Time Course of Dichoptic Masking in Normals and Suppression in Amblyopes

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Purpose. To better understand the relationship between dichoptic masking in normal vision and suppression in amblyopia we address three questions: First, what is the time course of dichoptic masking in normals and amblyopes? Second, is interocular suppression low-pass or band-pass in its spatial dependence? And third, in the above two regards, is dichoptic masking in normals different from amblyopic suppression?

Methods. We measured the dependence of dichoptic masking in normal controls and amblyopes on the temporal duration of presentation under three conditions; monocular (the nontested eye—i.e., dominant eye of normals or nonamblyopic eye of amblyopes, being patched), dichoptic-luminance (the nontested eye seeing a mean luminance—i.e., a DC component) and dichoptic-contrast (the nontested eye seeing high-contrast visual noise). The subject had to detect a letter in the other eye, the contrast of which was varied.

Results. We found that threshold elevation relative to the patched condition occurred in both normals and amblyopes when the nontested eye saw either 1/f or band-pass filtered noise, but not just mean luminance (i.e., there was no masking from the DC component that corresponds to a channel responsive to a spatial frequency of 0 cyc/deg); longer presentation of the target (corresponding to lower temporal frequencies) produced greater threshold elevation.

Conclusions. Dichoptic masking exhibits similar properties in both subject groups, being low-pass temporally and band-pass spatially, so that masking was greatest at the longest presentation durations and was not greatly affected by mean luminance in the nontested eye.

Keywords: amblyopia, suppression, dichoptic masking, spatial, temporal, presentation duration

Amblyopic suppression may involve the active inhibition of the amblyopic eye by the nonamblyopic eye during conditions in which both eyes are open. It is thought by some[1,2] to be the primary problem from which amblyopia is the secondary consequence and has formed the basis of a new treatment of amblyopia.[2–5] In some cases, it is thought to be the consequence of an imbalance in the reciprocal contralateral inhibitory interactions that occur prior to binocular summation[6]; in other cases, the imbalance may simply relate to the degree of signal attenuation by the amblyopic eye.[7]

A current issue that is yet to be resolved is whether suppression in amblyopes involves the same mechanism as dichoptic inhibition in normal.[8–10] One important dimension along which one can compare these two phenomena is their time course. Previous studies in this area have used a wide range of presentation times,[6,7,11] with the underlying assumption that the time course of suppression and dichoptic inhibition are comparable. Only two studies[12,13] have specifically investigated the time course of suppression in amblyopes and dichoptic inhibition in normals. These studies both used a binocular rivalry paradigm rather than the more conventional masking paradigm and found conflicting results. One study[13] argues for a similar time course for the two phenomena, while the other[12] argues that they are different.

We set out to provide a definitive answer to this question by using a standard dichoptic masking approach in normal and amblyopic observers for the discrimination of a low contrast letter target in one eye while viewing a high contrast noise mask in the other eye. Specifically, we ask three questions: first, what is the time course of dichoptic masking in normals and amblyopes? Second, is suppression low-pass or band-pass in its spatial dependence? And third, in the above two regards, is suppression in amblyopes different from dichoptic masking in normals? To answer these questions, we varied the duration of the target letter by changing the standard deviation of the Gaussian temporal envelope (see Fig. 1) and assessed contrast thresholds for letter identification in three conditions: when the nonamblyopic eye saw full-field two-dimensional (2D) noise—that is, either 1/f noise or band-pass noise; when the nonamblyopic eye saw only a mean-luminance background (i.e., a DC component, which may produce masking[14]) and when the nonamblyopic eye was patched. The 2D noise masks contain signals across a wide range of spatial frequencies (1/f noise) or a narrow range of spatial frequencies (band-pass noise), while the mean-luminance mask contains only a DC

