Visual Psychophysics and Physiological Optics

Dichoptic Perceptual Training in Children With Amblyopia With or Without Patching History

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Purpose. Dichoptic training is becoming a popular tool in amblyopia treatment. Here we investigated the effects of dichoptic demasking training in children with amblyopia who never received patching treatment (NPT group) or were no longer responsive to patching (PT group).

Methods. Fourteen NPT and thirteen PT amblyopes (6–16.5 years; 24 anisometropic, two strabismus, and one mixed) received dichoptic demasking training for 17 to 22 sessions. They used the amblyopic eye (AE) to practice contrast discrimination between a pair of Gabors that were dichoptically masked by a band-filtered noise pattern simultaneously presented in the fellow eye (FE). Dichoptic learning was quantified by the increase of maximal tolerable noise contrast (TNC) for AE contrast discrimination. Computerized visual acuities and contrast sensitivity functions for both eyes and the Randot stereoacuity were measured before and after training.

Results. Training improved maximal TNC by six to eight times in both groups, along with a boost of AE acuities by 0.15 logMAR ($P < 0.001$) in the NPT group and 0.06 logMAR ($P < 0.001$) in the PT group. This visual acuity improvement was significantly dependent on the pretraining acuity. Stereoacuity was significantly improved by 41.6% ($P = 0.002$) in the NPT group and 64.2% ($P < 0.001$) in the PT group. The stereoacuity gain was correlated to the pretraining interocular acuity difference ($r = -0.49$, $P = 0.010$), but not to the interocular acuity difference change ($r = -0.28$, $P = 0.15$). Training improved AE contrast sensitivity in the NPT group ($P = 0.009$) but not the PT group ($P = 0.76$). Moreover, the learning effects in 12 retested observers were retained for 10 to 24 months.

Conclusions. Dichoptic training can improve, and sometimes even restore, the stereoacuity of amblyopic children, especially those with mild amblyopia (amblyopic VA $\leqq$0.28 logMAR). The dissociation of stereoacuity gain and the interocular acuity difference change suggests that the stereoacuity gain may not result from a reduced interocular suppression in most amblyopes. Rather, the amblyopes may have learned to attend to, or readout, the stimulus information to improve stereopsis.

Keywords: dichoptic learning, amblyopia, patching history, children, stereopsis

Amblyopia is a developmental disorder of the visual cortex that arises from abnormal visual experience (e.g., strabismus or anisometropia) in early childhood.[1,2] During normal binocular viewing, information from the amblyopic eye is suppressed, whereas the stronger eye dominates perception.[2–7] A weakened ability of the amblyopic eye to modulate cortical response gain was created by an imbalance of interocular suppression that favors the dominant eye.[4] In addition to decreased visual acuity, amblyopia is accompanied by binocular dysfunctions such as impaired stereoacuity.[8,9] Therefore it has been argued that amblyopia is intrinsically a binocular problem, rather than a monocular one. This may explain why the conventional patching treatment, which forces the use of amblyopic eye (AE) with the fellow eye (FE) patch-covered, improves AE visual acuity more than stereoacuity.[10–14]

In the past decades, studies have shown that perceptual learning can improve visual functions in patients with amblyopia (see Levi et al.[15] for a comprehensive review). Earlier perceptual learning studies mostly performed monocular training in AE with FE patched.[16–20] For example, we reported that monocular training of a grating acuity task (cutoff spatial frequency) improved visual acuity in amblyopic children (ages similar to those in the current study) by 0.08 to 0.13 logMAR.[16] However, monocular training does not directly address interocular suppression. More recent studies used dichoptic training, targeting binocular discordance directly via reducing interocular suppression, strengthening binocular fusion, or promoting binocular vision. Many dichoptic training studies use signal integration training paradigms,[21–27] which require observers to integrate dichoptically presented task elements for successful task completion. To manipulate interocular suppression directly, previously we adopted a different dichoptic demasking training paradigm (detailed provided in Methods and Results), in which the observers were trained to discriminate the contrast or orientation of a Gabor stimulus presented to the amblyopic eyes while resisting dichoptic noise masking from the fellow eyes.[28,29] The amblyopic observers were significantly more capable of discounting dichoptic noise masking after training. Moreover, dichoptic training further improved stereoacuity, but not AE visual acuity, in monocularly well-trained adults with amblyopia.[28] These results support Levi et al.[15] on the potential extra advantages of dichoptic training.

