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 pro-

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	$6/20^{-1}$	None
					L plano	6/6	
ZC	15.2	M	Aniso	None	R −1.50	6/6	None
					L +0.50/+2.00×85	6/15	
ZH	13.4	M	Aniso	None	R plano	$6/5^{+}$	None
					L +3.00/−2.00×15	6/37.5	

BM1477.6(M)-3477.8(Aniso)-5166.8(None)-7548(R)-264.5(plano)-10463.3(6/5)]TJ/F41ne

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.

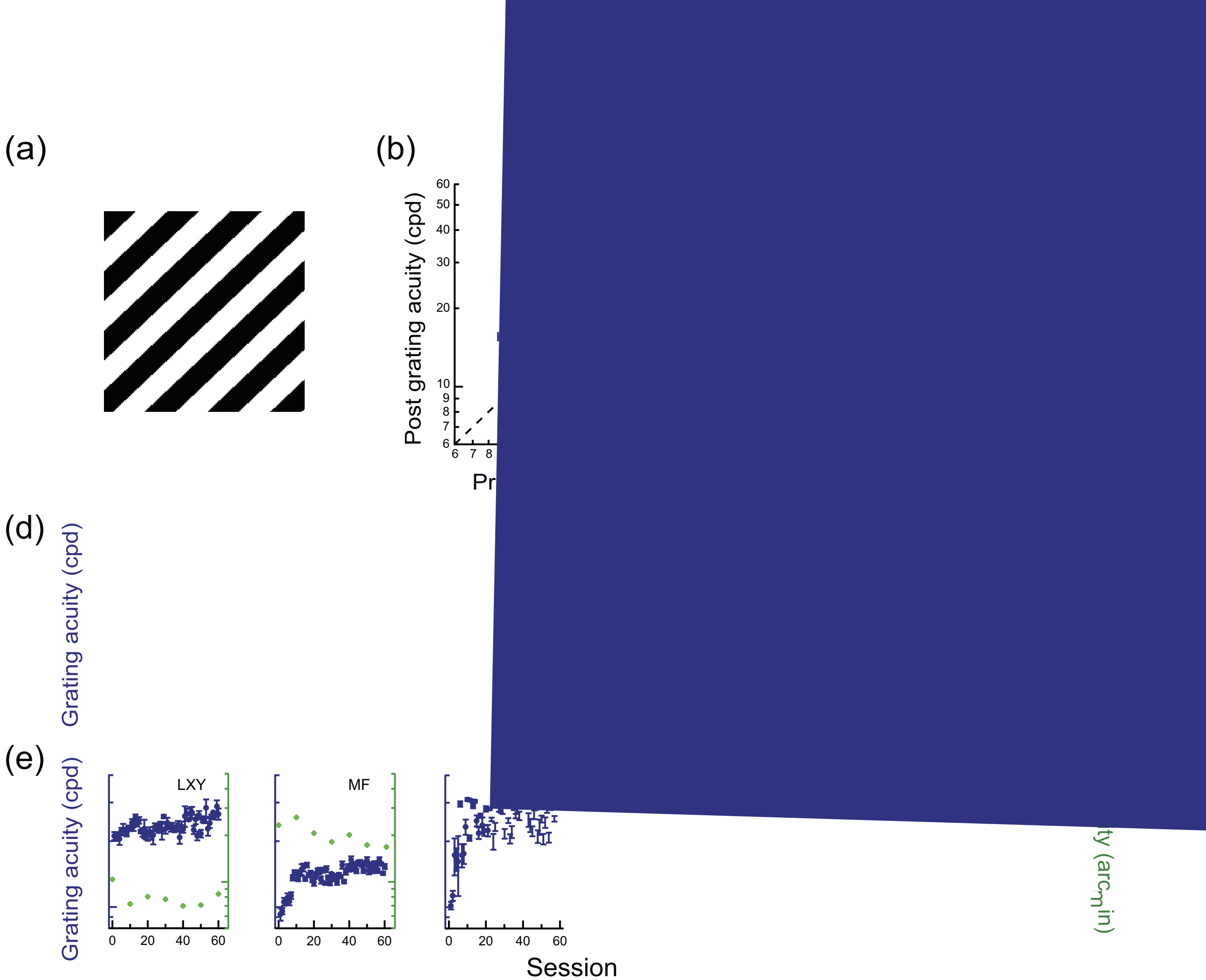
Results

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 post-training 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