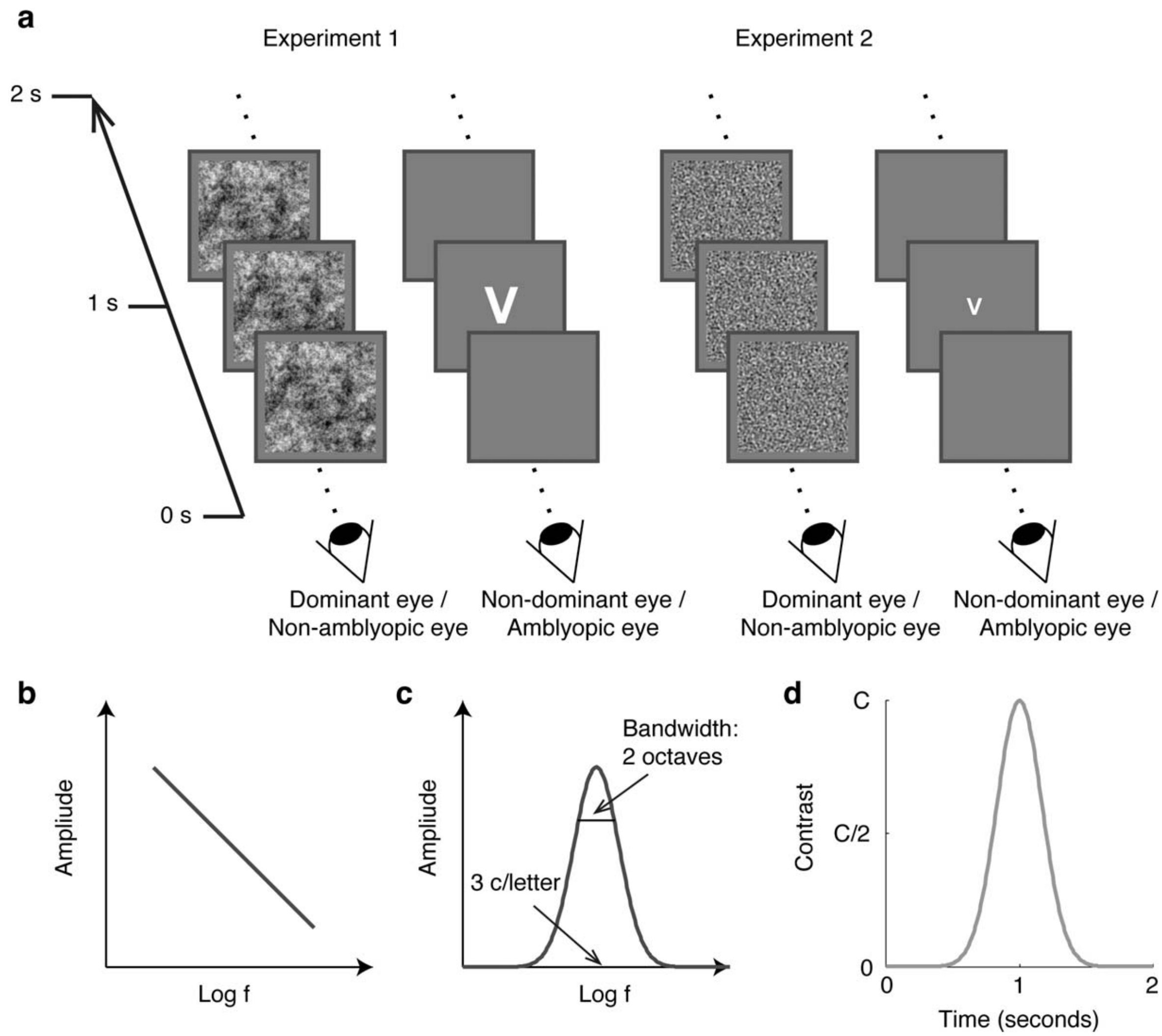

Figure 1. Illustration of the dichoptic-masking task. (**a**) The noise mask was dichoptically presented to one eye for 2 seconds while the test letter was presented to the other eye for various durations. A larger size of letter relative to the frame is shown here for illustration. (**b**) In experiment 1, the noise had a 1/f amplitude spectrum in the Fourier domain. (**c**) In experiment 2, the noise was filtered white noise with peak spatial frequency of three cycles/letter and bandwidth of ±1 octave. (**d**) The presentation of the letter was controlled by a Gaussian temporal modulation of the contrast of the letter. The Gaussian distribution peaked at 1 second and had a standard deviation of 8, 17, 40, 170, and 500 ms in different tested blocks (standard deviation of 17 ms is illustrated here).