Binocular approaches for amblyopic children, such as dichoptic games, that rebalance contrast between two eyes to overcome suppression have been reported to induce visual acuity gains.[30–39] However, their effects on stereoacuity are unclear. Some studies report that binocular treatments improved stereoacuity in some amblyopic children.[35,40,41] For example, Kelly et al.[40] reported that 20% of 41 amblyopic children (age 4–10 years) experienced stereoacuity improvements after nine to ten hours of binocular treatments (dichoptic game or movie). But other studies have shown no improvement in binocular functions.[31–33] For example, Li et al.[31] found that passive viewing of dichoptic movies for two weeks failed to improve stereoacuity in eight amblyopic children (age 4–10 years). The diverse outcomes could result from differences in treatment type, treatment duration, and sample inhomogeneity.[15] Therefore it remains to be determined whether binocularity in children benefits from binocular treatments and what factors are associated with the outcomes.

Here we investigated the effects of dichoptic de-masking training on visual functions, especially stereoacuity, in children with amblyopia, and related the training effects to the history of patching treatment and the severity of amblyopia. These amblyopic children learned to use AE to perform contrast discrimination while resisting dichoptic noise masking simultaneously presented in FE. Learning was quantified by the maximal tolerable noise contrast (TNC) for AE contrast discrimination. To assess the improvements of visual functions, monocular visual acuity and contrast sensitivity, as well as binocular stereoacuity, were measured before and after training.

METHODS

O

Twenty-seven amblyopic observers aged 6 to 16.5 years took part in this study. They were trained in the Tengzhou Central People's Hospital, Tengzhou City, Shandong province of China. Thirteen observers (seven boys and six girls, mean ± SD = 10.9 ± 2.8 years; Table 1) had been patch treated for more than 1.5 years, starting at the age of 6.6 ± 3.1 years, by the three ophthalmologist authors (LXY, FG, FC). The visual acuity of these observers had improved by 0.43 ± 0.18 logMAR on the tumbling E chart (missing SA2 data). There had been no acuity improvement in the previous six months before the current training. These observers formed the patch-treated (PT) group. The fourteen other observers (ten boys and four girls, mean ± SD = 10.4 ± 2.0 years; Table 2) had never received patching treatment. They formed the never patch-treated (NPT) group. Among them, four amblyopes (SB5, SB8, SB11, SB13) had worn their corrective lenses for six months, and they received no other therapy beyond glasses before training. The other 10 observers had untreated amblyopia before training. They were either newly diagnosed amblyopes (SB1, SB4, SB7, SB10, SB12, SB14) or amblyopes who were diagnosed younger (SB2, SB3, SB6, SB9) but did not take any treatment because of poor compliance. They were prescribed new glasses and wore them for at least two weeks (mean ± SD = 4.1 ± 2.4 weeks) before data collection. All observers had undergone part-time occlusion therapy during training. The prescribed dose during training was about 2.5 h/d on average. Besides, we obtained the pre-patching and post-patching visual acuity data of 15 age-matched amblyopic observers from the medical archives at the Beijing Tongren Hospital. These amblyopes received 2965 ± 362 hours of patching treatment starting at similar ages (10.2 ± 0.6 years).

Each observer's vision was best-corrected before training with a tumbling E acuity chart at the designated viewing distance of 5 m. Testing and training were performed with the observer wearing the best optical correction, and the visual acuity values reported throughout the article are for best-corrected acuity. The study adhered to the tenets of the Declaration of Helsinki and was approved by the ethics committees of Tengzhou Central People's Hospital. Informed consent was obtained from each observer's parent or guardian after an explanation of the nature and possible consequences of the study.

A

The setup was identical to those described in Liu and Zhang.[28,29] Briefly, the stimuli were generated with Psychtoolbox-3[42] and presented on a 21-inch Sony G520 CRT monitor (2048 pixel × 1536 pixel, 0.19 mm × 0.19 mm pixel size, 75 Hz frame rate; Sony, Tokyo, Japan). The head of the observer was stabilized by a chin-and-head rest. Experiments were run in a dimly lit room. For cutoff frequency (grating acuity) and contrast sensitivity measurements, 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). For other tasks, an 8-bit look-up table was used (mean luminance = 50 cd/m^2).

S D

The experiment consisted of pretraining assessment, dichoptic demasking training, and posttraining assessment (Fig. 1A). Pretraining and posttraining assessments measured visual acuities and contrast sensitivity functions for AE and FE, respectively, and stereoacuity (Fig. 1B). Dichoptic demasking training took 21 sessions on average (mean ± SD = 20.7 ± 1.6 for the NPT group and 20.6 ± 1.8 for the PT group). Each training session consisted of 14 to 21 staircases and lasted for approximately 1 to 1.5 hours. The training frequency ranged from two to five daily sessions per week, which was more frequent during summer and winter breaks and varied among observers. The experiment lasted 3 months on average (mean ± SD = 85 ± 23 days). Three NPT observers (SB10, SB11, SB12) did not complete the pretraining contrast sensitivity assessment. One PT observer (SA13) did not complete the pretraining computerized-E acuity assessment. His/her Tumbling E chart acuity was used as VA (visual acuity) in data analysis.

