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Perceptual learning improves contrast sensitivity and visual acuity in adults with anisometropic amblyopia

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Abstract

To evaluate the effects of perceptual learning on contrast-sensitivity function and visual acuity in adult observers with amblyopia, 23 anisometropic amblyopes with a mean age of 19.3 years were recruited and divided into three groups. Subjects in Group I were trained in grating detection in the amblyopic eye near pre-training cut-off spatial frequency. Group II received a training regimen of repeated contrast-sensitivity function measurements in the amblyopic eye. Group III received no training. We found that training substantially improved visual acuity and contrast-sensitivity functions in the amblyopic eyes of all the observers in Groups I and II, although no significant performance improvement was observed in Group III. For observers in Group I, performance improvements in the amblyopic eyes were broadly tuned in spatial frequency and generalized to the fellow eyes. The latter result was not found in Group II. In a few cases tested, improvements in visual acuity following training showed about 90% retention for at least 1 year. We concluded that the visual system of adult amblyopes might still retain substantial plasticity. Perceptual learning shows potential as a clinical tool for treating child and adult amblyopia.

Keywords: Amblyopia; Contrast detection; Contrast sensitivity; Perceptual learning; Visual acuity

1. Introduction

Amblyopia is a developmental disorder of spatial vision in the absence of any detectable structural or pathologic abnormalities that cannot be corrected by refractive means (Ciuffreda, Levi, & Selenow, 1991; McKee, Levi, & Movshon, 2003). It has been widely accepted that amblyopia develops as a result of abnormal visual experience during a so-called "sensitive period", although the neural mechanisms of amblyopia are still not entirely clear (Daw, 1998; Kiorpes & McKee, 1999). In clinical practice, only infant and young child amblyopes are treated, while older children (>8 years) and adults are mostly left untreated because it is widely believed that the various therapies are no longer effective for them (Campos, 1995; Flynn, Schiffman, Feuer, & Corona, 1998; Greenwald & Parks, 1999; Loudon, Polling, & Simonsz, 2002; Polat, Ma-Naim, Belkin, & Sagi, 2004).

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Can amblyopia in adults and older children be effectively treated? The clinical practice of not treating adult and older child amblyopes is based largely on the classical notion that neural plasticity in the visual system diminishes with age after the sensitive period (Berardi, Pizzorusso, Ratto, & Maffei, 2003). For amblyopes, once they have passed the sensitive period for spatial vision (usually before 6–8 years of age), the visual system is fully (though erroneously) developed and therefore no longer subject to therapeutic modifications. On the other hand, several studies reported marked visual acuity improvements in adult amblyopes (Birnbaum, Koslowe, & Sanet, 1977; Kupfer, 1957; Polat et al., 2004; Simmers & Gray, 1999; Wick, Wingard, Cotter, & Scheiman, 1992). In addition, a large number of recent studies have demonstrated remarkable plasticity in the adult visual system (Chino, 1995; Dragoi, Sharma, & Sur, 2000; Levine, 1988; Pizzorusso, Medini, Berardi, Chierzi, & Fawcett, 2002; Safran & Landis, 1996). Of particular interests are studies that demonstrated large performance improvements in normal adult observers following training or practice in various spatial vision tasks such as visual detection and spatial localization (Fahle, 1997; Shiu & Pashler, 1992), motion (Zanker, 1999), and vernier acuity (Fahle & Edelman, 1993). Often quite specific to some "low level" attributes of the stimuli, such as retinal location, orientation, and motion direction, these improvements are attributed to perceptual learning, reflecting neural plasticity in the adult visual system (Fahle, 2004; Gilbert, Sigman, & Crist, 2001).