signal (i.e., a spatial frequency of 0 cyc/deg). If suppression is primarily caused by low spatial frequency mechanisms, we expect to see threshold elevation from both the mean luminance and noise masks. Alternatively, suppression might be band-pass (having zero response at 0 cyc/deg), and thresholds will not be affected by mean luminance. In addition, using various durations of the target letter enables us to assess the temporal properties of dichoptic masking—that is, the dependence of the masking effect on the duration of the target presentation. A positive correlation between the masking effect and the duration indicates a low-pass temporal property, since prolonged presentation (i.e., large standard deviation of the Gaussian temporal envelope) corresponds to low temporal frequencies, whereas a negative correlation would suggest a high-pass temporal character. Furthermore, the comparison between normals and amblyopes enables us to assess whether suppression from the nonamblyopic eye to the amblyopic eye can be accounted for by normal dichoptic masking. The spatial frequency range we investigated here was limited to low-mid frequencies, as have a number of previous studies.[1,7,15–20]

We found that threshold elevation relative to the patched condition (i.e., the masking effect) occurred in both normals and amblyopes when the nontarget eye saw either 1/f or band-pass noise, but not just mean luminance; longer presentation of the target produced greater threshold elevation. These results indicate similar low-pass temporal dependence and band-pass spatial dependence of suppression in amblyopes and dichoptic masking in normals.

Methods

Participants

Fifteen adult amblyopes (A1–A15) were recruited for the current study. They were diagnosed as having amblyopia due to anisometropia ($n = 2$), strabismus ($n = 8$), or both ($n = 5$) during childhood. Subjects had previously received a range of treatments, including surgery, glasses, and patching, but still had unbalanced visual acuity across the eyes ($\geq$0.1 in logMAR) and/or poor stereovision ($\geq$100 arc seconds). Further clinical