Table 1. The Characteristics of the Amblyopic and Fellow Eyes in the PT Group

							A		S (A)		P T		
O	A ( )	G	T	S	E	C	P	P	P	P	S A /L ( )	S A	T S
SA1	9.5	Male	A	None	AE (L)	+5.00	0.48	0.35	F	200	7.5/2	0.92	22
					FE (R)	Plano	−0.09	−0.11				0	
SA2	16.5	Female	A	None	AE (L)	+3.50/−2.00 × 15	0.29	0.21	F	70	3/9	Unknown	22
					FE (R)	−3.50	−0.03	−0.05				Unknown	
SA3	7.2	Male	A	None	AE (R)	+3.50	0.13	0.11	200	40	5/2	0.92	22
					FE (L)	+3.75	0.05	0.01				0.40	
SA4	10.4	Male	A	None	AE (L)	+2.50/+0.75 × 115	0.59	0.51	F	200	6/4.5	1	21
					FE (R)	Plano	0.08	0.05				0	
SA5	6.0	Female	A	None	AE (L)	+3.00	0.24	0.18	F	50	4/2	0.82	22
					FE (R)	+0.75	0.15	0.11				0.10	
SA6	10.2	Male	A	None	AE (L)	+6.00/+2.00 × 80	0.43	0.37	F	200	5/2	0.82	22
					FE (R)	+2.50/−2.00 × 85	0.11	−0.05				0.52	
SA7	10.2	Female	A	None	AE (R)	+6.00	0.24	0.23	400	140	5/2	0.52	22
					FE (L)	+5.50	0.09	0.05				0.10	
SA8	11.8	Male	A	None	AE (L)	+0.75/+2.75 × 90	0.27	0.24	400	20	10/1.5	0.30	22
					FE (R)	+1.25/+0.75 × 80	0.06	0.01				0	
SA9	14.0	Male	A	None	AE (L)	+2.50	0.23	0.19	50	20	12/2	0.60	17
					FE (R)	Plano	−0.10	−0.12				−0.18	
SA10	14.0	Male	A	None	AE (R)	+6.00/+0.50 × 120	0.32	0.22	140	20	12/1.5	0.70	18
					FE (L)	+0.25/+0.50 × 60	−0.15	−0.14				0	
SA11	10.0	Female	A	None	AE (R)	+4.25 × 95	0.13	0.12	30	20	8/2	0.22	17
					FE (L)	+3.50 × 75	0	−0.01				0	
SA12	11.5	Female	A	None	AE (R)	+3.50	0.13	0.11	50	20	4/2	0.40	18
					FE (L)	+4.00/+0.75 × 130	0.08	0.07				0.10	
SA13	10.7	Female	S	R 15$^{\Delta}$ EsoT	AE (R)	−0.75	0.22	0.10	F	F	4/2	1	22
					FE (L)	−0.75/−0.50 × 10	0	−0.10				0.30	

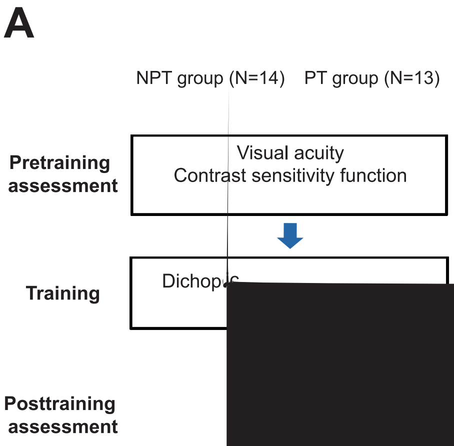
Pretraining and posttraining visual acuities were measured with a computerized crowded-E acuity test (except SA13 whose E chart acuity was used instead). The starting acuity was tested with a Tumbling E chart. The stereoacuity was evaluated with the Randot Stereo Test. Strabismus diagnosed by a cover test at a distance of 33 cm.

