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

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

							Visual Acuity		Stereoacuity (Arcsec)		Patch Treatment		
Observer	Age (y)	Gender	Type	Strabismus	Eye	Correction	Pre	Post	Pre	Post	Starting Age/Length (y)	Starting Acuity	Training Sessions
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.

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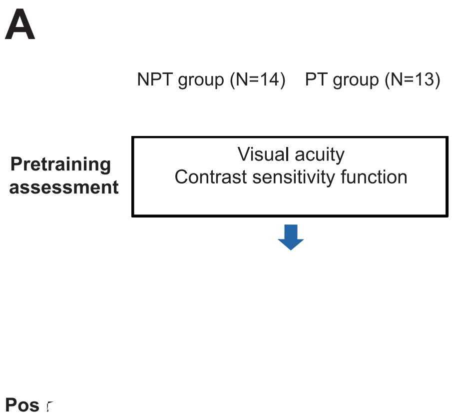
Table 2. The Characteristics of the Amblyopic and Fellow Eyes in the NPT Group

Observer	Age (y)	Gender	Type	Strabismus	Eye	Correction	Visual Acuity Pre	Visual Acuity Post	Stereoacuity (Arcsec) Pre	Stereoacuity (Arcsec) Post	Treatment History	Training Sessions
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$^{\Delta}$ 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 y, no patching	22
					FE (R)	+6.75/+1.00 × 80	0.16	0.16				
SB6	11.7	Male	S	L 30$^{\Delta}$ 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 y, 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 y, 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 y, 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, amblyopic eye; FE, fellow eye; 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
Pos

C

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 keypress 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.

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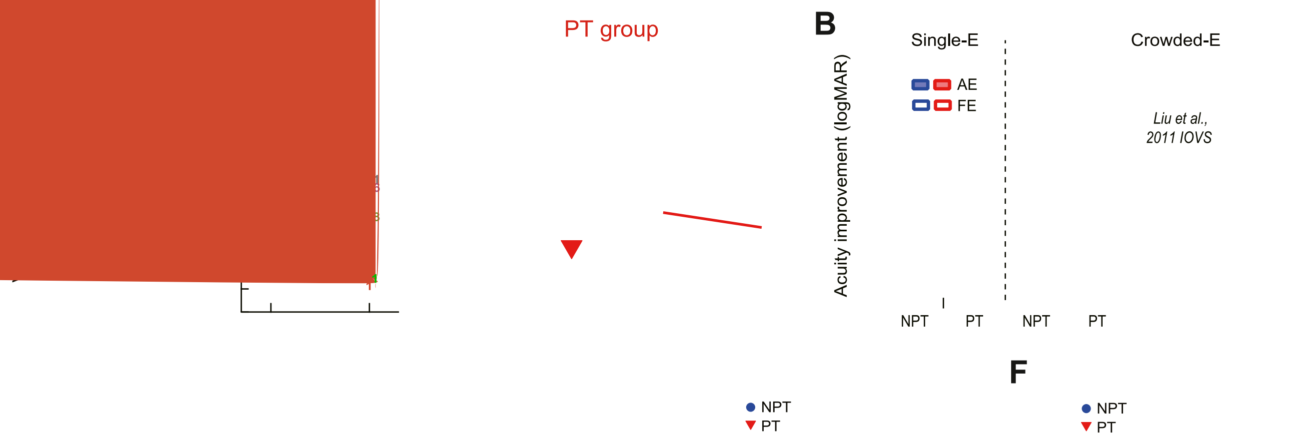

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A
NPT grou
3
6
B
D
E

small, may bear clinical significance when added to previous VA gains after patching. The VA gains by perceptual learning in the NPT eyes, which might benefit from both refractive correction and part-time occlusion,[55,56] were comparable to those (0.16 logMAR) in the age-matched control group after extended patching treatment (~3000 hours), suggesting that perceptual learning combined with traditional treatment may speed up the time to recovery in children with amblyopia. Also, improved acuity was shown in some PT FEs after training. The FEs of many amblyopes are not as good as those in normally sighted people, because recent scientific evidence showed that ocular motor, visual, and visuomotor deficits were present with fellow eye monocular viewing and with binocular viewing.[57–60] Training may have general effects on FE acuity. Nevertheless, our results suggest that monocular and dichoptic perceptual learning are both effective in improving AE visual acuity.

However, binocular training may have advantages over monocular training in stereoacuity improvements. Previous studies have shown that for amblyopic children who are no longer responsive to patching treatment, even if their AEs have achieved normal visual acuity, they rarely restored normal binocularity.[11,12,61,62] In our study, all PT children except one in our study showed stereoacuity improvement. Five in our study had their stereoacuities improved by ≥2 octaves after dichoptic training, reaching clinical significance.[49,50] Overall these children had greater stereoacuity gains than PT children after monocular grating acuity training in our previous study,[16] suggesting that dichoptic training that targeted reducing interocular suppression may be more efficient in improving binocular function for children who are no longer responsive to patch treatment. These data are also consistent with recent findings of ours[28] that dichoptic demasking training may produce extra gains of stereoacuity, but not visual acuity, in adults with amblyopia after prolonged monocular training. Our results thus support the argument of Levi et al.[15] for the potential advantages of dichoptic training.

The stereoacuity improvement varied in NPT children. Five had no measurable stereoacuity after training (initial interocular difference > 0.3 log unit), but five with milder amblyopia (initial interocular difference ≤0.3 log unit) regained normal stereoacuity. A recent study also reported that many stereoblind children remained stereoblind after two weeks of binocular training.[41] In this study, most children had moderate to severe amblyopia (initial interocular difference ≥0.3 log unit). So were children in our NPT group. Therefore dichoptic training may be more effective for those with mild amblyopia, as suggested by Figure 4C, which is also consistent with a meta-analysis on the behavioral training effects for adult amblyopia.[63]

What is learned in dichoptic learning and how can it result in improving visual acuity and stereoacuity? Previously we investigated the mechanisms of amblyopic dichoptic demasking learning by testing two hypotheses.[29] The low-level hypothesis assumed that dichoptic training reduces physiological interocular suppression in the amblyopic visual cortex, which restores at least part of the functionality of binocular vision. In contrast, the high-level hypothesis assumed that training might lead to better attention or reading out contrast or orientation signals from dichoptically presented noise to discount the effects of direct interocular suppression to improve visual function.[63] The results supported the high-level hypothesis by demonstrating that AE dichoptic de-masking learning of contrast and orientation discrimination can transfer nearly completely to an orthogonal orientation with double training,[64,65] so that new orientation or contrast signals can be read out from noise equally effectively. High-level brain areas may learn the rules of reweighting the noisy visual inputs from the amblyopic visual cortex for better readout.[29] Our current results dissociated stereoacuity gain and the change of interocular suppression. The PT group exhibited greater stereoacuity gain even though the interocular suppression was unchanged, which is not expected if the amblyopic observers learn to discount interocular suppression directly through dichoptic training. It is likely the amblyopic observers may learn to be more capable of picking up the trained stimulus signals under the influence 9(b)8(y)-3864influe6-38up thn26(nois.g)-354.3(T)-0.2(he)-39

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