Visual Psychophysics and Physiological Optics

The Therapeutic Impact of Perceptual Learning on Juvenile Amblyopia with or without Previous Patching Treatment

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Purpose. To investigate the therapeutic impact of perceptual learning on juvenile amblyopia that is no longer responsive to patching treatment (PT group) or was never patch treated (NPT group).

Methods. Ten PT and 13 NPT subjects aged 8 to 17 years were trained with a grating acuity task for 40 to 60 sessions. Half in each group were further trained with single or crowded tumbling E acuity tasks for 8 to 10 sessions.

Results. Training improved grating acuity by −2.1% in the PT eyes and 36.1% in the NPT eyes, along with a boost of single and crowded E acuities by 0.9 or 0.7 lines in the PT eyes and 1.5 and 1.2 lines in the NPT eyes, in contrast to a nearly 5-line improvement in the same PT eyes after previous patching treatment. Stereoacuity was improved in some PT and NPT eyes. The single and crowded E acuity improvements were not significantly dependent on the pretraining acuity. The single and crowded E acuity and stereoacuity improvements were uncorrelated with grating acuity improvement, suggesting some random training impacts on different tasks and individuals. Further direct single and crowded E acuity training generated an additional 0.2- and 0.2-line boost for PT eyes and a 0.4- and 0.5-line boost for NPT eyes, resulting in overall single and crowded E acuity gains of 1.4 and 1.0 lines for PT eyes and 2.2 and 1.8 lines for NPT eyes.

Conclusions. Perceptual learning has a small but significant therapeutic impact on both PT and NPT juvenile eyes, which is most likely to have clinical values for eyes with mild amblyopia. Early diagnosis and treatment are most important and effective. (*Invest Ophthalmol Vis Sci.* 2011;52:1531–1538) DOI:10.1167/iovs.10-6355

Amblyopia is an eye condition associated with anisometropia, strabismus, or compromised form vision in early childhood and is typically diagnosed by significantly reduced visual acuity without detectable structural or pathologic causes.[1–3] Conventional patching treatment is most effective in treating amblyopia when the child is younger than 6 or 7 years (the sensitive period). Recent studies have shown that amblyopic vision can be improved through perceptual learning in older children and adults.[1] Perceptual learning refers to improvement, through practice, in discrimination of many basic visual features, such as contrast, orientation, Vernier acuity, and texture.[4–7] Levi and Polat[8] and Levi et al.[9] first reported that training in Vernier acuity improves performance in adult amblyopes, which also leads to improved visual acuity. Later studies found perceptual learning in tasks such as contrast detection and position discrimination in juvenile and adult amblyopes, and learning also transfers in various degrees to visual acuity.[10–17] These findings raise the hope that perceptual learning could become a new therapeutic means for treating amblyopia beyond the sensitive period.[1]

In the present study, we investigated the impact of perceptual learning on juvenile amblyopia for two specific goals. First, although conventional patching can greatly improve amblyopic vision in young children,[18] visual acuity may not always be fully restored.[19] It is important to know whether the residual visual acuity loss in amblyopic eyes that are no longer responsive to patching treatment can be further recovered by perceptual learning. Second, it is still uncertain how much juvenile amblyopic eyes that have never undergone patching treatment can benefit from perceptual learning. Li et al.[13] recently reported that extended positional acuity training leads to a substantial recovery of visual acuity in two previously untreated juvenile amblyopic eyes. A larger sample is needed to establish the therapeutic value of perceptual learning in never-treated juvenile amblyopia.

To maximize the impact of perceptual training, juvenile amblyopes with and without a history of patching treatment were first trained with a grating acuity task in which they had to identify the orientation of a grating patch near the cutoff spatial frequency of the contrast sensitivity function. Previous studies have established the efficacy of training near the cutoff spatial frequency.[17] The grating acuity task uses a self-adaptive staircase method to quickly converge the stimulus to the cutoff frequency to challenge the amblyopic vision. Therefore, in theory, the grating acuity task is an easy and most efficient way to train amblyopic vision at the cutoff frequency. Moreover, since perceptual learning of various visual tasks has been shown to transfer only partially to visual acuity, we re-enrolled half the subjects in each group to further practice the visual acuity task directly. Our results showed a small but significant perceptual learning effect on the visual acuity of both patch-treated and never-treated

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juvenile amblyopic eyes, which is most likely to have clinical value in treating juvenile eyes with mild amblyopia.

METHODS

Observers

Twenty three amblyopic subjects aged 8 to 17 years were trained in the Tengzhou Central People's Hospital, Tengzhou City, or the Zaozhuang Municipal Hospital, Zaozhuang City, in the Shandong province of China. Ten subjects (7 boys, 11.8 ± 0.9 years, Table 1; the error bars indicate 1 SEM) had been patch treated for more than 2 years, starting at the age of 7.4 ± 1.2 years, by the first and third authors, who are ophthalmologists. Their visual acuity had improved by 0.495 ± 0.088 log units or 4.95 ± 0.88 lines on a logarithmic visual acuity chart (averaged from nine subjects' data, with subject SYs prepatching visual acuity missing), but there had been no acuity improvement in the 6 months before the current training started. These 10 subjects formed the patch-treated (PT) group. The other 13 subjects (10 boys, 11.6 ± 0.9 years; Table 2) had never had patch treatment. They formed the never patch-treated (NPT) group. Each subject's vision was best corrected before training by the first and third authors who supervised the current training. The training frequency ranged from two to five daily sessions per week, which was more frequent during summer and winter breaks and varied among subjects. The training lasted 6 months on average, ranging from 3 to 10 months. In addition, we obtained the pre- and postpatching visual acuity data of 15 juvenile amblyopes 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; age-matched control group). The study adhered to the tenets of the Declaration of Helsinki and was approved by the ethnics committees of both hospitals. Informed consent was obtained from each subject's parents after an explanation of the nature and possible consequences of the study.