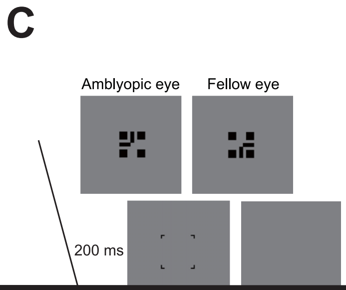
A, anisometropic; S, strabismic; AE, amblyopic eye; FE, fellow eye; L: left; R: right; EsoT, esotropia; ExoT, exotropia; F, failed the Randot Stereo Test.

Table 2. The Characteristics of the Ambl opic and Fellow E es in the NPT Group

									S			
							A		(A)			T
O	A ( )	G	T	S	E	C	P	P	P	P	T H	S
SB1	12	Female	A	None	AE (R)	+3.00	0.61	0.44	F	200	No treatment	21
					FE (L)	Plano	0	−0.14				
SB2	8.8	Male	A	None	AE (L)	+6.25/+0.75 × 95	0.68	0.43	F	F	No treatment	20
					FE (R)	+1.75/+0.75 × 90	−0.02	−0.08				
SB3	9.3	Male	A & S	L 15^{Δ} EsoT	AE (L)	+3.00/+1.25 × 90	0.96	0.69	F	F	No treatment	21
					FE (R)	+1.50	−0.04	−0.02				
SB4	7.5	Male	A	None	AE (L)	+3.50/−3.50 × 115	0.33	0.16	400	40	No treatment	22
					FE (R)	+4.00/−2.00 × 175	0.15	0.12				
SB5	11.8	Male	A	None	AE (L)	+6.50/+0.75 × 100	0.39	0.36	F	200	Glasses for 0.5 , no patching	22
					FE (R)	+6.75/+1.00 × 80	0.16	0.16				
SB6	11.7	Male	S	L 30^{Δ} EsoT	AE (L)	−0.50/−1.25 × 170	0.57	0.35	F	F	No treatment	22
					FE (R)	−1.50 × 175	0.24	0.22				
SB7	10.7	Female	A	None	AE (R)	+1.00/+1.00 × 50	0.18	0.15	140	40	No treatment	20
					FE (L)	Plano	−0.03	−0.02				
SB8	7.2	Female	A	None	AE (R)	+2.25/+1.50 × 60	0.45	0.32	F	30	Glasses for 0.5 , no patching	22
					FE (L)	+1.25/+1.50 × 95	0.22	0.18				
SB9	11.7	Male	A	None	AE (R)	+4.00	0.51	0.39	F	F	No treatment	22
					FE (L)	Plano	0.03	0.01				
SB10	12	Male	A	None	AE (R)	+0.50	0.21	0.02	200	30	No treatment	17
					FE (L)	+4.00	−0.12	−0.12				
SB11	9.5	Male	A	None	AE (R)	+4.50/−5.50 × 5	0.14	0.14	70	30	Glasses for 0.5 , no patching	22
					FE (L)	+4.50/-6.00 × 175	0.14	0.14				
SB12	9.0	Female	A	None	AE (R)	+2.50/+0.75 × 95	0.44	0.26	200	70	No treatment	21
					FE (L)	Plano	0.04	0.06				
SB13	14.5	Male	A	None	AE (R)	+6.00	0.60	0.54	400	400	Glasses for 0.5 , no patching	20
					FE (L)	Plano	−0.17	−0.10				
SB14	9.5	Male	A	None	AE (R)	+3.00/+1.00 × 70	0.77	0.54	F	F	None	18
					FE (L)	+1.00 × 105	0.15	0.09				

A, anisometropic; S, strabismic; AE, ambl opic e e; FE, fellow e e; L: left; R: right; EsoT, esotropia; ExoT, exotropia; F, failed the Randot Stereo Test.


A
NPT group (N=14)
PT group (N=13)
Pretraining assessment
Visual acuity
Contrast sensitivity function
Training
Dichop
Posttraining assessment


C
Amblyopic eye
Fellow eye
200 ms

[redacted]

chart because both were influenced by visual crowding. The stroke and opening width of the E letters were one-fifth of the letter height.

The E acuities were all measured with a single-interval staircase procedure. The stimulus stayed on until a key press by the observer. The task was to judge the orientation of the tumbling E (left, right, up, or down). All thresholds were estimated following a three-down/one-up staircase rule. Each staircase consisted of two preliminary reversals and four experimental reversals. The step size of the staircase was 0.05 log units. The geometric mean of the experimental reversals was taken as the threshold for each staircase run. Three staircases were run to determine single-E or crowded-E acuities. The computerized E-acuities test (the step size of the staircase was 0.05 log units) might be more reliable than the clinical E-chart test (size of optotypes changed by 0.1 log unit from line to line); therefore we only use the computerized acuity tests to evaluate VA.

