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. Recently, we reported that dichoptic de-masking training can further boost stereoacuity, but not visual acuity, in adults with amblyopia after extensive monocular perceptual training. Here, we investigated whether this dichoptic training targets on interocular suppression directly, or improves vision through high-level brain mechanisms.

. Eleven adults with amblyopia first used amblyopic eyes (AEs) to perform contrast ($n = 6$) or orientation ($n = 5$) discrimination training, while resisting dichoptic noise masking from fellow eyes (FEs). Learning was indicated by increased maximal tolerable noise contrast (TNC) for AE contrast/orientation discrimination. After dichoptic training, six observers continued to use AEs to perform monocular training for nine sessions.

. (1) Training of dichoptic de-masking doubled maximal TNC, but learning did not transfer much to the same task at an orthogonal orientation or a different task, showing orientation/task specificities. (2) Following a training-plus-exposure (TPE) protocol, AEs then received exposure of the orthogonal orientation by performing the other orientation/contrast discrimination task at the orthogonal orientation. After this TPE training, dichoptic learning with the original discrimination task transferred to the orthogonal orientation. (3) Dichoptic training improved AE's acuity (1.2 lines), stereoacuity (60.2%), and contrast sensitivity (mainly at higher spatial frequencies). (4) Additional monocular training did not produce further acuity and stereoacuity gains.

. The initial orientation/task specificities exclude the possibility that dichoptic training reduces physiological interocular suppression. The later transfer of learning to an orthogonal orientation with TPE training suggests improvement in high-level brain processing. Dichoptic training may strengthen top-down attention to AEs to counter the impacts of attentional bias to FEs and/or physiological interocular suppression and improve stereoacuity.

Keywords: amblyopia, dichoptic training, perceptual learning, orientation specificity, task specificity

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Amblyopia is a developmental visual disorder due to abnormal binocular visual experience (e.g., strabismus and anisometropia) in early childhood that disrupts the development of the visual cortex.[1,2] Imbalanced visual inputs from two eyes may lead to interocular suppression or inhibition of the amblyopic eye (AE) by the strong fellow eye (FE).[3] As a consequence, visual acuity, stereoacuity, as well as many other visual functions, are compromised.[4,5]

Many studies have demonstrated that perceptual learning improves vision in adults with amblyopia.[6,7] Although amblyopia affects both binocular and monocular visual functions, earlier perceptual learning studies mostly perform monocular training in the AE with the FE patched. More recent studies employ dichoptic training, targeting abnormal binocular functions directly via reducing interocular suppression, strengthening binocular fusion, and promoting binocular vision. Many dichoptic training studies use signal integration training paradigms, in which the task elements are separated between the two eyes and must be integrated for successful task completion.[8–15] Dichoptic training may assist information integration from the two eyes to help recover stereovision in amblyopic patients.[6]

In a previous study, we adopted a different dichoptic de-masking training paradigm (details provided in Methods and Results sections), in which the observers were trained to discriminate the contrast or orientation of a Gabor stimulus presented to the AE while discounting the masking effect from a noise masker presented to the FE.[16] Dichoptic de-masking training was performed by a group of monocularly well-trained adult amblyopic observers to isolate the effects of dichoptic training. The observers were significantly more capable of discounting dichoptic noise masking after training. Moreover, dichoptic training produced extra gains of stereoacuity, but not visual acuity, in these monocularly well-trained amblyopic observers, supporting Levi et al.[6] on the potential advantages of dichoptic training.

Like in adults with normal vision, monocular perceptual learning in those with amblyopia is often specific to the trained orientation. The orientation specificity has been attributed to training induced neural plasticity in the amblyopic early visual

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S1	24	F	A
S2	24	M	A
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S4	26	F	
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udy, we investigated the mechanisms of
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otheses. The low-level hypothesis supposes
c training reduces physiological interocular
n in the amblyopic visual cortex, which restores at
rt of the functionality of binocular vision. This
esis would predict no orientation specificity because
siological interocular suppression is orientation invari-
nt,[24,25] and no task specificity because the task specificity is
elated to high-level attentional mechanisms,[26] and may
indicate learning of different rules for different tasks.[22] In
contrast, the high-level hypothesis supposes that dichoptic

tropic and strabismic) aged 19 to 28 years (mean = 23 years) participated. All had a visual acuity of 0 logMAR or better in FEs, and a visual acuity difference of two lines (0.2 logMAR) or greater between the AEs and FEs. They were new to psychophysical experiments. Their vision was best corrected before training by an ophthalmologist. Five of eleven observers wore their existing lenses during training, which were worn for a period of at least 6 months. The other six observers received new lenses during training, which were wore only when they undertook the experiments (20~28 hours). Full ophthalmic histories were obtained. Clinical details of all observers are summarized in the Table. Informed consent was collected from each observer prior to data collection. The study followed the tenets of the Declaration of Helsinki and was approved by the institutional review board of Peking University.