The value of perceptual learning as a potential therapy for amblyopia has been evaluated since the pioneering work of Campbell, Hess, Watson, and Banks (1978). The results have been somewhat mixed (Ciuffreda, Goldner, & Connelly, 1980; Mehdorn, Mattheus, Schuppe, Klein, & Kommerell, 1981; Schor & Wick, 1983; Terrell, 1981). However, unlike most of the studies on perceptual learning in the normal population, these studies typically used high contrast stimuli and relatively short training periods (e.g., 7 min) that were pre-determined irrespective of the progress and subject's ophthalmological characteristics (history, type, and degree of amblyopia, for example). We now understand from the recent literature that significant performance improvements in perceptual learning may require thousands of practice trials. Two recent studies (Levi & Polat, 1996; Levi, Polat, & Hu, 1997) using intensive training found that repetitive practice did lead to substantial improvements in vernier acuity in the amblyopic eyes of adult amblyopes. The authors also found that the improvement in vernier acuity of two novice observers was accompanied by a commensurate improvement in Snellen acuity. In a latest publication, Polat et al. (2004) demonstrated that perceptual learning could significantly (about 2-fold) improve contrast sensitivity and visual acuity in patients with amblyopia. Focusing on the lack of functional spatial interactions in amblyopes, Polat and colleagues used training procedures that emphasized lateral interactions. In this study, we used simpler basic visual stimuli (sine-wave gratings) to evaluate effects of perceptual learning on visual acuity and contrast-sensitivity functions (CSF) of amblyopic eyes in young adults and older children. The use of simpler visual stimuli might lead to a better understanding of the basis of neural plasticity in amblyopia.

Both reduction of visual acuity and contrast sensitivity are hallmarks of amblyopia (Asper, Crewther, & Crewther, 2000; Kiorpes, Tang, & Movshon, 1999). Whereas visual acuity reflects limits of spatial resolution, contrast-sensitivity function assesses spatial vision over a full range of spatial frequencies and is widely believed to reflect the overall gain of the visual system to visual input in different spatial frequencies. Models with CSF as the front-end spatial frequency filter can account for human performance in a wide range of visual tasks, including letter identification (Chung, Legge, & Tjan, 2002; Chung, Levi, Legge, & Tjan, 2002) and face recognition (Kornowski & Petersik, 2003). Here, we assessed visual acuity and contrast-sensitivity functions of the amblyopic and fellow eyes of anisometropic amblyopes prior to and after intensive training in contrast detection either at a single spatial frequency near each individual's cut-off frequency on the CSF or over a range of spatial frequencies (i.e., repeated measures of CSF). We focused on amblyopes of anisometropic nature because they are the pre-dominant group. Other types of amblyopia, e.g., strabismic amblyopia, may be rather different (Barrett, Bradley, & McGraw, 2004; Bonneh, Sagi, & Polat, 2004; Hess & Pointer, 1985; Levi & Klein, 1982; Polat, Bonneh, Ma-Naim, Belkin, & Sagi, 2005). Our aim was to evaluate whether these training methods can improve visual functions of amblyopes and to compare their efficacies.

2. Materials and methods

2.1. Subjects

Twenty-three naive observers with natural-occurring amblyopia and written informed consent completed this study. The age of the observers ranged from 14 to 27 years, with a mean of 19.3 years and a standard deviation of 3.7 years. All observers (23) have anisometropic amblyopia. Two out of 23 observers (Subjects #8 and #17 in Group II) are bilateral. Detailed characteristics of these observers, including amblyopia type, optical correction, and corrected visual acuity, were performed by an ophthalmologist (the fourth author). The optical correction and corrected visual acuity of the observers are listed in Table 1 along with their age, gender, and training orientation and spatial frequency. All observers

Table 1
Observer characteristics

Group	S	Sex	Age	Eye[b]	Correction	Acuity[a]	Orientation	Training SF (c/deg)
I	1	F	16	AE	−4.00DS/−1.50DC × 180	3.0	90°	10
				FE	−2.00DS	0.9		
	2	M	15	AE	+2.00DS	23.8	90°	3
				FE	Plano	0.7		
	3	M	21	AE	+2.00DS	4.7	0°	12
				FE	Plano	0.7		
	4	M	22	AE	+1.50DS	3.8	90°	10
				FE	Plano	0.9		
	5	F	16	AE	+3.50DS	7.1	90°	9.1
				FE	−1.00DS	1.2		
	6	F	17	AE	+7.00DS/+1.50 × 90	7.1	90°	3
				FE	+1.25DS	0.7		
	7	F	21	AE	+7.50DS	6.0	0°	4
				FE	Plano	0.6		
II	8	F	24	AE	+3.00DS	2.4	90°	
				FE	−1.00DS	1.9		
	9	M	20	AE	+2.75DS/+1.75 × 0	3.8	90°	
				FE	Plano	0.9		
	10	M	20	AE	+2.00DS/+1.00DC × 90	1.9	90°	
				FE	−0.50DS	1.4		
	11	M	19	AE	+5.50DS/+0.50DC × 90	3.8	0°	
				FE	+1.50DS	0.9		
	12	F	16	AE	+3.00DS	5.8	0°	
				FE	Plano	0.6		
	13	M	25	AE	−13.00DS/−2.00DC × 10	5.3	0°	
				FE	Plano	0.9		
	14	M	14	AE	+1.25DS/1.75DC × 85	3.8	90°	
				FE	Plano	0.9		
	15	M	20	AE	+5.00DS	5.3	90°	
				FE	−1.75DS	0.9		
	16	F	22	AE	+8.75DS	3.8	90°	
				FE	+6.00DS	0.6		
	17	F	25	AE	Plano	1.9	90°	
				FE	Plano	1.9		
III	18	F	20	AE	+4.50DS	5.3	90°	
				FE	−3.00DS	0.8		
	19	F	14	AE	−1.75DS/−0.37DC × 90	7.5	90°	
				FE	+3.00DS/0.50DC × 180	0.9		
	20	M	18	AE	+7.50DS/+2.00DC × 90	7.5	90°	
				FE	−2.00DS	0.6		
	21	M	15	AE	+1.25DS/1.75DC × 85	3.7	0°	
				FE	Plano	0.9		
	22	F	18	AE	+2.00DS	4.2	90°	
				FE	Plano	0.9		
	23	F	27	AE	−3.50DS	2.3	90°	
				FE	−2.50DS	1.4		