S . Stereoacuity is the smallest detectable depth difference that can be seen in binocular vision. The Randot Stereo Test (Stereo Optical Co, Inc, Chicago, IL, USA) was used to test stereoacuity under normal room lighting. Contoured circles at 10 levels of disparity ranging from 400 to 20 arcsec provide a graded sequence for testing. Observers wore polarizing glasses and looked at the test material at a viewing distance of 40 cm. Note that in Figure 4A, and for the convenience of data analysis, the stereoacuity for those who failed the Randot Stereo Test was set at 500 arcsec, a value below the lowest measurable score.

C S . Acuity measures only the smallest resolvable details, but not the ability to see larger ones. The contrast sensitivity function (CSF) provides a more comprehensive evaluation of spatial vision. CSF describes an observer's sensitivity (i.e., 1/contrast threshold) to sinusoidal gratings of various spatial frequencies. Therefore CSF is an additional tool to document changes in visual functions during the treatment of amblyopia.[44]

Contrast sensitivity was measured with a Gabor stimulus ($\sigma = 0.9°$, orientation = ± 45° from vertical). The spatial frequencies of the Gabor were 3/4, 1/2, 1/4, and 1/16 times the cutoff spatial frequency determined with a cutoff frequency measurement before training. For the cutoff frequency measurement task, the stimulus was a 0.29° × 0.29° sharp-edged full-contrast square-wave grating tilted ± 45° from vertical.

The contrast sensitivity and cutoff frequency measurement were all measured with a single-interval staircase procedure at a viewing distance of 4 m. The stimulus stayed on until a key press by the observer. The task was to judge the orientation of the grating (tilted to the left or right from vertical). Each staircase consisted of two preliminary reversals and six experimental reversals. The step size of the staircase was 0.05 log units for contrast sensitivity measurements and 0.03 log units for cutoff frequency measurements. Three staircases were run to determine cutoff frequency and the contrast sensitivity to each spatial frequency. The order of all staircases for all spatial frequencies followed a randomly permuted table. Each observer's AE and FE had different tables. Staircases were run consecutively for one eye before being switched to the other eye.

The mean CSFs were fitted with a difference of Gaussians function: $y = A_1 e^{-(x/\sigma_1)^2} - A_2 e^{-(x/\sigma_2)^2}$. Here y stood for the contrast sensitivity, x for the spatial frequency, A_1 and A_2 for the amplitudes, and σ_1 and σ_2 for the standard deviations.