Apparatus

The stimuli were generated by computer (MatLab-based WinVis program; Neurometrics Institute, Oakland, CA) and presented by one of two 21-in. CRT monitors (model G520; Sony, Tokyo, Japan; or model FS201A, NESO, Shanghai, China) at 1024 × 768 pixels, 0.37 × 0.37 mm per pixel, 85-Hz frame rate, for grating acuity and contrast sensitivity testing and at 2048 × 1536 pixels, 0.19 × 0.19 mm per pixel, 60-Hz frame rate, for E acuity testing. The luminance of the monitors was linearized by an 8-bit look-up table for E acuity testing and by a 14-bit look-up table with a video attenuator for grating acuity and contrast sensitivity testing. The mean luminances of the Sony and the NESO monitors were 56.7 and 47.5 cd/m^2, respectively, with the 8-bit look-up table, and 27.0 and 22.0 cd/m^2, respectively, with the 14-bit look-up table. Viewing was monocular with the fellow eye covered by a black eye patch. A chin-and-head rest was used to stabilize the head. Experiments were run in a dimly lit room. In addition, a Randot Stereo Test (Stereo Optical Co., Inc., Chicago, IL) was used to test stereoacuity under normal room lighting.

Stimuli

Grating acuity was tested with a 1° × 1° sharp-edged, full-contrast, square-wave grating tilted ±45° from vertical (Fig. 1a).

Contrast sensitivity was measured with a Gabor stimulus (Gaussian windowed sinusoidal grating). The spatial frequencies of the Gabor were 1, 3/4, 1/2, 1/4, and 1/16 times the cutoff spatial frequency of the contrast sensitivity function predetermined with the grating acuity task. The SD was 0.9°, and the orientation was tilted ±45° from vertical. For both the grating acuity and contrast sensitivity tasks, the viewing distance was 8 m with the use of a front-surface mirror. Each contrast sensitivity function was fitted with a difference of Gaussian functions: $y = A_1e^{-(x/\sigma_1)^2} - A_2e^{-(x/\sigma_2)^2}$, where y is the contrast sensitivity, x is the spatial frequency of the grating, A_1 and A_2 are the amplitudes of the Gaussians, and σ_1 and σ_2 are the standard deviations of the Gaussians.

Single E acuity was tested with one tumbling E letter (a minimal-luminance black letter on a full-luminance white background; see Fig. 3a). Crowded E acuity was tested with a tumbling E letter target surrounded by four additional same-sized tumbling E letters on four sides at an edge-to-edge gap of one letter size (see Fig. 3b). The crowded E acuity was functionally similar to the conventional visual chart acuity, since both may be influenced by the crowding effect. The stroke and opening width of the E letters were one fifth of the letter height. The viewing distance was 5 m.

Procedures

Each subject practiced the grating acuity task (Fig. 1a) with the amblyopic eye for 40 to 60 1-hour sessions (mean = 52.5 ± 2.9 sessions for the PT

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

Subject	Age (y)	Sex	Type	Strabismus (Dist)	Eye: Refractive Error	Line Acuity	Patch Treatment Starting Age|Starting Acuity|Length (y)
LS	10.8	M	Aniso	None	R plano	6/6	6.8|6/40|4
					L +2.50/+0.75×94	6/10	
RXC	10.3	M	Aniso	None	R +5.50/+0.75×32	6/10	7.8|6/20|2.5
					L +1.50	6/4	
XC	16.0	M	Aniso	None	R −0.50/−0.12×12	6/4	13.5|6/24|2.5
					L +0.50/−0.25×145	$6/12^{-2}$	
SY	15.6	M	Aniso	None	R +2.75	6/15	13.6|unknown|2
					L −0.50	6/7.5	
MA	11.7	M	Ametr	None	R +6.50	6/15	4.0|6/40|7.7
					L +6.00	6/7.5	
XX	8.5	F	Strab	L 30^{Δ}EsoT	R +2.00	6/6	4.0|6/120|4.5
			Aniso		L +6.00	$6/12^{-1}$	
RX	8.1	M	Ametr	None	R +5.25/+0.50×70	$6/6^{-1}$	5.0|6/50|3.1
					L +6.00	6/10	
DR	8.5	F	Aniso	None	R +5.00	6/6	4.0|6/40|4.5
					L +6.00	$6/10^{-1}$	
CY	10.8	M	Aniso	None	R +0.50	6/6	7.6|6/20|3.2
					L +3.00	6/7.5	
LY	10.5	F	Aniso	None	R +2.00	6/6	7.9|6/30|2.6
					L +4.00	6/24	

Aniso, anisometropia; ametr, ametropia; strab, strabismus.

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

Subject	Age	Sex	Type	Strabismus (Dist)	Eye: Refractive Error	Line Acuity	Patch Treatment
MI	8.0	F	Aniso	None	R +5.00 L plano	$6/20^{-1}$ 6/6	None
ZC	15.2	M	Aniso	None	R −1.50 L +0.50/+2.00×85	6/6 6/15	None
ZH	13.4	M	Aniso	None	R plano L +3.00/−2.00×15	$6/5^{+}$ 6/37.5	None
BM	16.4	M	Aniso	None	R plano L +3.00/+1.50×135	6/5 6/60	None
MZ	8.0	M	Aniso	None	R +4.50/+ 1.00×65 L + 0.75	6/24 6/6	None
MF	9.0	M	Aniso	None	R −11.25/−0.50×80 L −0.75/−0.25×5	$6/24^{+1}$ 6/7.5	None
YC	8.5	M	Aniso	None	R +0.75 L +3.00/+1.50×80	6/5 $6/12^{+2}$	None
LX	11.4	F	Strab Aniso	R 60^{Δ}EsoT	R +6.00 L plano	$6/50^{-1}$ 6/6	None
YG	8.0	M	Ametr	None	R +1.50 L +1.00	$6/20^{+2}$ 6/7.5	None
TC	11.3	M	Aniso	None	R plano L +3.75/+0.75×90	6/4 $6/30^{-1}$	None
LXY	11.8	M	Ametr Astig	None	R plano L +2.00×80	$6/5^{-3}$ 6/12	None
MK	10.9	M	Strab Ametr	R 40^{Δ}EsoT	R +1.25×100 L 1.25/+0.50×60	$6/12^{+}$ $6/6^{-2}$	None
CT	17.5	F	Aniso	None	R plano L +3.00	6/6 6/20	None