[a] MAR, minimum angle of resolution; visual acuity was tested with the Chinese. Tumbling E Chart and defined as the score associated with 75% correct judgments. Different tester performed post-training assessment.

[b] AE, amblyopic eye; FE, fellow eye.

wore their corrective lenses during the experiment. Subjects with astigmatism were assigned gratings oriented either in or perpendicular to their astigmatic direction. Due to the small number of subjects with astigmatism, the assignment was only roughly balanced.

Observers were randomly assigned into three treatment groups. There were 7 (18.3 ± 2.9 years), 10 (20.5 ± 3.7 years), and 6 observers (18.7 ± 4.6 years) in Group I, II, and III, respectively.

2.2. Apparatus and stimuli

The experiments were controlled by a Power Macintosh G3 computer running Matlab programs based on version 2.44 of PsychToolBox (Brainard, 1997). The stimuli were presented on a Sony G220 color monitor driven by the internal graphics card (ATI mach 64_3DU) with a spatial resolution of 640 × 480 pixels, a refresh rate of 85 Hz, and a mean luminance of

27 cd/m^2. Using a special circuit that combines two 8-bit output channels of the graphics card, the display system can produce gray levels with 14 bits gray-level resolution (Li, Lu, Xu, Jin, & Zhou, 2003). All displays were viewed monocularly in fovea at a distance of 2.28 m in a dimly lit room. An opaque eye patch was used to cover the eye that was not being tested in a given condition.

The signal stimuli were vertical or horizontal 3.06×3.06 deg sinusoidal luminance modulations ("sine-wave gratings") presented in the center of the display. To minimize edge effects, a 0.5 deg half-Gaussian ramp was added to each side of the stimulus to blend the stimuli to the background. Depending on the experimental condition, sine-wave gratings of different spatial frequencies were used.

2.3. Experimental design

The experiment consisted of three consecutive phases: pre-training assessment, training, and post-training reassessment. In pre- and post-training assessments, CSF and visual acuity for both eyes were measured for all the observers. The pre-training assessment took a total of 1.5 h, split across 2 days. It was followed by on average 12.7 sessions (range from 9 to 19) of training and 2 days of post-training assessment. Training was terminated after first three consecutive sessions with similar performance. The order of testing in the pre-training and the post-training assessments was counterbalanced for each observer. For some observers, retention of the improvements in CSF and visual acuity was also assessed several times after the initial post-training.

Contrast sensitivity (CS), defined as 1/threshold, was calculated from sine-wave grating detection thresholds at spatial frequencies 0.5, 1, 2, 4, 8, 10, 12, 14, and 16 c/deg for the amblyopic eye, and 0.5, 1, 2, 4, 8, 12, and 16 c/deg for the fellow eye. The two additional spatial frequencies (10 and 14 c/deg) were used in the amplyopic eye to obtain more detailed measures of the CSF at high spatial frequencies. For a given observer, independent of group assignment, the orientation of the signal sine-wave gratings was either 0 or 90 deg (listed in Table 1), but consistent across spatial frequencies and eyes. Visual acuity was assessed with the Chinese Tumbling E Chart (Mou, 1966)[1] and defined as the score associated with 75% correct judgments.