RESULTS

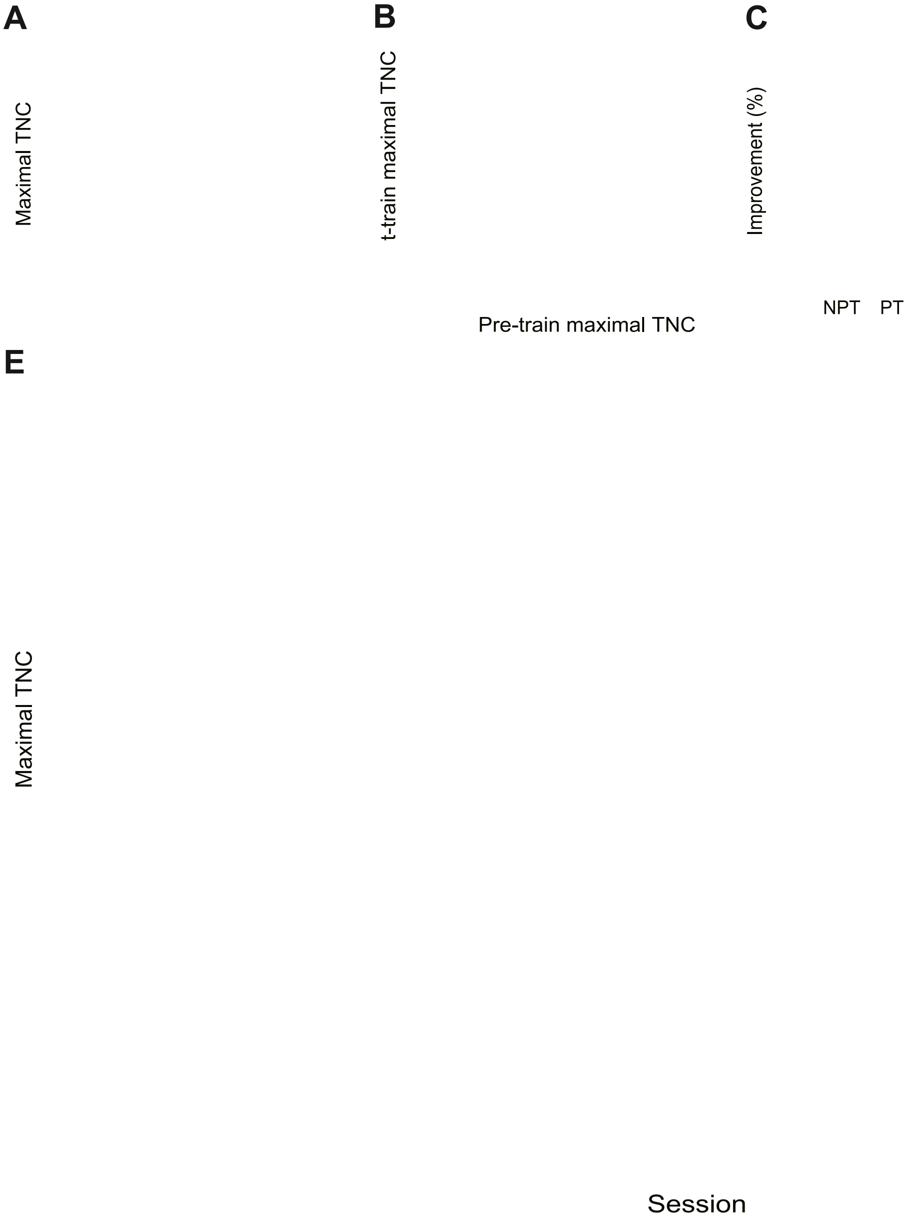
P L I D D

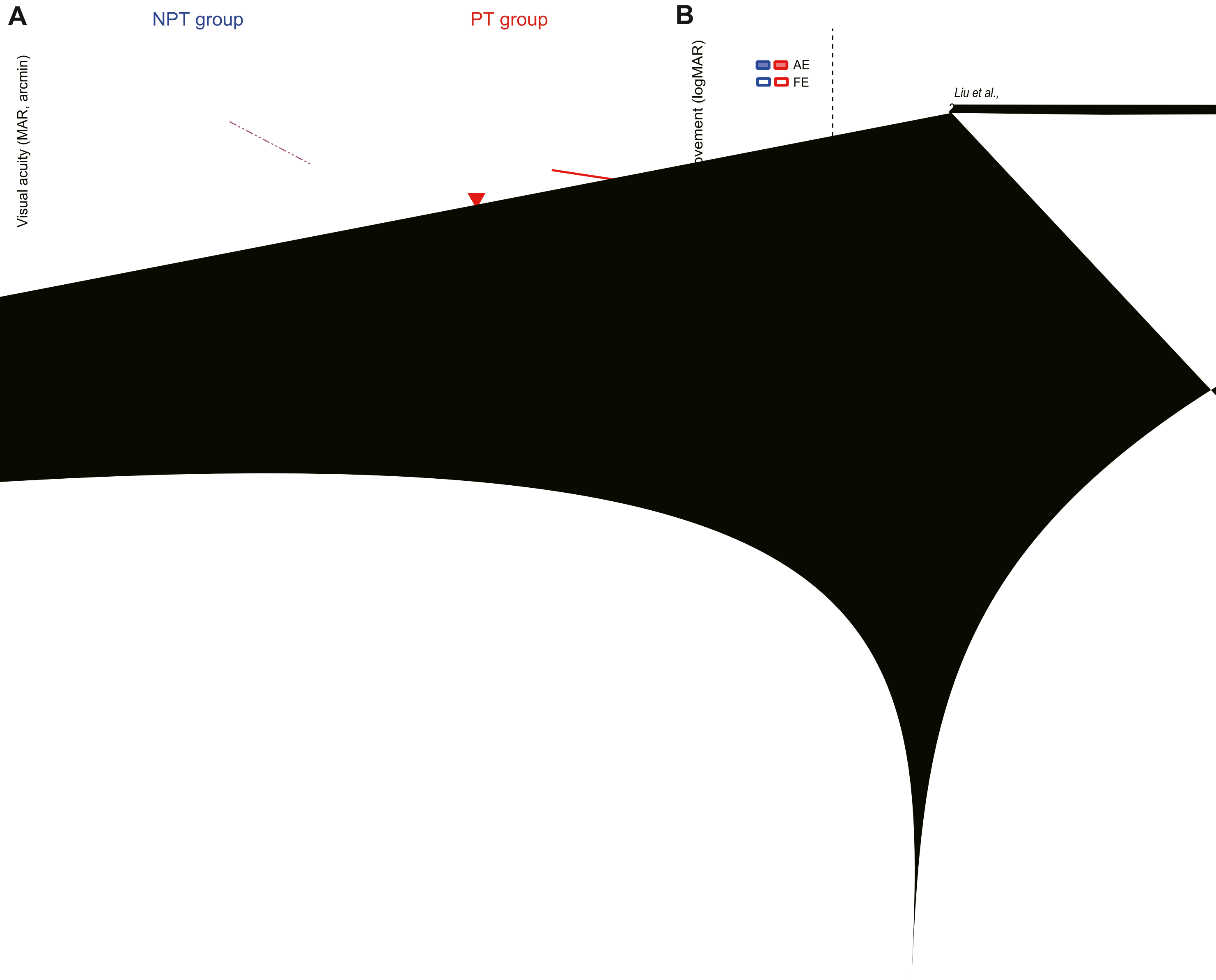
During the dichoptic training, the AE performed contrast discrimination under dichoptic noise masking from the FE (Fig. 1C). Significant learning was evident as the maximal TNC increased during the course of dichoptic training (Figs. 2A and 2B). We used the percent improvement (PI = (threshold_post/threshold_pre - 1)*100) to quantify the amount of learning. Training improved the maximal TNC of the NPT group by 747% ± 342% ($t_{13} = 2.22$, $P = 0.045$, Cohen's d = 0.59; two-tailed paired *t*-test here and later unless specified), from a root mean square contrast of 0.015 ± 0.003 to 0.070 ± 0.012 (Figs. 2A–2C). Likewise, training improved the maximal TNC of the PT group by 580% ± 164% ($t_{12} = 3.55$, $P = 0.004$, Cohen's d = 0.99), from a root mean square contrast of 0.023 ± 0.005 to 0.090 ± 0.011 (Figs. 2A–2C). A mixed-design ANOVA suggested a significant main factor of training ($F_{1,25} = 63.38$, $P < 0.001$, $\eta^2 = 0.72$), a nonsignificant main factor of group ($F_{1,25} = 2.01$, $P = 0.17$, $\eta^2 = 0.07$), and a nonsignificant interaction between training and group ($F_{1,25} = 0.60$, $P = 0.45$, $\eta^2 = 0.023$). Moreover, the amount of dichoptic demasking learning appeared to depend on the pretraining maximal TNC, as shown by the Deming regression fit on the log-log plot (slope = −1.53, $R^2 = 0.57$, $P < 0.001$) (Fig. 2D), suggesting that those with poorer pretraining maximal TNC tended to have more room for dichoptic learning. This correlation was consistent with previous studies[45,46] showing that the learning speed and amount were strongly coupled to pretraining performance levels.