The basic experimental design is represented schematically in Figure 1A. Prior to training the visual acuities and contrast sensitivity functions for both amblyopic and fellow eyes, as well as the stereoacuity, were measured. Eleven observers were assigned into two groups randomly. Following a dichoptic TPE protocol: (1) The first group ($n = 6$) practiced contrast discrimination at a vertical orientation for nine sessions. Then they received exposure to the orthogonal orientation through an irrelevant orientation discrimination task for five sessions. (2) The second group ($n = 5$) first practiced orientation discrimination at a horizontal orientation for five sessions. Then they received exposure to the orthogonal orientation through an irrelevant contrast discrimination task for another five sessions. After the dichoptic TPE training, the visual acuities, contrast sensitivity functions, and stereoacuity were remeasured. A subset of observers ($n = 6$; S1, S2, S3, S5, S7, and S11 in the Table) then performed monocular orientation training for nine sessions. After this monocular training the visual acuities and stereoacuity were remeasured.

The setup was identical to that in Liu and Zhang.[16] The stimuli were generated with Psychtoolbox-3 software[27] and presented on a 21-in Sony G520 CRT monitor (2048 × 1536 pixel, 0.19 × 0.19 mm/pixel, and 75-Hz frame rate). The head of the observer was stabilized by a chin-and-head rest. Experiments were run in a dimly lit room. For grating acuity and contrast sensitivity testing, a 14-bit look-up table achieved with a video attenuator was used to linearize the luminance of the monitor (mean luminance = 27 cd/m^2), and for other tasks an 8-bit look-up table was used (mean luminance = 50 cd/m^2).

The dichoptic stimuli (Fig. 1B) consisted of a pair of collinear vertical or horizontal Gabors (Gaussian windowed sinusoidal gratings) presented in AE and a band-pass filtered white noise masker in FE. The two Gabors had the same spatial frequency at 40% of AE's cut-off frequency, standard deviation at 1 wavelength (the reciprocal of spatial frequency), orientation at 0° or 90°, phase at 90°, and a center-to-center distance of 4 wavelengths. The cut-off frequency of AE (Mean = 14.4 cpd, SD = 3.6 cpd) was assessed by a grating acuity test for each observer before training. The viewing distance was 1.2 m. In contrast discrimination trials, one Gabor's contrast was set at 0.80, and the other Gabor's contrast was $0.80 - 1.414 \times$ contrast discrimination threshold (with no masker presented in FE). The contrast discrimination threshold was premeasured for each observer with the same Gabor stimulus at a reference contrast of 0.80 (AE's contrast just-noticeable difference (JND) threshold: mean = 0.189, SD = 0.031). In orientation discrimination trials, the global orientation of two always aligned Gabors were tilted upper or lower from horizontal. The orientation offset was 1.414 times the orientation discrimination threshold premeasured for each observer with no masker presented in FE (AE's orientation JND threshold: mean = 1.5°, SD = 0.3°). The contrast of two Gabors was identical at 0.80.

The band-pass filtered noise masker was 512 × 512 pixels (4.4° × 4.4°) in size. To create the noise masker, a 512 × 512 pixels zero-mean white noise field was first generated, with each element being 2 × 2 pixels. The white noise field was then filtered in the frequency domain by a 1-octave band-pass filter centered at the same frequency of the Gabors. A new noise masker was generated every trial.

The stimulus for monocular orientation discrimindenti-10.4(nente-16.

observer pressed the space bar to initiate the trial as soon as the whole cross appeared stable. Immediately after the key press, a black square contour (1.5° × 1.5°, the contour lines were 2-arcmin thick) was presented for 200 ms to prime attention to AE. After that the Gabor stimuli and the noise masker were presented dichoptically for 200 ms.

In the contrast discrimination trials, the observers were asked to judge which Gabor had a higher contrast. In the orientation discrimination trials, they were asked whether the 2-Gabor stimuli tilted upper or lower from horizontal. A staircase varied the root mean square contrast of the noise masker upon AE's contrast or orientation judgment. The staircase followed a 3-up-1-down rule that resulted in a 79.4% convergence rate. Specifically, three consecutive correct responses would raise the noise contrast by one step, and one incorrect response would lower the noise contrast by one step. The step size of the staircase was 0.05 log units. Each staircase consisted of eight reversals (∼40–50 trials). The geometric mean of the last six reversals was taken as the maximal tolerable noise contrast (TNC) for successful contrast or orientation discrimination.