Aniso, anisometropia; ametr, ametropia; strab, strabismus; astig, astigmatism.

group and 57.9 ± 1.6 sessions for the NPT group), 6 to 12 staircases per session, and one session on a given day. The single E acuity and stereoacuity were measured every 10 sessions throughout the training courses. Before and after training, the contrast sensitivity function and the single and crowded E acuities in both eyes and the stereoacuity were measured.

The grating acuity, contrast sensitivity, and E acuities were all measured with a one-interval, forced-choice staircase procedure. The stimulus was presented for an unlimited time until a key press by the subject. The subject's task was to judge the orientation of the grating (tilted left or right from vertical) or the tumbling E (left, right, up, or down). Auditory feedback was given on incorrect responses.

Each staircase followed the 3-down-1-up rule, which converged on a 79.4% correct level on the underlying psychometric function. Because of the young age of many subjects, each staircase was short and consisted of two preliminary reversals and four experimental reversals (~25–30 trials). The step size of the staircase was 0.05, 0.05, and 0.03 log units for grating acuity, contrast sensitivity, and E acuity measurements, respectively. The geometric mean of the experimental reversals was taken as the threshold.

RESULTS

Experiment 1: Perceptual Learning of Grating Acuity and Its Impact on Contrast Sensitivity Function, E Acuities, and Stereoacuity

Perceptual Learning of the Grating Acuity Task. The PT eyes had better pretraining grating acuity on average than did the NPT eyes (25.1 ± 1.5 cyc/deg vs. 17.5 ± 1.8 cyc/deg, $P = 0.005$, two-tailed parametric *t*-test). After training, the grating acuity of the PT eyes changed insignificantly, from 25.1 ± 1.5 to 24.5 ± 1.6 cyc/deg (mean percentage improvement [MPI] = −2.1% ± 3.6%; $P = 0.29$; one-tailed paired *t*-test, which was used to calculate the *P* values throughout the study, except where specified otherwise; Figs. 1b–d). This insignificant change indicated that the previous patching treatment had recovered grating acuity to its upper limit. However, the posttraining grating acuity of the PT eyes was still lower than that of the fellow eyes (31.7 ± 2.7 cyc/deg; $P = 0.018$).

Grating acuity improved significantly in the NPT eyes, from 17.5 ± 1.8 cyc/deg before training to 22.5 ± 1.9 cyc/deg after training (MPI = 37.4% ± 13.4%; $P = 0.008$; Figs. 1b, 1c, 1e). The observed improvement was mainly contributed by six NPT subjects whose grating acuity improved by 25% or more (MPI = 74.8% ± 19.9%; $P = 0.007$; Figs. 1b, 1e). The session-by-session training results of these subjects indicated varied learning speed, taking 10 to 40 sessions for learning to maximize (Fig. 1e). The MPI of the remaining seven subjects was 5.4% ± 3.7% ($P = 0.098$). Overall, the grating acuity improvement had a strong correlation with the pretraining acuity (Pearson $r = 0.83$, $P < 0.001$) in the NPT eyes. Those with poorer pretraining acuity tended to have more room for grating acuity improvement. The posttraining grating acuity of the NPT eyes was also lower than that of the fellow eyes (34.5 ± 2.6 cyc/deg; $P < 0.001$).

Contrast Sensitivity Changes after Grating Acuity Training. Contrast sensitivity functions (CSFs) were measured in both eyes of each subject, with Gabor stimuli before and after grating acuity training. The Gabor spatial frequencies were 1, 3/4, 1/2, 1/4, and 1/16 times the pre- or post-training cutoff spatial frequency measured in the previous grating acuity task. To compare the pre- and post-training CSF functions between the amblyopic and fellow eyes, the sensitivities at spatial frequencies of 1, 2, 4, 8, 16, and 32 cyc/deg were calculated on the basis of data fitting (the sensitivity was set to 0 beyond the cutoff frequency). In the PT eyes, the CSF functions of the amblyopic eyes were similar to those of the fellow eyes before grating acuity training ($F_{1,9} = 0.168$, $P = 0.691$, repeated-measures ANOVA) and were not significantly changed after grating acuity training ($F_{1,9} = 0.509$, $P = 0.494$; examples shown in Fig. 2a). In the NPT eyes, the CSF functions of the amblyopic eyes were significantly different from those of the fellow eyes before grating acuity training ($F_{1,12} = 9.16$, $P = 0.011$) and were changed marginally significantly after training