Observers were only trained in their amblyopic eyes (or the more severe one for two bilateral amblyopes). Different training protocols were assigned to the three groups of observers. Observers in Group I were trained in a sine-wave grating detection task near each individual's cut-off spatial frequency (listed in Table 1), defined as the spatial frequency at which the estimated contrast threshold from pre-training CSF measurements was 0.50. Observers in Group II practiced the CSF task over the entire range of spatial frequencies tested in the amblyopic eyes over many days. Observers in Group III received no training. For Group III, the two sets of visual acuity and CSF assessments were separated by at least 10 days.

2.4. Procedure

Each trial started with a 259 ms fixation cross in the center of the display. This was followed by two intervals of 118 ms separated by a 500 ms inter-stimulus interval (ISI) and demarcated by a brief tone in the beginning of each interval. The signal sine-wave grating appeared in only one of the intervals for 118 ms. The observer was asked to indicate the interval that contained the signal by pressing one of two keys on the computer keyboard. During training, a brief tone followed each correct response; during pre- and post-training assessments, a brief tone followed each response regardless of its accuracy. The response also initiated the next trial.

Contrast thresholds at 79.3% correct in the two-interval, forced-choice, sine-wave grating detection task were estimated using an adaptive staircase method. The 3/1 staircase method, expected to asymptote at 79.3% correct, decreased signal contrast by 10% (multiplied the previous value by 0.9) after every three consecutive correct responses and increased signal contrast by 10% after every incorrect response. In assessing CSF, threshold for detecting a sine-wave grating at a particular spatial frequency was estimated from 100 trials. A reversal results when the staircase changes its direction (changing from increasing to decreasing contrast or vice versa). Following the standard practice in psychophysics, we excluded the first three (if the number of total reversals was odd) or four (if even) reversals. The average contrast of the remaining reversals was taken as the contrast threshold for detecting grating of a certain spatial frequency. The starting contrast for each staircase was set close to the expected threshold based on results from pilot testing. CSF for each eye was measured in separate sessions. All the staircases for all the spatial frequencies on a given CSF were interleaved. Seven hundred trials and about 35 min were used to measure a CSF in the fellow eye; 900 trials and about 45 min were used in the amblyopic eye.

For Group I, each training session consisted of nine 120-trial blocks, often run in immediate succession. For Group II, each training session consisted of 900 trials, 100 trials per spatial frequency. Observers were given instruction trials before data collection.

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[1] The chart we used was developed by Mou (1966). It has been accepted by Ministry of Health, PR China, as national standard (GB11533-1989). Due to language differences, it only uses "E" in different orientations instead of multiple letters.

2.5. Statistical analysis and model fit

Data from the two orientations were compared using between-subject analysis of variance (ANOVA). Pre-training and post-training CSF's as well as the magnitude of CSF improvements in the trained and untrained eyes were compared using within-subject ANOVA. The average CSF's of each group prior to and after training was fit with a Difference of Gaussian (DOG) model that allowed us to estimate the maximum sensitivities and cut-off spatial frequencies (Rohaly & Buchsbaum, 1988, 1989). For Group I, contrast sensitivities at the trained spatial frequency in the beginning and the end of training were compared using within-subject t tests. For all groups, pre- and post-training visual acuity was compared using within-subject t tests. The magnitudes of contrast sensitivity and visual acuity improvements among the three groups were compared using between-subject ANOVA.

For each observer, the magnitude of improvement for each measure (e.g., contrast sensitivity, average CSF's, and visual acuity) was calculated as:

$$I_{\text{individual}} = 20\log_{10}\frac{\text{post-training Measure}}{\text{pre-training Measure}}\ \text{dB}. \qquad (1)$$

We report I group $= \sum I_{\text{individual}}/N$ (N is the total number of individuals) for each group as the average magnitude of improvements for that group. We then convert the average dB improvement to percent improvement:

$$P_{\text{group}} = (10^{I_{\text{group}/20}} - 1) \times 100\%. \qquad (2)$$

3. Results

Statistical analysis revealed no significant differences between pre-training CSFs of 0 deg and 90 deg in either (trained or untrained) eye for all three groups ($F(1,45) = 0.48$, $p > 0.10$ and $F(1,40) = 3.47$, $p = 0.07$; $F(1,54) = 0.611$, $p > 0.10$ and $F(1,49) = 2.532$, $p > 0.10$; $F(1,41) = 0.181$, $p > 0.10$ and $F(1,27) = 0.669$, $p > 0.10$ for trained and untrained eyes of Group I, II, III, respectively.) We pooled data from the two orientations in all the subsequent data analyses and report.