TABLE 1. Clinical Details of Amblyopes

Subject No.	Age/Sex	Type	Refractive Error (OD/OS)	LogMAR Visual Acuity (OD/OS)	Distance Tropia	History and Stereo
A1	22/F	RE	−0.25/−2.25 × 7	−0.1	Ø	Diagnosis at 1–2 y, patching and glasses at 5 y. Stereo vision 200 arc s
		Aniso, LE	−5.75/−1.75 × 160	0.5	Ø	
A2	28/M	Mixed, RE	+2.5/−1.25 × 20	0.48	XT8°	Diagnosis at age 11; patching tried but not compliant. Patching attempted again at 20 y. ARC with central suppression. Stereo vision 200 arc s
		LE	Plano	0.1	Ø	
A3	41/M	Strab, RE	+6.75/−2.50 × 30	0.18	ET10°, occasionally alternates	Diagnosis at 4 y, strabismus surgery at 4 y, glasses and patching at 4 y. Stereo vision 800 arc s
		LE	+5.00/−1.75 × 162	−0.1	Ø	
A4	21/F	RE	+0.5 DS	0	Ø	Diagnosed at age 5 y, no surgery, glasses since 5 y, no stereo
		Mixed, LE	+4.50/−1.00 × 30	0.2	ET14°	
A5	40/M	Strab, RE	−2.75/−1.00 × 105	0.25	ET6°	Diagnosis and patching at 6 y, glasses at 16 y, no stereo
		LE	−2.75/−1.00 × 80	−0.2	Ø	
A6	44/F	RE	+4.75/−0.75 × 162	−0.2	Ø	Diagnosis amblyopia before 6 mo, eye turn diagnosis at 6–12 mo, strabismus surgery at 18 mo, glasses at 1 y old, occasional patching at 10 y old, no stereo
		Strab, LE	+5.50/−1.00 × 121	0.5	ET3°	
A7	45/M	Strab, RE	Plano	−0.1	ET8°	Diagnosis and glasses and surgery at 4 y old, surgery again at 5 y old, no glasses since 20 y of age, no stereo
		LE	+0.75/−0.50 × 110	0.32	Ø	
A8	21/F	Mixed, RE	+5.50/−2.00 × 27	0.4	ET5°	Diagnosis and glasses at age 4 y, patching at age 7 y, 1 h a day, no stereo
		LE	+4.25/−0.50 × 132	−0.2	Ø	
A9	42/F	RE Aniso	+4.50/+0.75 × 135	0.5	Ø	Diagnosed approximately 15 y of age, no patching. Stereo vision 200 arc s
		LE	+0.50 DS	−0.12	Ø	
A10[1]	29/M	RE	−1.00 DS	0	Ø	Diagnosed approximately 11 y of age, glasses at 11 y, no stereo
		Aniso, LE	+3.00 DS	0.1	Ø	
A11	39/M	Mixed, RE	+2.50/−3.25 × 170	0.42	Ø	Diagnosed in infancy, strabismus surgery age 4 y, no stereo
		LE	+1.50 DS	−0.2	Ø	
A12	25/F	RE	−2.75/−0.75 × 25	0.52	Ø	Diagnosed 8 y old, no surgery, patching and glasses at 8 y old. Stereo vision 100 arc s
		Strab, LE	−3.25/−1.25 × 10	−0.1	XT6°, intermittent	
A13	37/M	Strab, RE	−3.00/−1.75 × 110	0.6	Small exo	Diagnosed as infant, glasses since 11 or 12 y old, no stereo
		LE	−3.50/−1.00 × 100	0.06	Ø	
A14	23/M	RE	−1.00 DS	−0.2	Ø	Diagnosed over 12 y of age, glasses since 2011. Stereo vision 400 arc s
		Strab, LE	−1.00/−0.25 × 160	0.12	ET2°	
A15	38/M	RE	−0.50 DS	−0.22	Ø	Diagnosis 3–5 y, ptosis surgery and patching before age 3 y, second ptosis surgery at 12 y. Stereo vision 200 arc s
		Ptosis, Strab, LE	+0.75 DS	0.24	ET3°	

Subject A10 had near-normal visual acuity as a result of early treatment, but very poor stereoacuity. We therefore included him in the study. Removing the data of subject A10 had no effect on any of the results we report. RE, right eye; LE, left eye; stra, strabismus; anis, anisometropia; mix, mixed (strabismus + anisometropia); XT, exotropia; ET, esotropia.[1]

details are provided in Table 1. Subjects A1 through A9 participated in experiment 1; subjects A1 through A4 and A10 through A15 participated in experiment 2. Eleven normal adults (see Table 2 for a summary of demographic details), with normal or corrected-to-normal vision, participated in the study as controls. Four normal adults participated in experiment 1; ten normal adults (three of whom had also participated in experiment 1) participated in experiment 2. Observers wore their prescribed optical correction, if necessary, during the experiment.

TABLE 2. Summary of the Normal Controls

Experiment No.	Observers, *n*	Sex	Age (Mean ± SE)
1	4	2 F/2 M	34.25 ± 9.39
2	10	6 F/4 M	28.30 ± 3.89

All observers were naïve to the purpose of the study. Written informed consent was obtained from each of them before testing began. This study complied with the Declaration of Helsinki and was approved by the institutional ethics committee of McGill University.

Apparatus

Stimuli were generated by a MacBook Pro (Mac; Apple, Inc., Cupertino, CA, USA) using visual psychophysics software (PsyKinematix; KyberVision, Montreal, Quebec, Canada)[21] and dichoptically presented using a head mounted goggle system with a separate display for each eye (Z800 pro, eMagin Corp., Bellevue, WA, USA). The two displays had a resolution of 800 × 600, a refresh rate of 60 HZ, and mean luminance of 160 cd/m². They comprised OLED screens, which have a linear luminance response,[22] meaning that gamma correction was not required.