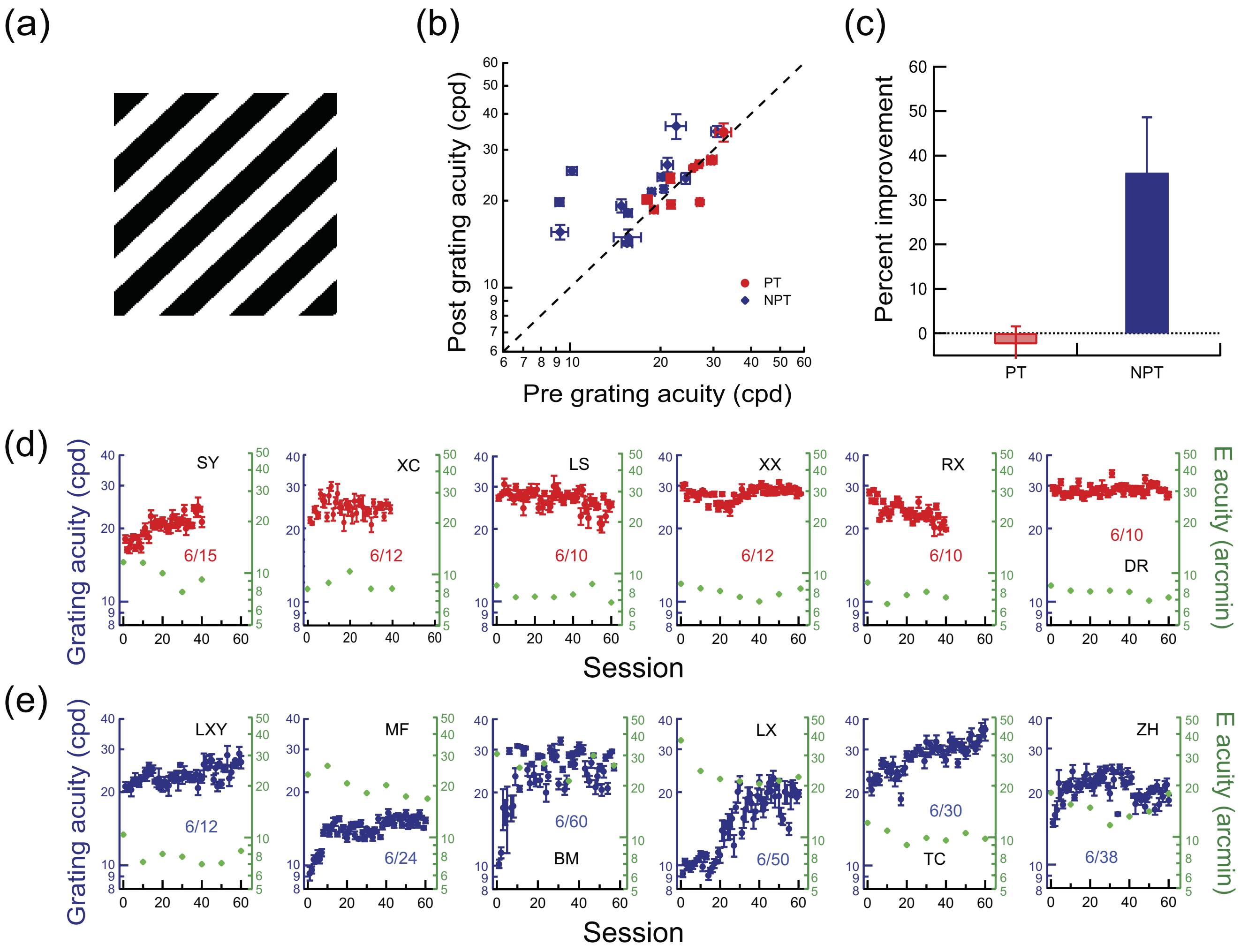

FIGURE 1. Perceptual learning of grating acuity. (**a**) Stimulus. (**b**) Pre- versus post-training grating acuity in NPT and PT eyes. Each point represents one subject's data. Learning is indicated by a point above the diagonal line. Error bars in this and all other figures indicate 1 SEM. (**c**) The MPI of grating acuity in PT and NPT eyes. (**d**) Session-by-session grating acuity data of six randomly selected PT subjects, as well as their single E acuity measured every 10 sessions through training (*green dots*; indicated by the *left* ordinate). The acuity value in each panel indicates pretraining Snellen acuity. (**e**) Session-by-session grating acuity data in the six NPT subjects who showed the most learning (≥25%), as well as their single E acuity measured every 10 sessions through training (*green dots*).

($F_{1,12} = 3.52$, $P = 0.085$; examples shown in Fig. 2b). The posttraining CSF functions of the amblyopic eyes were still significantly different from those of the fellow eyes ($F_{1,12} = 10.16$, $P = 0.008$). Among the six subjects in the NPT group who showed most improved grating acuity (Fig. 2b), two (MF and BM) showed better contrast sensitivity at lower spatial frequencies, consistent with one previous report.[11]

Single or Crowded E Acuity Changes after Grating Acuity Training. Many studies have shown that perceptual learning leads to improvement in visual acuity,[8–11,15,17,20–22] which would justify the use of perceptual learning for the treatment of amblyopia. We also found that PT and NPT eyes showed significantly improved single and crowded E acuities after grating acuity training ($F_{1,21} = 17.2$, $P < 0.001$; Figs. 3a, 3b). Specifically, the single E acuity improved from 9.7 ± 0.6 to 7.9 ± 0.6 arc min (0.09 ± 0.02 log units, $P < 0.001$) in the PT eyes and from 17.9 ± 2.5 to 12.9 ± 1.8 arc min (0.15 ± 0.02 log units, $P < 0.001$) in the NPT eyes (Fig. 3a). The crowded E acuity improved from 12.6 ± 1.5 to 10.6 ± 0.8 arc min (0.07 ± 0.03 log units, $P < 0.013$) in the PT eyes, and from 25.9 ± 6.1 to 21.2 ± 6.0 arc min (0.11 ± 0.02 log units, $P < 0.001$) in the NPT eyes (Fig. 3b). The crowded E acuity tended to be worse than the single E acuity across the groups and in both pre- and posttraining conditions ($F_{1,21} = 5.25$, $P < 0.032$), indicating a certain degree of crowding. In addition, the crowded E acuity improvement in the NPT eyes was comparable to the acuity improvement on the visual chart (0.16 ± 0.05 log units, $P = 0.016$; Figs. 3b, 3c, green symbols) in the age-matched control group (see the Methods section) after extended patching treatment (~3000 hours; $P = 0.38$, two-tailed parametric *t*-test). However, the impact of perceptual learning in general is much less significant than that of patching treatment starting at a young age. In the same PT eyes, the previous patching treatment, starting at a mean age of 6.7 years, improved visual acuity by 0.50 ± 0.09 log units.

