vertical lines at 10% and 70% contrast in Fig. 8a). These predictions would also be more in line with the results previously reported[7–9] for monocular matching tasks at different contrasts. These simulations can then at least rule out any explanation in terms of an output attenuation of the response of the amblyopic eye and in turn suggest an explanation based on a mixture of input attenuation and reduced contrast gain (i.e., increased suppression, see Table 3).

In conclusion, the form of the perceived suprathreshold contrast imbalance, measured under conditions in which the unstimulated eye is open and viewing a mean luminance as a function of spatial frequency, parallels that of the interocular contrast sensitivity ratio in amblyopia. This suggests a complete breakdown of contrast constancy, contrary to previously reported results obtained under purely monocular conditions.[7] These observations would confirm the inhibition hypothesis—the amblyopia being the consequence of a binocular dysfunction, with a model of amblyopic suppression being a mixture of input attenuation and reduced gain.

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Appendix

We implemented a simple version of the interocular normalization model[13,15,34] in which the response of the fellow eye $resp_F$ would be given by:

$$resp_F = \frac{C_F^p}{Z + C_F^q + C_{AO}^q} \qquad (3)$$

where C_F is the input contrast in the fellow eye, C_{AO} is the input contrast in the amblyopic eye, and Z, p, and q are model parameters, representing, respectively, the normalization parameter and the rate of acceleration of the nonlinear contrast responses on the numerator and denominator, here fixed at 0.01, 2.4, and 2.[35–38]

For a range of contrasts C_F in the fellow eye, we simulated the matching contrast in the amblyopic eye C_A, such as $resp_F = resp_A$ for the successive and simultaneous matching conditions, according to four possible mechanisms, by adding an extra parameter in different places of the response of the amblyopic eye $resp_A$. In the normalization term, the contrast of the other eye: whether the amblyopic C_{A0} or fellow C_{F0} was set to 0% for the successive matching simulation and to 70% for the simultaneous matching.

1. Input attenuator:

$$resp_A = \frac{(wC_A)^p}{Z + (wC_A)^q + C_{F0}^q} \quad (4)$$

   input contrast is reduced by a multiplicative coefficient $w < 1$ (in this simulation, we set $w = 0.4$). Note that in that case the response of the fellow eye would also be affected, and Equation 3 would become:

$$resp_F = \frac{C_F^p}{Z + C_F^q + (wC_{A0})^q} \quad (5)$$

2. Output attenuator:

$$resp_A = a\frac{C_A^p}{Z + C_A^q + C_{F0}^q} \quad (6)$$

   general eye response is reduced by a multiplicative coefficient $a < 1$ (here we set $a = 0.7$). In that case and the following ones, the response of the fellow eye would not be affected and would remain as described in Equation 3.

3. Offset subtraction:

$$resp_A = \frac{C_F^p}{Z + C_A^q + C_{F0}^q} - b \quad (7)$$

   general eye response is reduced by a subtractive coefficient $b > 0$ (here $b = 0.1$).

4. Contrast gain change:

$$resp_A = \frac{C_A^p}{s + Z + C_A^q + C_{F0}^q} \quad (8)$$

   contrast gain is changed by increasing the normalization denominator by a constant amount $s > 0$ (here $s = 0.07$).

Note that the input attenuator model is the only mechanism that can account for the similar results observed with the successive or simultaneous matching tasks assuming $wC_A = C_F$.

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