Design

In experiments 1 and 2, the effect of masking and suppression was assessed by presenting a low-contrast letter target to the nondominant eye of controls or the amblyopic eye of amblyopes, with a high-contrast noise mask presented to the other eye. To evaluate the time course of the dichoptic masking, we varied the presentation duration of the target letter and assessed the contrast detection threshold in three conditions: when the nonamblyopic eye was patched, when the nonamblyopic eye saw only a mean-luminance background, and when the nonamblyopic eye saw full-field 2D noise. The threshold elevations at different durations were calculated by subtracting the appropriate thresholds (in dB) from those measured in the patched condition.

On a given trial, the noise mask was presented for 2 seconds. The presentation duration of the letter was controlled by a Gaussian temporal modulation of the contrast of the letter. The Gaussian function peaked 1 second after the mask onset and had a standard deviation (i.e., the sigma parameter of the Gaussian) of 8, 17, 40, 170, or 500 ms in different test blocks. Two noise types were used in the study. In experiment 1, the noise had an amplitude spectrum with a 1/f falloff (pink noise). In experiment 2, the noise was band-pass filtered white noise with a center spatial frequency of three cycles/letter and bandwidth of ±1 octave.

Stimuli

The subject's task was to identify a white letter (Z, X, C, or V) on the mean luminance background in the tested eye. In experiment 1, the letters subtended 2.3° of visual angle. In experiment 2, the letter subtended 0.6° of visual angle for all the observers, except subject A4 and A13. These two observers had poorer acuity so a slightly larger letter of size of 1.1° of visual angle was used. The contrast of the letter was defined as the ratio of the peak letter-background luminance difference to the luminance of the background (i.e., the Weber contrast), and was temporally modulated by a Gaussian function during the 2-second period of each trial.

In each trial, the nontarget eye was presented with full-field 2D noise, or a whole screen mean luminance background, or was patched with black fabric. The noise mask had an RMS contrast of 13%. In experiment 2, subjects A1, A12, and A13 could not see the test letter even at the longest duration (standard deviation of 500 ms) when the noise was presented, so a lower noise contrast (RMS contrast of approximately 6.5%) was used to enable us to quantify the time course of the masking effect. For all subjects, the noise mask was square with a width of 20.9° of visual angle. Both the noise mask and the target letter were centered in a red square frame which had a width of 22.7° of visual angle. An illustration of the noise and letter display in the two experiments is shown in Figure 1.

Procedure

In a typical trial, the mask (noise, mean luminance or patched) was dichoptically presented for 2 seconds, during which the test letter was presented preceded by an auditory signal. Subjects were asked to identify the letter (Z, X, C, or V) presented to their tested eye by pressing the appropriate key on the keyboard. Auditory feedback was provided to indicate the correctness of the response. The next trial started 500 ms after the response. The contrast of the target letter was temporally modulated by a Gaussian envelope with different standard deviations in different blocks. The letter contrast was determined by a 2-down, 1-up staircase method. The peak contrast was decreased proportionally by 25% before the first reversal and 12.5% thereafter after each two consecutive correct responses and was increased by 12.5% after each incorrect response. Each staircase contained only one tested condition (i.e., duration and mask type) and was terminated at the sixth reversal point. To better determine the threshold, each staircase was repeated three times. The last five reversals of each repetition were averaged to obtain the threshold (i.e., 15 reversal points in total). Before beginning each staircase, subjects also 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 the amblyopic eye with another vertical line in the middle of the screen seen by the nonamblyopic eye. The coordinates of the two lines were then used to present the target letter and noise mask in the experiment.

Statistical Methods

For each group, the effect of target duration on the threshold elevation was analyzed with one-way repeated measures ANOVA. Correlations between the target duration and the threshold elevation were measured by Pearson's correlation coefficient (r). The threshold elevations (for the noise masking condition) and the contrast thresholds (for the patched condition) across the five target durations were compared between amblyopes and controls using a between-subject ANOVA.