Perceptual learning in general resulted in more E acuity improvement in the NPT eyes than in the PT eyes ($F_{1,21} = 5.20$, $P = 0.033$; Fig. 3c). However, within each group, the E acuity improvement was not significantly dependent on the severity of amblyopia. When the amblyopic eyes in each group were equally split into the better and worse subgroups according to their pretraining acuities (single E acuity: 8.3 ± 0.3 vs. 11.0 ± 0.7 arc min; crowded E acuity: 9.4 ± 0.4 vs. 15.9 ± 0.9 arc min), the single and crowded E acuity improvements in the

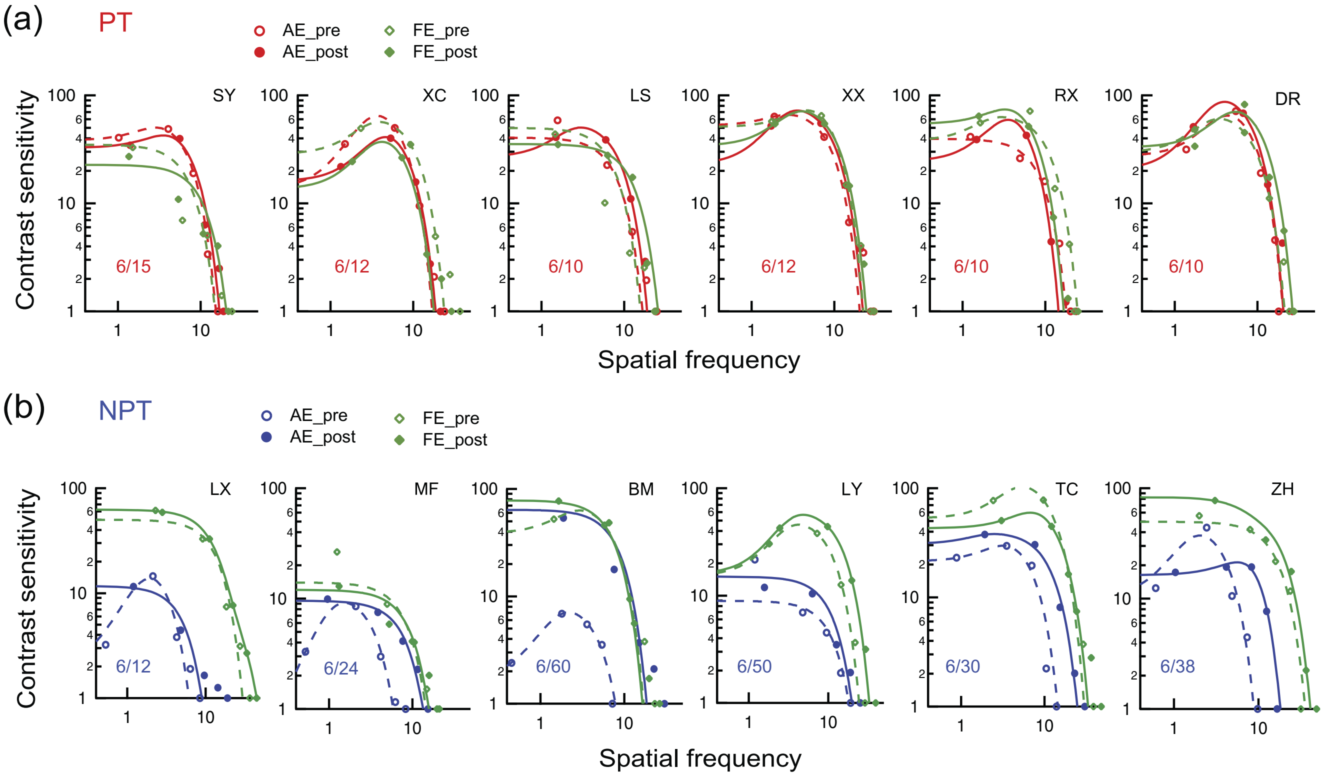

Figure 2. The impact of grating acuity learning on CSF functions in the trained amblyopic eyes and untrained fellow eyes. Only results from the same subjects in Figures 1d and 1e are shown. (**a**) PT eyes and (**b**) NPT eyes. The acuities shown indicate pretraining Snellen acuities. AE, amblyopic eye; FE, fellow eye.

better subgroup did not differ significantly from those in the worse subgroup in the PT eyes (single E improvement: 0.11 ± 0.04 vs. 0.08 ± 0.01 log units, $P = 0.50$; crowded E improvement: 0.04 ± 0.02 vs. 0.09 ± 0.05 log units, $P = 0.31$; two-tailed parametric *t*-test; $n = 5$ in each subgroup). Nor did the improvements differ between the better and the worse subgroups in the NPT eyes (pretraining single E acuity: 11.5 ± 0.4 vs. 25.1 ± 3.6 arc min; pretraining crowded E acuity: 12.1 ± 1.1 vs. 40.0 ± 10.3 arc min; single E improvement: 0.16 ± 0.04 vs. 0.15 ± 0.03 log units, $P = 0.75$; crowded E improvement: 0.10 ± 0.03 vs. 0.11 ± 0.04 log units, $P = 0.89$; two-tailed parametric *t*-test; $n = 6$ in each subgroup, excluding