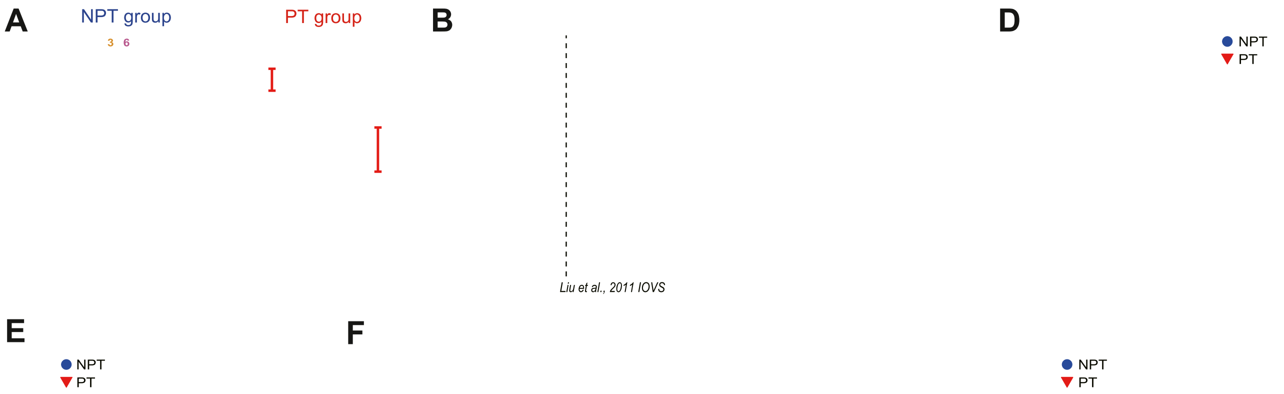
To quantify the learning rate, we used an exponential function: Maximal TNC = $y0 + a\,(1\text{-}e^{-x/\tau})$ to fit the training-induced change of maximal TNC (smooth curves in Figs. 2A and 2E), where x was the training session, $y0$ the maximal TNC at $x = 0$, a the asymptotic maximal TNC with sufficient training, and τ the time constant corresponding to the training time needed to reach 63% of asymptotic performance.[47,48] The time constants were 11.36 ± 3.73 and 9.26 ± 1.60 sessions for NPT and PT groups, respectively (Fig. 2A), which were not significantly different between each other (independent-samples *t*-test, $P = 0.28$). Besides, the other two parameters $y0$ and a were not significantly different between NPT and PT groups (independent-samples *t*-test, $y0$: $P = 0.85$; a: $P = 0.46$). There were large individual variabilities, as indicated by the different improvements of maximal TNC or the time constants of learning across observers. However, no significant correlation was evident between these two indexes ($r = 0.18$, $P = 0.36$). Although learning is variable in different observers (17–22 sessions), there is no correlation of training frequency to the improvement of Maximal TNC ($r = 0.14$, $P = 0.49$) and to the time constant ($r = 0.38$, $P = 0.052$).