Results

Experiment 1. 1/f Noise and Large Letter

Figure 2 shows the averaged results of experiment 1, in which the noise had a 1/f spectral distribution in the Fourier domain and the target letter was relatively large. For both amblyopes and normal controls, it is clear that the threshold in all masking conditions decreased rapidly as the effective presentation duration of target letter (i.e., the Gaussian standard deviation, sigma) increased (Figs. 2a, 2c). The thresholds when the nonamblyopic eye was patched were similar to those when the nonamblyopic eye viewed a mean luminance background. Thresholds increased relative to these two conditions when the nonamblyopic eye viewed the noise mask. To better illustrate the effect of time course on dichoptic masking, threshold elevation relative to the patched condition is plotted in Figures 2b and 2d. Threshold elevation in the noise-masking condition increased with increasing target duration. There was no clear threshold elevation in the mean luminance condition. Repeated measures one-way ANOVAs showed that threshold elevation significantly varied with target duration in the noise-masking condition for both amblyopes ($F[4,32] = 4.257$, $P = 0.007$) and controls ($F[4,12] = 5.239$, $P = 0.011$). There was a significant positive correlation between threshold elevation and duration in the noise-masking condition both for amblyopes ($r = 0.927$, $P = 0.023$) and controls ($r = 0.883$, $P = 0.047$). However, threshold elevation did not vary with target duration in the mean luminance condition for either amblyopes ($F[4,32] = 1.528$, $P = 0.217$) or controls ($F[4,12] = 1.002$, $P = 0.444$).

We also compared threshold elevation in the noise-masking condition between amblyopes and controls; they were not significantly different ($F[1,11] = 1.920$, $P = 0.193$). The difference in contrast threshold (in the patched condition) between amblyopes and controls across the five target durations was also not significant ($F[1,11] = 1.361$, $P = 0.268$).

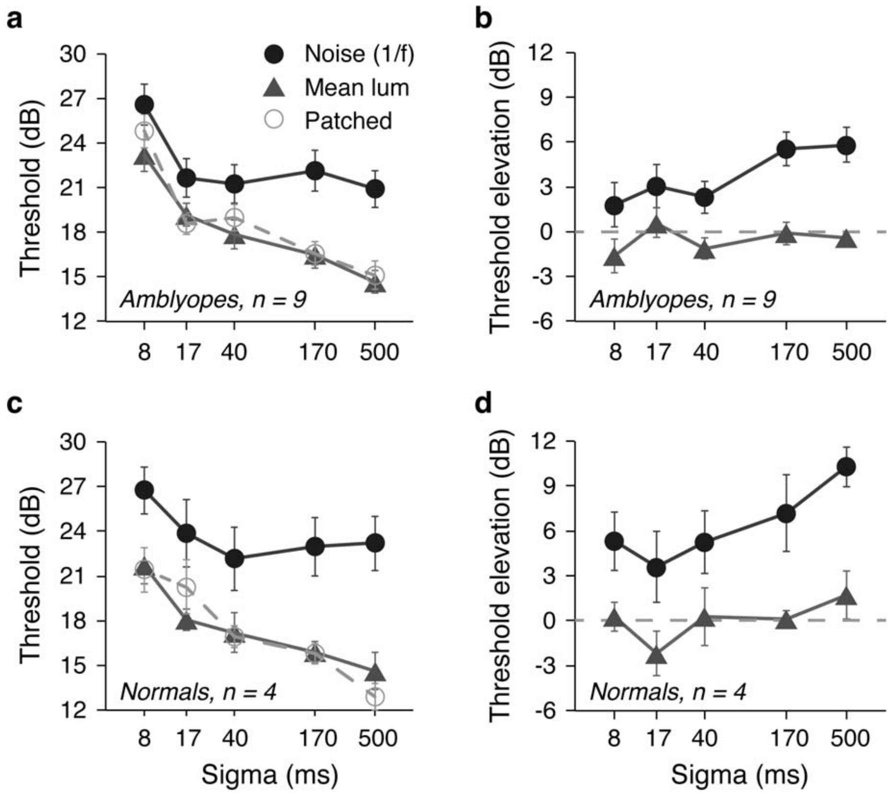

FIGURE 2. Results of experiment 1. The function relating averaged threshold to target presentation duration (sigma) for the three dichoptic-masking conditions presented to amblyopes (**a**) and normal controls (**c**). The threshold elevation compared with the patched condition of amblyopes (**b**) and controls (**d**). *Error bars* show ±1 SEM.