3.1. Group I

Training of the amblyopic eyes near each individual's cut-off spatial frequency resulted in highly significant ($t(6) = 5.19$, $p < 0.01$) improvements of contrast sensitivity at the trained spatial frequency. Averaged across observers, contrast sensitivity improved by 9.8 dB (calculated from pre-training and post-training CSF evaluation; or 209%; range, 0.1–20.9 dB; median = 8.3 dB; SE = 2.7 dB). The average learning curve, i.e., CS as a function of the common training sessions of all the observers in the group (i.e., 9 sessions), is shown in Fig. 1. Learning rates were estimated by using log–log linear regressions of the learning curves, consistent with power-law learning. Taking pre-training and post-training evaluation into account, training improved contrast sensitivity with an average of 0.42 log units per log unit of training session ($r^2 = 0.91$, $p < 0.0001$). Excluding data from pre- and post-training sessions, the slope of improvement is 0.31 log units per log unit of training session ($r^2 = 0.87$, $p < 0.01$).

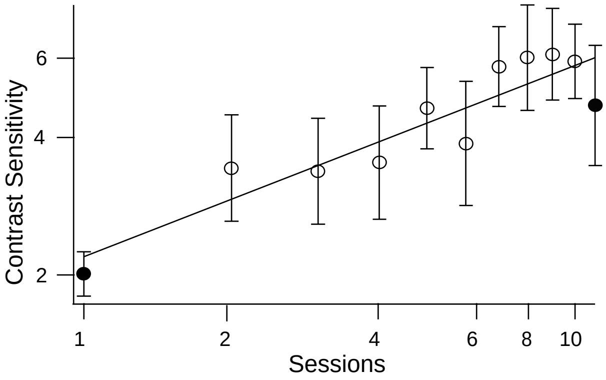

Fig. 1. Average learning curve of Group I. The first and last data points (filled circles) were derived from pre-training and post-training CSF measurements, respectively. Data from the training phase are represented by open circles. The number of training sessions varied between observers, from 9 to 19 (12.7 ± 3.4 SD) sessions. Only the first ("common") nine sessions are illustrated here. Data were fitted with a linear function with a slope of 0.42 and r^2 of 0.91 ($p < 0.0001$).

For the amblyopic eyes, training near the cut-off spatial frequency also improved contrast sensitivity over a wide range of spatial frequencies (Fig. 2A). Averaged across observers and spatial frequencies, contrast sensitivity improved about 5.7 dB (or 92%; SE, 1.3 dB; range, 0.06–9.8 dB; median, 5.3 dB). A within-subject analysis of variance showed that contrast sensitivity varied significantly with both spatial frequency ($F(8,24) = 40.98, p < 0.0001$) and practice level ($F(1,6) = 26.15$, $p < 0.01$). Interaction of the two factors was also significant ($F(6,24) = 2.93$, $p < 0.05$). In other words, training significantly increased contrast sensitivity and the improvement depends on the spatial frequency. For the average observer, the maximum contrast sensitivity (labeled as "MS" in Fig. 2) improved 2.7 dB (or 36.8%; $t(6) = 3.41$, $p < 0.01$), from 51 before to 70 after training; the cut-off spatial frequency also increased 2.7 dB (or 36.8%; $t(6) = 3.09$, $p < 0.05$), from 12 to 17 c/deg.

Following training in the amblyopic eyes, there was also marked contrast sensitivity improvement in the untrained fellow eyes. At the trained spatial frequency, contrast sensitivity in the fellow eyes improved 4.3 dB (or 64%; SE, 1.4 dB; range, −0.1 to 8.2 dB; median, 4.7 dB), averaged over the six observers tested ($t(6) = 2.23$, $p < 0.05$). The magnitude of improvement in the fellow eyes was not statistically different from that in the amblyopic eyes ($t(6) = 1.18$, $p > 0.10$). Moreover,