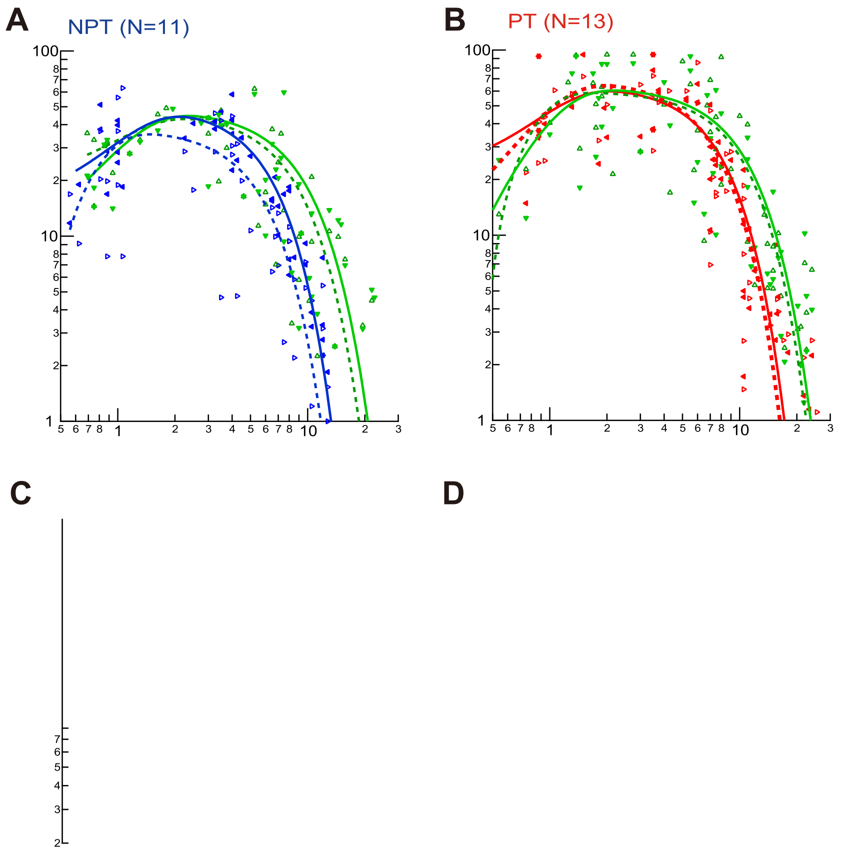
A C A D D T

Figure 3A shows the AE visual acuities of the NPT and PT groups before and after training. A repeated-measures ANOVA suggested a significant main effect of training ($F_{1,24} = 17.02$, $P < 0.001$, $\eta^2 = 0.42$), indicating significantly improved AE visual acuities of both groups and a significant main effect of acuity test type ($F_{1,24} = 19.83$, $p < 0.001$,


A
Maximal TNC
B
t-train maximal TNC
Pre-train maximal TNC
C
Improvement (%)
NPT
PT
E
Maximal TNC
Session


A
NPT group
PT group
Visual acuity (MAR, arcmin)
B
AE
FE
ovement (logMAR)
Liu et al.,


A
NPT group
3
6
PT group
B
Liu et al., 2011 IOVS
D
● NPT
▼ PT
E
● NPT
▼ PT
F
● NPT
▼ PT


A
NPT (N=11)
B
PT (N=13)
C
D
100
10
1
5 6 7 8 1 2 3 4 5 6 7 8 10 2 3

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Investigative Op th
Dichoptic
Training in
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