($F_{1,12}$ = 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

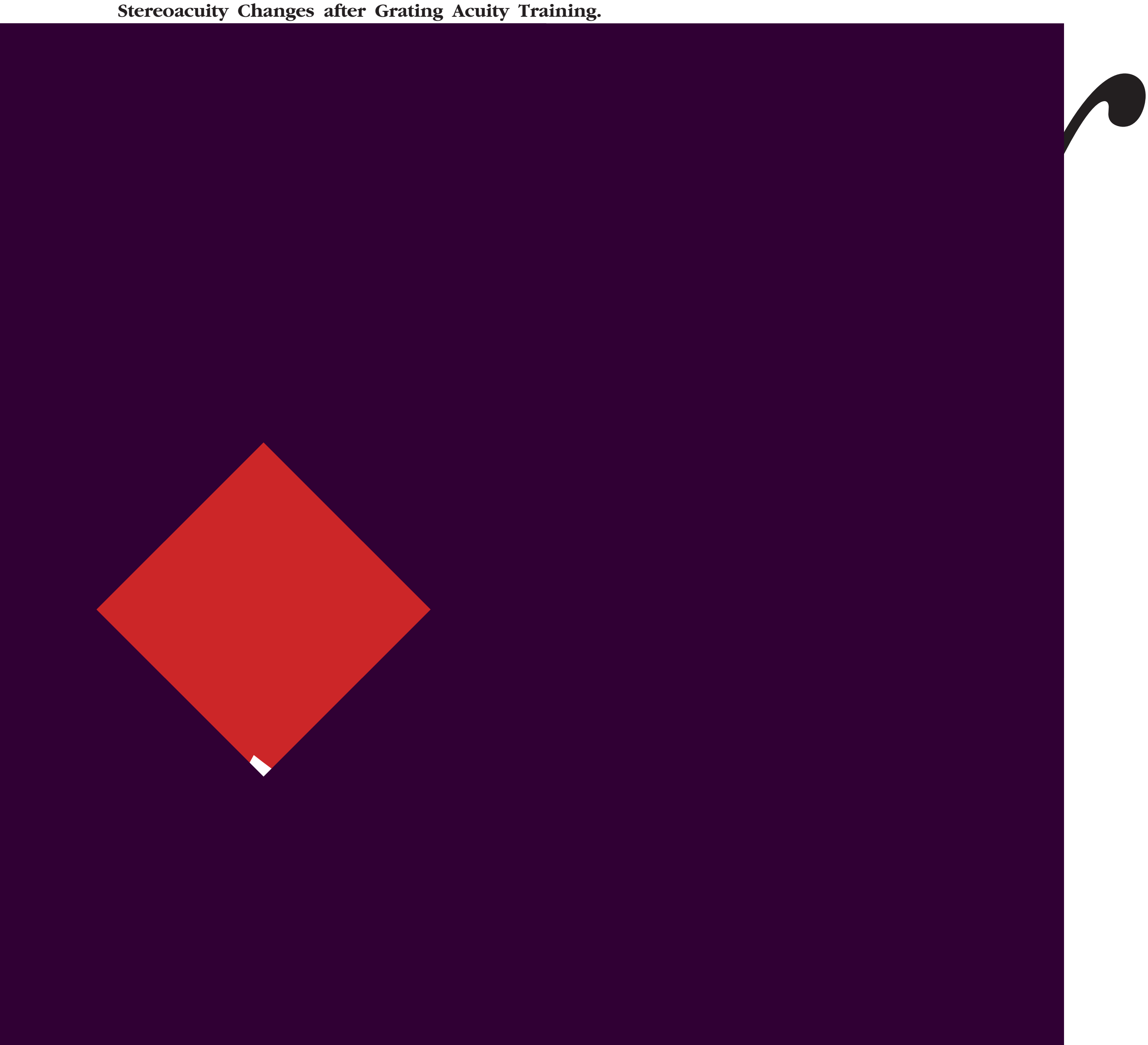

6
4
1

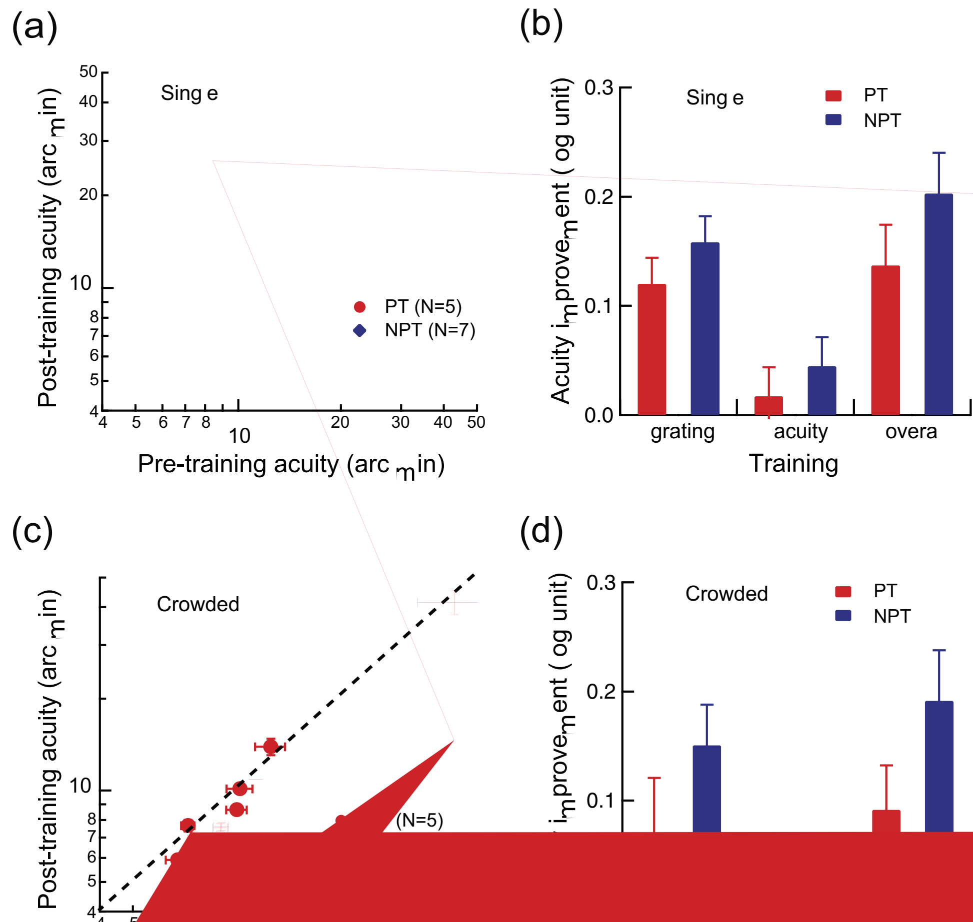
subject TC, who had a median pretraining single E acuity of 13.04 arc min and crowded E acuity of 18.22 arc min). These results imply that only eyes with mild amblyopia stand a good chance of regaining normal vision after perceptual learning.

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.





Follow-up Measurements

We remeasured the visual ac
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NPT eyes (0.22 versus 0.18

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veniles and adults.
g was evident in only
PT eyes (Fig. 1), and that
ot predict E acuity improve-
ained the contrast sensitivity to
y, which was higher than 8 cyc/deg
to 30 cyc/deg in the PT and NPT eyes
1b). On the other hand, it is possible that
make correct judgment of the gap orientation
y tumbling Es on the basis of frequency compo-
at are much lower than the cutoff frequency. For
ple, the subject may use the low-order geometric mo-
ent 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 am-

blyopic 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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