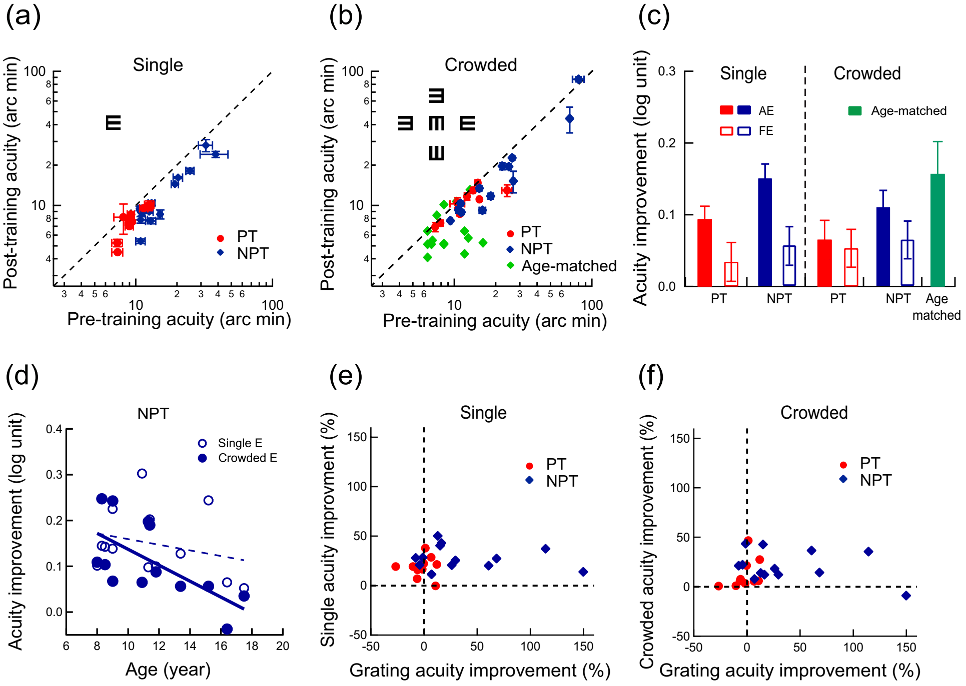

Figure 3. The impact of grating acuity training on single and crowded E acuities. (**a**) Single E acuities before and after grating acuity training in PT and NPT eyes. (**b**) Crowded E acuities before and after grating acuity training in PT and NPT eyes, as well as visual chart acuity before and after extended patching treatment in an age-matched control group. (**c**) Mean percentage of improvement of single and crowded E acuities in the trained PT and NPT amblyopic eyes and untrained fellow eyes. Data from 1 PT subject and 2 NPT subjects were excluded from analysis because, by mistake, the acuity in the fellow eyes was not best corrected during testing. The visual acuity data of the age-matched control group are also presented. (**d**) The correlations of age with single E acuity improvement fitted with a *dashed line* and with crowded E acuity improvement fitted with a *solid line*. (**e**) The correlation between single E acuity improvement and grating acuity improvement. (**f**) The correlation between crowded E acuity improvement and grating acuity improvement.

subject TC, who had a median pretraining single E acuity of 13.04 arc min and crowded E acuity of 18.22 arc min). These results imply that only eyes with mild amblyopia stand a good chance of regaining normal vision after perceptual learning.

When compared with the trained PT and NPT amblyopic eyes, the untrained fellow eyes showed similar gains in crowded E acuity ($F_{1,20}$ = 1.67, P = 0.21; Fig. 3c), suggesting that some general learning may be responsible for the visual acuity improvement. The trained amblyopic eyes showed more gains in single E acuity than did the fellow eyes ($F_{1,20}$ = 13.17, P = 0.002), probably because the amblyopic eyes practiced single E acuity during grating acuity training (every 10 sessions).

We found that the E acuities tended to be improved more at a younger age in the NPT eyes (Fig. 3d). This trend was insignificant between age and single E acuity improvement ($r = -0.27$, P = 0.38), but was significant between age and crowded E acuity improvement ($r = -0.65$, P = 0.017). No such trend was evident in the PT eyes. However, we could not find a direct link between E acuity improvement and grating acuity improvement. Both single and crowded E acuity improvements did not correlate with grating acuity improvement (r = 0.07 and −0.01, respectively; Figs. 3e, 3f).

Stereoacuity Changes after Grating Acuity Training. The stereoacuity was improved by 17.2% ± 13.2% (P = 0.11) in the PT eyes and 48.0% ± 10.7% ($P < 0.001$) in the NPT eyes (Figs. 4a, 4b). The improvement was contributed by three of the nine PT subjects (33.3%) and 9 of the 11 NPT subjects (81.8%). Among them, one PT and one NPT subject who failed the initial stereoacuity test (marked by a lowercase f in Fig. 4a) showed restored stereoacuity up to 50 arc sec (Fig. 4a). For the convenience of data analysis, the stereoacuity for those who failed the Randot Stereo Test was set at 500 arc sec, the lowest score.

Like E acuities, the stereoacuity improvement observed in the three PT and nine NPT subjects did not correlate with grating acuity improvement in the amblyopic eyes ($r = -0.51$, P = 0.09; Fig. 4c). It did not correlate with single E acuity improvement (r = 0.47, P = 0.12; Fig. 4d) and crowded E acuity improvement (r = 0.15, P = 0.64; Fig. 4e) in the amblyopic eyes nor with the improvement in interocular acuity difference (r = 0.46, P = 0.14; Fig. 4f).

Experiment 2: Further Direct Perceptual Learning of Single and Crowded E Acuities

In the previous grating acuity training, the stimuli were 45° and 135° tilted square-wave gratings. These stimuli were made of oblique bars that were different from the horizontal and vertical bars of the tumbling Es. Moreover, the tumbling Es were often much smaller than the 1° × 1° gratings used in grating acuity training (e.g., the size of a 6/12 tumbling E = 10 × 10 arc min), so that the test results were potentially influenced by spatial uncertainty, especially at very small stimulus sizes. Because the transfer of perceptual learning is proportional to the similarity between the trained and tested tasks, these difference between the grating stimuli and tumbling Es might have contributed to the relatively small improvements in E acuities in the previous experiment.