To ensure effective noise masking (i.e., an observer did not close his/her fellow eye), in 20% of the trials a white digit ("1" or "2," 1.1° × 1.7° in size) was centered on the noise masker in FE while a blank screen was presented in AE. The observer needed to report the digit by key press (the mean correct rate = 95.5 ± 1.5%). Auditory feedback was given on incorrect responses in all trials.

The dichoptic TPE protocol consisted of a first training phase and a second exposure phase. Before and after the first training phase (i.e., contrast/orientation discrimination training), the following conditions were tested to evaluate the learning and transfer effects: (1) maximal TNC for AE's contrast/orientation discrimination at the trained orientation (groups 1, 2), and (2) maximal TNC for AE's contrast (group 1) or orientation discrimination (group 2) at an untrained orthogonal orientation. Each condition was measured for five staircases (∼200–250 trials). After the second exposure phase (orientation/contrast discrimination training at an orthogonal orientation), only condition (2) was re-tested to evaluate the learning and transfer effects. All staircases were run following a randomly permuted table for each observer. The duration varied from 1 to 2 hours, depending on the conditions. In the training and exposure phases, each daily session consisted of 20 staircases (for a total number of 800∼1000 trials) and lasted for approximately 2 hours. More details can be found in the Results section below.

During monocular training, orientation discrimination threshold was measured with a 2AFC staircase procedure in AE. In each trial, a foveal fixation cross was flashed for 400 ms before the onset of the stimulus. Then the reference and the test stimuli were presented separately in two 200-ms stimulus intervals in a random order, separated by a 500-ms interstimulus interval. Threshold was estimated following a 3-down-1-up staircase rule that resulted in a 79.4% convergence rate. The step size of the staircase was 0.05 log units. Each staircase consisted of two preliminary reversals and six experimental reversals. The geometric mean of the experimental reversals was taken as the threshold for each staircase run. Each session consisted of 20 staircases (for a total number of 800∼1000 trials) and lasted for approximately 2 hours.

Several studies have suggested that the interocular contrast ratio is a reliable objective measurement of interocular suppression.[9,28] Therefore, we adopted the interocular contrast ratio, which was the maximal TNC for AE divided by the maximal TNC for FE, to assess the strength of interocular suppression. Specifically, in the pre- and posttests, the Gabors and the noise masker were switched between eyes, so that the noise masker was presented to AE and the Gabor stimuli were presented to FE. Thus, the maximal TNCs for FE contrast

. The stereoacuity was evaluated using the Randot Stereo Test (Stereo Optical Co., Inc., Chicago, IL, USA) with polarizing glasses at a 40-cm viewing distance under normal room lighting. The stereo test was administered and scored according to the manufacturer's instructions. A graded sequence test was provided by contoured circles at 10 levels of disparity ranging from 400 to 20 arcsec. Randot forms with disparities at 500 and 250 arcsec were also used to provide additional steps of disparity.

Eleven adult amblyopic observers with no prior monocular training experience were randomly divided into two groups. The first group of six initially practiced AE contrast discrimination at a vertical orientation with dichoptic noise masking for nine sessions (Fig. 2A). We used the percent improvement (PI = [threshold_post/threshold_pre-1] × 100) to index the learning and transfer effects. After the first training phase, the maximal TNC for AE contrast discrimination was significantly improved by 173.1 ± 39.8% ($t_5 = 4.35$, $P = 0.007$, Cohen's $d =$ 1.78; 2-tailed paired *t*-test in this and later analyses unless specified), from a root mean square 3 1 Tf.3161 0 7(Coh8f07 -1.138f07 73.4(2 ged either (Fig. 2B, MPI = 11.39 ± 18.51%, $t_4 = 0.62$, $P =$ [illegible] Cohen's $d = 0.28$). In the pretest, the interocular contrast [illegible] which we used as an index for interocular suppression [illegible] Methods), was 0.18 for the two groups when data were [illegible] ged, suggesting strong interocular suppression. In the [illegible] test, the interocular contrast ratio was significantly [illegible] ased to 0.56 ($t_{10} = 3.53$, $P = 0.005$, Cohen's $d = 1.06$), [illegible] esting reduced interocular suppression. As would be [illegible] ussed later, this reduction does not necessarily suggest [illegible] ced physiological interocular suppression, but is likely a [illegible] t of reduced interocular functional imbalance due to [illegible] itive learning effects.