Experiment 2. Band-Pass Noise and Small Letter

The above results in experiment 1 indicate a low-pass temporal dependence of suppression in amblyopes and dichoptic masking in normals; the longer the stimulus was presented, the stronger the noise masking. On the other hand, mean luminance in one eye does not affect the visibility of stimuli in the other eye, which suggests that the spatial dependence of suppression in amblyopes and dichoptic masking in normals is spatially band-pass. To ascertain whether these effects could be generalized to other stimuli, we conducted a second experiment with a letter that was a factor of 4 smaller (subtended 0.6°) and with band-pass noise centered at a letter spatial frequency (i.e. three cycles/letter and bandwidth of ±1 octave).

Similar effects of time course of presentation on dichoptic masking were found in experiment 2 (Fig. 3). The threshold elevation significantly varied with the target presentation duration in the noise-masking condition in both amblyopes (Fig. 3b, $F[4,36] = 2.656$, $P = 0.049$) and normal controls (Fig. 3d, $F(4,36) = 3.249$, $P = 0.023$). There was again a significant positive correlation between the threshold elevation in the noise masking condition and the target duration for both amblyopes ($r = 0.974$, $P = 0.005$) and controls ($r = 0.927$, $P = 0.023$). However, threshold elevation did not vary significantly with target duration in the mean luminance condition for either amblyopes ($F[4,36] = 1.308$, $P = 0.285$) or controls ($F[4,36] = 2.127$, $P = 0.098$).

We also compared threshold elevation for the noise-masking condition between amblyopes and controls across the five target durations; they were not significantly different ($F[1,18] = 2.142$, $P = 0.161$). The difference in contrast thresholds (i.e., patched condition) between amblyopes and controls across the five target durations was also not significant ($F[1,18] = 1.642$, $P = 0.216$).

GENERAL DISCUSSION

We asked three questions: First, what is the time course of dichoptic masking in normals and suppression in amblyopes? Second, is suppression low-pass or band-pass in its spatial dependence? And third, in the above two regards, is dichoptic masking in normals different from amblyopic suppression?

We demonstrate a low-pass temporal dependence of suppression in amblyopes and dichoptic masking in normals. This is evidenced by the time course of the masking effect, in which the longer the stimulus was presented, the stronger the masking. Such low-pass temporal property is consistent with a previous work in studying the effect of dichoptic cross-orientation masking in normals with brief durations.[8] Our measurements extend to durations of 500 ms (in standard deviation units, or 1175 ms full-width-at-half-height) and within this time frame, amblyopic suppression and normal dichoptic masking are comparable in their dynamics. It is unclear if this would be the case for more sustained presentation, during which binocular rivalry alternations might occur. The spatial dependence of suppression in amblyopes and dichoptic masking in normals is band-pass, as mean luminance (i.e., DC component, with a spatial frequency of 0 cyc/deg) in one eye does not affect the visibility of stimuli in the other eye. To this extent, the two phenomena are spatiotemporally comparable.

Current theories on binocular interaction are in agreement with the involvement of interocular contrast gain control in both normals and amblyopes,[9–11,15–17,23–26] in which the visual input in one eye is suppressed by the stimuli in the other eye,