To achieve the best training efficiency, we continued to train the subjects directly with the single and crowded E acuity tasks. We were able to call back half the subjects in each group (five PTs and seven NPTs) and had them practice the single and crowded E acuity tasks in alternating blocks of trials (staircases) for 8 to 10 1-hour daily sessions.

After this additional training, the single and crowded E acuities in the five PT eyes were nearly unchanged (single E: 0.02 ± 0.03 log units, P = 0.29 ; Figs. 5a, 5c; crowded E: 0.02 ± 0.02 log units, P = 0.18; Figs. 5b, 5d). The overall improvement after grating acuity and E acuity training was 0.14 log units for the single E acuity (Fig. 5b) and 0.10 log units for the crowded E acuity (Fig 5d), equivalent to 1.4 and 1 lines on a visual acuity chart, respectively. In contrast, the single and crowded E acuities in the seven NPT eyes (Figs. 5a, 5c) improved significantly (0.04 ± 0.03 log units, P = 0.040, and 0.05 ± 0.01 log units, P = 0.002, respectively; Figs. 5b, 5d). These improvements added to the initial acuity improvements after grating training, so that the combined training improved single E acuity by 0.22 log units or 2.2 lines (Fig. 5b) and crowded E acuity by 0.18 log units or 1.8 lines (Fig. 5d).

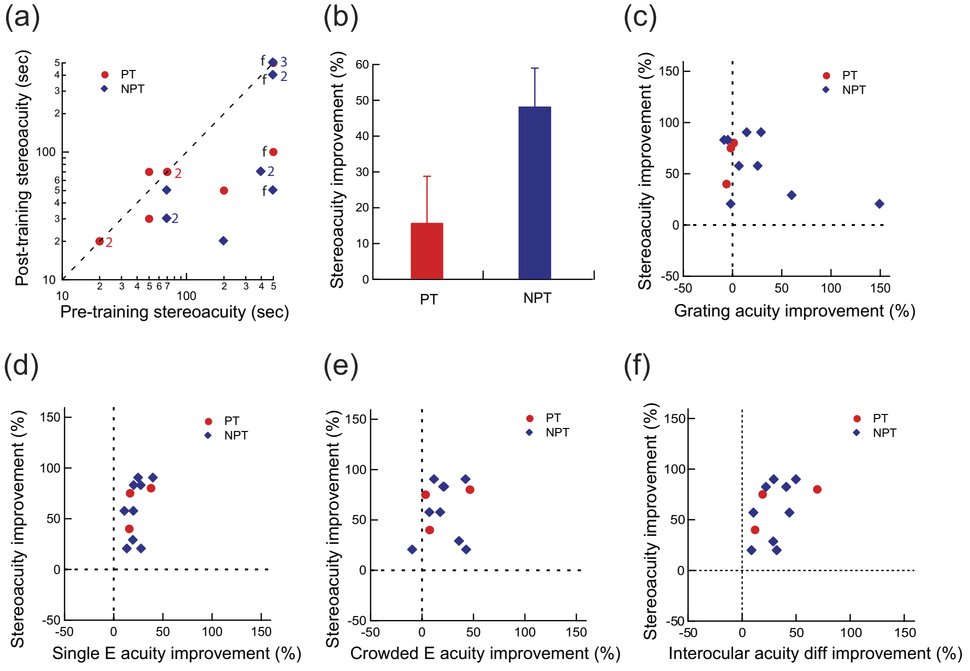

FIGURE 4. The impact of grating acuity training on stereoacuity. **(a)** Stereoacuity before and after grating acuity training. One PT subject and 2 NPT subjects whose fellow eyes were not properly corrected were excluded from the analysis. **(b)** MPI of stereoacuity in PT and NPT eyes. **(c–f)** The improvement of stereoacuity against the improvement of grating acuity, single E acuity, crowded E acuity, and interocular difference in visual acuity.