[illegible] or contrast discrimination learning (group 1), when the [illegible] ulus was switched to an orthogonal orientation after the [illegible] training phase, no significant change of maximal TNC was [illegible] erved (MPI = 22.2 ± 15%, $t_5 = 1.48$, $P = 0.20$, Cohen's $d =$ [illegible], the first two red solid circles in Fig. 2A). Similarly, the [illegible] imal TNC for AE orientation discrimination (group 2) was [illegible] significantly changed at an orthogonal orientation either [illegible] I = 68.5 ± 36.3%, $t_4 = 1.89$, $P = 0.13$, Cohen's $d = 0.85$, the [illegible] two red solid diamonds in Fig. 2B). When data from two [illegible] ups were combined, there was significant difference [illegible] ween the improvements at the trained orientation and the [illegible] rained orthogonal orientation ($t_{10} = 5.37$, $P < 0.001$, [illegible] hen's $d = 1.62$), showing orientation specificity in dichoptic [illegible] masking learning.

In addition, we found that dichoptic de-masking learning [illegible] s mostly specific to the trained [illegible] tched to untrained ori [illegible] re was no signif [illegible] AE [illegible] entation discri [illegible] mina- [illegible] n training (M [illegible] ohen's [illegible] .03, the f [illegible] . Likew [illegible] hoptic [illegible] n trans [illegible] le to [illegible] = 5.1 [illegible] =0.2 [illegible] rst two [illegible] ang [illegible] two [illegible] m [illegible] ifferenc [illegible] the u [illegible] , sugg [illegible] ed tas [illegible]

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[illegible] also worked on orientation specificity in dichoptic de-m [illegible] sking learning. After initial [illegible] trast discrimination training, t [illegible] mblyopic observers in [illegible] tice an AE [illegible] discrimina- [illegible] orientation discrimination by 65.5 ± 41.9% (Fig. 2A, $t_5 =$ 1.56, $P = 0.18$, Cohen's $d = 0.64$), the maximal TNC for [illegible] contrast discrimination at the same orthogonal orient [illegible] was further improved by 193.9 ± 61.5% ($t_5 = 3.15$, P [illegible] Cohen's $d = 1.29$). The total improvement was 230.3 [illegible] % ($t_5 = 3.71$, $P = 0.01$, Cohen's $d = 1.52$), whi [illegible] not significantly different to the total improvement [illegible] rained orientation ($t_5 = 1.02$, $P = 0.35$, Cohen's $d =$ [illegible] dicating complete de-masking learning transfer of [illegible] c learning for AE contrast discrimination to an or [illegible] orientation. Moreover, the task specificity results [illegible] t the possibility that the improved contrast discrim [illegible] at the orthogonal transfer orientation resulted from [illegible] tion training around the same orientation alone.

The transfer effects were [illegible] ed in group 2. After initial orientation training, the o [illegible] s received exposure to the orthogonal transfer orie [illegible] through an irrelevant contrast discrimination trainin [illegible] under dichoptic noise masking. After that, the maxi [illegible] C for AE orientation discrimination at the orthogonal [illegible] tion was further improved by 73.6 ± 22.1% (Fig. 2B [illegible] 3.34, $P = 0.03$, Cohen's $d = 1.49$). In general, the [illegible] mprovement was as much as that at the trained or [illegible] n ($t_4 = 0.86$, $P = 0.44$, Cohen's $d = 0.38$), showin [illegible] ntial and nearly complete learning transfer. The consi [illegible] nd nearly complete learning transfer shown in the [illegible] groups suggests that dichoptic de-masking learning i [illegible] s with amblyopia is mainly a high-level process, which [illegible] be further elaborated in the Discussion section.

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[illegible] rvers, after dichoptic [illegible] ty measured by a [illegible] lines in AEs [illegible] ohen's [illegible]

[illegible] changed after dichop [illegible] 0.37, $t_{10} = -1.24$, $P = 0.24$, Cohen's $d = 0.37$), indicating that training improved uncrowded acuity slightly more than crowded acuity.

[illegible] The dichoptic training improved stereoacui- [illegible] of 900 [illegible] her stereoacuity to be 600 arcsec. The improvement of

improve top-down attention to the amblyopic eye, so as to

learning improves adult amblyopic vision through rule-based

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