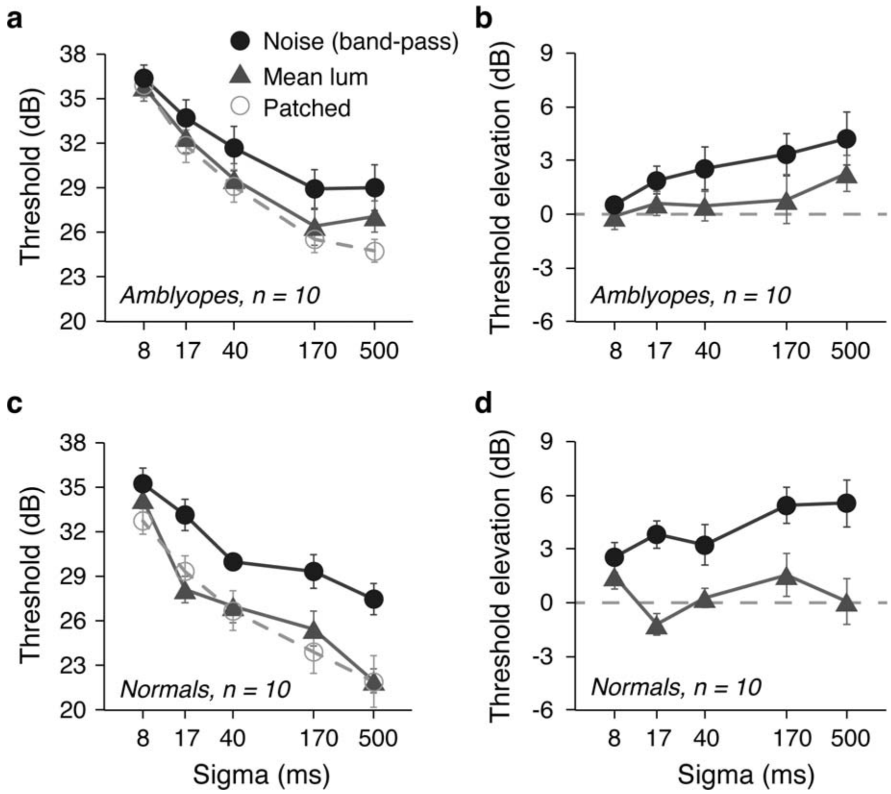

FIGURE 3. Results of experiment 2. Thresholds as a function of stimulus presentation duration (sigma) for the three dichoptic-masking conditions presented to amblyopes (**a**) and normal controls (**c**); The threshold elevation compared to the patched condition of amblyopes (**b**) and controls (**d**). *Error bars* show ±1 SEM.

and the strength of the suppression is proportional to the contrast of the stimuli. This is consistent with the band-pass spatial property we found here, as the dichoptic masking effect only occurs with a noise mask not with a mean luminance mask (i.e., the contrast of the mask was zero). On the other hand, there is evidence that longer presentation produces more effective interocular contrast gain control,[23] which is also consistent with the low-pass temporal dependence of dichoptic masking, since brief presentation might be too short to produce strong interocular suppression.

Previously, dichoptic masking effects were studied in normals and/or amblyopes with a pedestal-masking paradigm comprising a two-interval forced choice task, in which both intervals contained a mask presented to one eye and only one interval contained a target signal presented to the other eye. Subjects were asked to indicate which interval contained the target. Using narrowband spatial stimuli (e.g., gratings), Holopigian et al.[27] and Harrad and Hess[6] documented a number of possible forms that amblyopic suppression could take, including both normal dichoptic masking (the passive effects of amblyopic eye attenuation), as well as anomalous inhibitory interactions (active suppressive effects not accounted for by normal dichoptic interactions combined with amblyopic threshold attenuation). For the stimuli used here, we find that suppression from the nonamblyopic eye to the amblyopic eye can be accounted for by normal dichoptic masking. Since the magnitude of suppression in amblyopes and dichoptic masking in normals is comparable when it involves masking from the nonamblyopic eye to the amblyopic eye, as exclusively used in this study. This is similar to previous observations by Huang et al.,[11] who reported similar dynamics between amblyopic suppression and normal dichoptic masking. Taken together, these results indicate that at least for the spatial frequency range investigated here (0.6–2.4 cyc/deg–peak letter frequency) no additional suppression of the amblyopic eye by the nonamblyopic eye once differences in detection threshold are factored out. In other words, there is no evidence within this low- to mid-spatial frequency range for an active process of suppression from the nonamblyopic eye to the amblyopic eye other than what would be expected from normal dichoptic masking. Future studies should also investigate the higher spatial frequency range where threshold is known to be raised in amblyopia and on the balance of interocular masking.

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