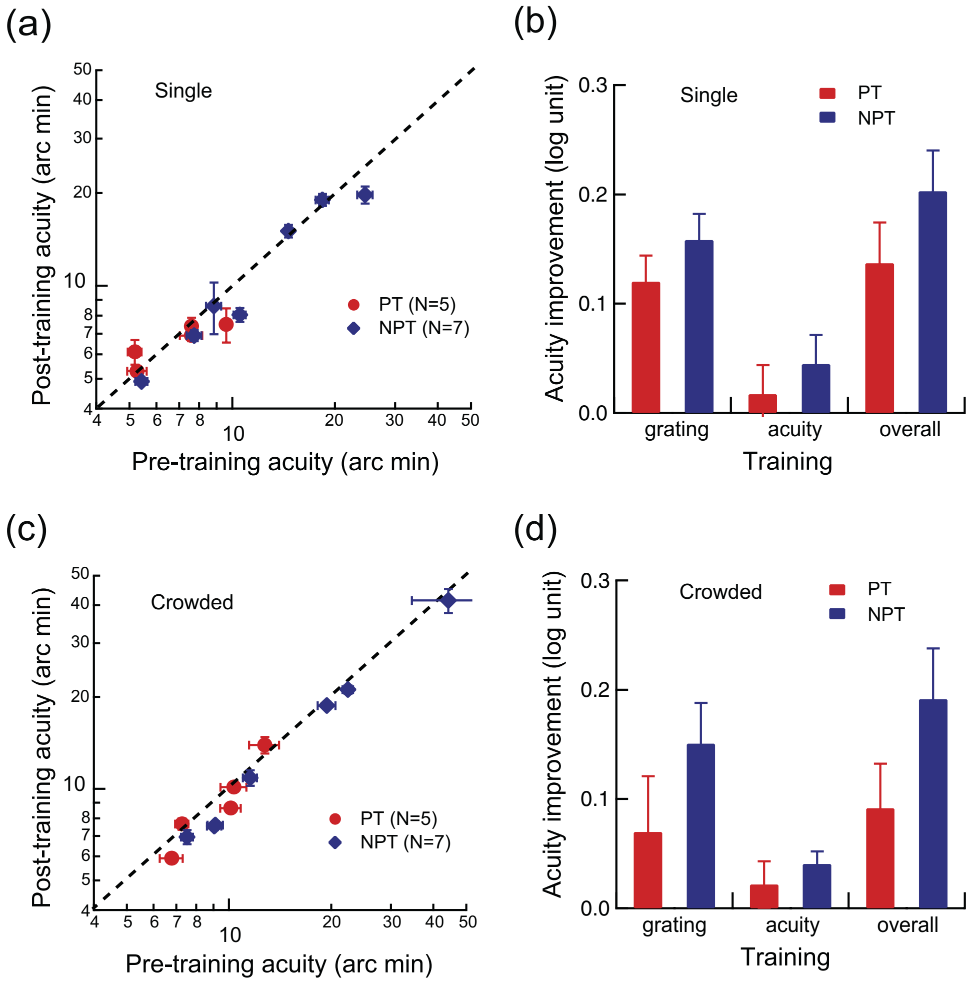

FIGURE 5. The impact of direct E acuity training after earlier grating acuity training. (**a**) Single E acuity before and after direct E acuity training. (**b**) Single E acuity improvement after earlier grating training, subsequent E acuity training, and the overall improvement. (**c**) Crowded E acuities before and after direct E acuity training. (**d**) Crowded E acuity improvement after earlier grating training, subsequent E acuity training and the overall improvement.

Follow-up Measurements

We remeasured the visual acuities in seven PT eyes and eight NPT eyes 1 year after training (mean, 12.4 ± 0.7 months). Among them, some received grating acuity training only and some received combined grating acuity and E acuity training. The visual acuities of the PT eyes regressed by 0.04 ± 0.04 log units ($P = 0.16$). The visual acuities of the NPT eyes regressed by 0.01 ± 0.03 log units ($P = 0.39$). These results indicate that training-induced visual acuity improvements persisted for nearly 1 year after the training had stopped.

DISCUSSION

In this study, grating acuity training had a small but significant therapeutic impact on the visual acuities of PT and NPT eyes and the impact was slightly larger if the grating acuity training is combined with direct E acuity training. Because of the relatively small sample size, our results are better regarded as preliminary, and the therapeutic value of perceptual learning on adolescent amblyopia should be further evaluated in larger sample sizes and by meta-analyses of results of multiple studies.

The combined grating acuity and E acuity training improved single and crowded E acuities by 0.14 and 0.10 log units in the PT eyes. This effect, although small, may bear clinical significance when added to previous visual acuity gains after patching, especially with the consideration that these PT eyes are no longer responsive to further patching treatment. The effect of combined training is larger in the NPT eyes (0.22 versus 0.18 log units), which is comparable to the outcomes of previous perceptual-learning studies. Many studies have shown visual acuity improvements in the neighborhood of 0.2 to 0.3 log units.[8–11,17,20] A few others showed either larger[15,21,22] or smaller[14,23] effects. The visual acuity improvements we obtained from the PT and NPT eyes are relatively small in magnitude and do not seem to correlate with pretraining acuities. This result suggests that perceptual learning may be most beneficial for treating mild amblyopia in juveniles and adults.

In our results, grating acuity learning was evident in only some of the NPT eyes but not in the PT eyes (Fig. 1), and that grating acuity improvement did not predict E acuity improvement (Fig. 3). Grating acuity trained the contrast sensitivity to the cutoff spatial frequency, which was higher than 8 cyc/deg and in many cases ~20 to 30 cyc/deg in the PT and NPT eyes before training (Fig. 1b). On the other hand, it is possible that an observer can make correct judgment of the gap orientation of near-acuity tumbling Es on the basis of frequency components that are much lower than the cutoff frequency. For example, the subject may use the low-order geometric moment information, such as the skewness of the light distribution of the tumbling E images (i.e., which side of the image is lighter) to judge gap orientation.[24] Because different visual processes may have been involved, grating acuity learning (as well as many other types of perceptual learning) in theory should have minimal transfer to E acuity, because of the task specificity in perceptual learning.[25] Alternatively, perceptual learning could improve the overall responsiveness of the amblyopic visual system to recover visual acuity indirectly. However, this potential improvement in responsiveness is probably small enough that only mild amblyopia could benefit from it for full vision recovery.

Because amblyopia is characterized by visual acuity loss that has no detectable structural or pathologic cause, it would be ideal to train visual acuity directly to gain the maximum therapeutic impact on amblyopic vision, rather than to rely on the often partial transfer of perceptual learning of other visual tasks. As mentioned, the commonly observed task specificity often makes the transfer of perceptual learning difficult or even unlikely. However, no such direct visual acuity training in amblyopic eyes has been performed in previous studies. Our second experiment trained E acuities directly, but the impact was not straightforward because of the earlier grating acuity training. A new study with exclusive visual acuity training is necessary to clarify this issue.

The small visual acuity gain from perceptual training may result at least partially from a general learning process, as the crowded E acuity was not significantly more improved in the trained NPT amblyopic eyes than in the untrained fellow eyes. In addition, the training-improved responsiveness of the amblyopic visual system may have contributed, which may affect different acuity tasks in different individuals randomly, as no correlation of performance improvement was evident among these tasks (Figs. 3, 4).

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