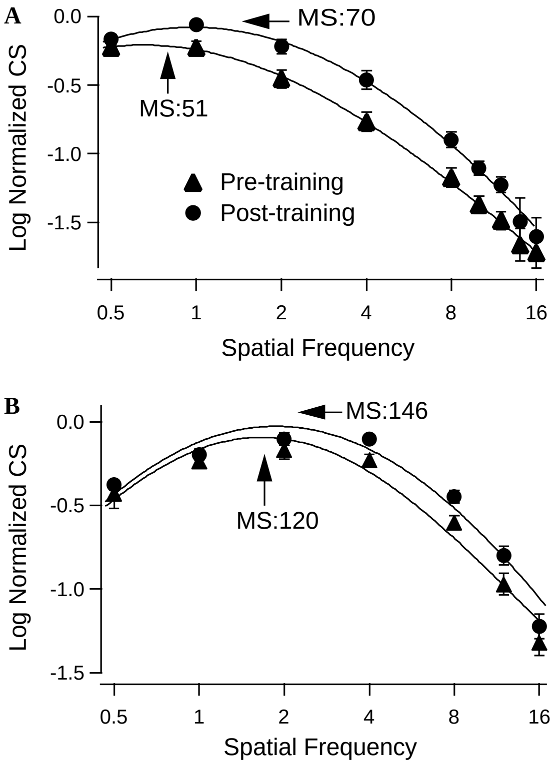

Fig. 2. Average contrast-sensitivity functions in the amblyopic eyes (A) and the fellow eyes (B) for observers in Group I. Triangles, pre-training; circles, post-training. For each observer, the maximum contrast sensitivity (of all the data points on the pre- and post-training CSF's) was set to 1.0. The CSF's were normalized to the maximum contrast sensitivity. Error bars indicate SEM. MS = maximum sensitivity. The smooth curves represent the best fitting DOG functions (Rohaly & Buchsbaum, 1988, 1989).

contrast sensitivity over a wide range of spatial frequencies also improved (Fig. 2B). Averaged across observers and spatial frequencies, contrast sensitivity improved 2.0 dB (or 26%; SE, 0.4 dB; range, 0.8–3.4 dB; median, 1.9 dB). Within-subject analysis of variance showed that contrast sensitivity varied significantly with both spatial frequency ($F(5,25) = 16.72$, $p < 0.0001$), practice level ($F(1,5) = 5.60$, $p = 0.06$), and interaction of the two factors ($F(5,25) = 2.59$, $p = 0.05$). For the average observer, the maximum contrast sensitivity improved 1.7 dB (or 22.1%; $t(6) = 2.66$, $p < 0.05$), from 120 before to 146 after training; the cut-off spatial frequency also increased 1.3 dB (or 16.7%; $t(6) = 1.15$, $p > 0.10$), from 35 to 41 c/deg.

We compared the magnitudes of contrast sensitivity improvements in the trained and untrained eyes across the seven common spatial frequencies tested in both eyes. Even though the magnitude of contrast sensitivity improvement depended significantly on spatial frequency ($F(5,25) = 3.184$, $p < 0.02$), it did not vary significantly between the two eyes ($F(1,5) = 2.159$, $p > 0.15$).

After training, visual acuity in the amblyopic eyes and fellow eyes improved 4.6 dB (or 69.8%; $t(6) = 4.38$, $p < 0.01$; SE, 1.0 dB; range, 1.9–10.0 dB; median, 3.8 dB) and 1.7 dB (or 21.6%; $t(7) = 5.16$, $p < 0.01$; SD, 0.4 dB; range, 0–3.5 dB; median, 1.3 dB), respectively (Table 2). Visual acuity of all observers improved in the trained amblyopic eyes. The magnitude of improvement in the amblyopic eyes was significantly greater than that in the fellow eyes ($t(6) = 2.83$, $p < 0.05$).

In Fig. 3, we plot visual acuity (logMAR) in the amblyopic eyes after training versus that before training for the seven observers. Visual acuity of all observers improved, signified by the clustering of most of the data points above the identity line. The best fitting linear regression curve has a slope of 0.58 ($r^2 = 0.93$, $p < 0.01$), suggesting greater visual acuity improvements for observers with worse initial visual acuities.

3.2. Group II

Ten subjects (they finished average 12.3 ± 3.1 sessions) demonstrated a mean of 5.0 dB (or 78.6%; SE, 1.0 dB; range, 1.2–9.7 dB; median, 4.3 dB) improvement of contrast sensitivity across frequencies (Fig. 4). Within-subject analysis of variance showed that contrast sensitivity varied significantly with both spatial frequency ($F(8,72) = 86.37$, $p < 0.0001$) and practice level ($F(1,9) = 7.378$, $p < 0.025$) but marginally significant interaction of the two factors ($F(8,72) = 1.901$, $p < 0.07$). For the average observer, the maximum contrast sensitivity improved 2.6 dB (or 35.6%; $t(9) = 2.94$, $p < 0.01$), from 70 before to 95 after training; the cut-off spatial frequency also increased 2.5 dB (or 33.3%; $t(9) = 3.19$, $p < 0.01$), from 12 to 16 c/deg.

Learning in the amblyopic eyes transferred little to the fellow eyes. The improvements of contrast sensitivity were only −0.3 dB (or −3.8%; SE, 0.3 dB; range, −2.1 to 0.5 dB; median, −0.2 dB) in the fellow eyes (Fig. 4B), averaged over subjects and spatial frequencies. This small amount of improvement was not statistically significant ($F(1,8) = 0.0001$, $p > 0.95$). For the average observer, the maximum contrast sensitivity improved −0.4 dB (or −4.1%; $t(8) = 0.32$, $p > 0.10$), from 94 before to 91 after training. The cut-off spatial frequency increased 1.0 dB (or 12.7%; $t(8) = 1.52$, $p = 0.083$), from 25 to 28 c/deg.

We also compared the magnitude of contrast sensitivity improvements in the trained and untrained eyes across the seven common spatial frequencies tested in both eyes. The magnitude of improvement in the trained eyes was marginally greater than that in the untrained eyes ($F(1,8) = 4.268$, $p < 0.07$).

After training, visual acuity in the amblyopic eyes and fellow eyes improved 3.3 dB (or 46.4%; $t(9) = 5.99$, $p < 0.001$; SE, 0.4 dB; range, 1.5–6.0 dB; median, 3.1 dB) and 0.6 dB (or 7.6%; $t(9) = 2.51$, $p < 0.05$; SE, 0.3 dB; range, 0–2.2 dB; median, 0.3 dB),

Table 2
Improvements in visual acuity for Groups I, II, and III

Group	Subject	AE			FE		
		Pre	Post	Improvement (dB)	Pre	Post	Improvement (dB)
I	1	3	2.4	1.9	0.9	0.7	2.2
	2	23.8	7.5	10.0	0.7	0.6	1.3
	3	4.7	2.4	5.8	0.7	0.6	1.3
	4	3.8	2.8	2.7	0.9	0.7	2.2
	5	7.1	4.2	4.6	1.2	0.8	3.5
	6	7.1	4.6	3.8	0.7	0.6	1.3
	7	6	4.2	3.1	0.6	0.6	0.0
Average				4.6			1.7
II	1	2.4	1.9	2.0	1.9	1.5	2.1
	2	3.8	2.5	3.6	0.9	0.9	0.0
	3	1.9	1.6	1.5	1.4	1.3	0.6
	4	3.8	2.7	3.0	0.9	0.9	0.0
	5	5.8	3.7	3.9	0.6	0.6	0.0
	6	5.3	3.7	3.1	0.9	0.9	0.0
	7	3.8	1.9	6.0	0.9	0.7	2.2
	8	5.3	3.7	3.1	0.9	0.8	1.0
	9	3.8	2.2	4.7	0.6	0.6	0.0
	10	1.9	1.5	2.1	1.9	1.8	0.5
Average				3.3			0.6
III	1	5.3	4.7	1.0	0.8	0.7	1.2
	2	7.5	7.5	0.0	0.9	0.9	0.0
	3	7.5	7.5	0.0	0.6	0.6	0.0
	4	3.7	4.2	−1.1	0.9	0.9	0.0
	5	4.2	3.8	0.9	0.9	0.9	0.0
	6	2.3	2.4	−0.4	1.4	1	2.9
Average				0.1			0.7

AE, amblyopic eye; FE, fellow (dominant) eye.

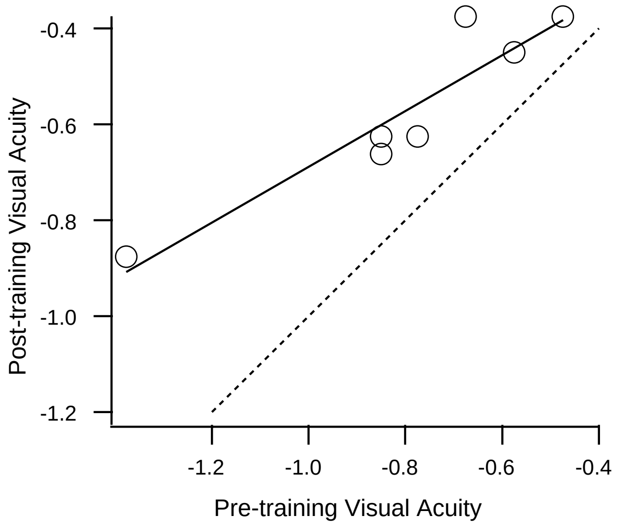

Fig. 3. Post- versus pre-training visual acuity for observers in Group I. Both abscissa and ordinate are in logMAR uints. The best fitting linear regression line ($r^2 = 0.93$, $p < 0.01$) has a slope of 0.58, suggesting greater visual acuity improvements for observers with initially worse visual acuities. The lower dashed line is the identity line (slope = 1), indicating the prediction of no improvement.

respectively (Table 2). The magnitude of improvement in the amblyopic eyes was significantly greater than that in the fellow eyes ($t(9) = 5.60$, $p < 0.001$).

3.3. Group III

The second measurement of the CSF in the amblyopic eyes showed an average 0.7 dB (or 8.6%; SE, 0.4 dB; range, −0.5 to 2.4 dB; median, 0.5 dB) improvement of contrast sensitivity in the amblyopic eyes across observers and frequencies (Fig. 5A). The improvement, however, was not significant ($F(1,6) = 0.474$, $p > 0.50$). For the average observer, the maximum contrast sensitivity improved 0.68 dB (or 8.2%; $t(5) = 0.98$, $p > 0.10$), from 82 to 88; the cut-off spatial frequency decreased 0.24 dB (or 2.8%; $t(4) = 0.94$, $p > 0.10$), from 17 to 16 c/deg.

In the fellow eyes, contrast sensitivity improved 1.4 dB (or 17.0%; SE, 0.3 dB; range, 0.1–2.4 dB; median, 1.5 dB) over observers and spatial frequencies (Fig. 5B). The improvement was only marginally significant ($F(1,4) = 4.970$, $p = 0.09$). For the average observer, the maximum contrast sensitivity improved 1.6 dB (or 20.7%; $t(4) = 1.49$, $p > 0.10$), from 103 to 125; the cut-

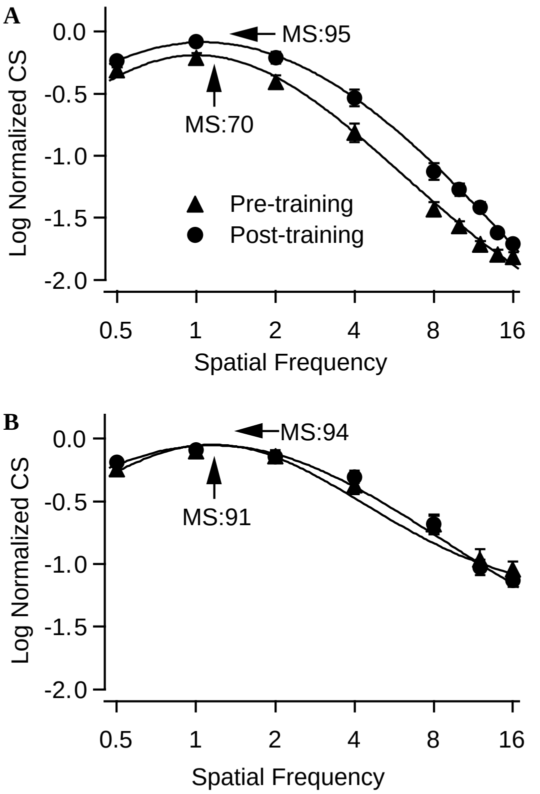

Fig. 4. Average contrast-sensitivity functions in the amblyopic eyes (A) and the fellow eyes (B) for observers in Group II. Triangles, pre-training; circles, post-training. For each observer, the maximum contrast sensitivity (of all the data points on the pre- and post-training CSF's) was set to 1.0. The CSF's were normalized to the maximum contrast sensitivity. Error bars indicate SEM. MS = maximum sensitivity. The smooth curves represent the best fitting DOG functions.

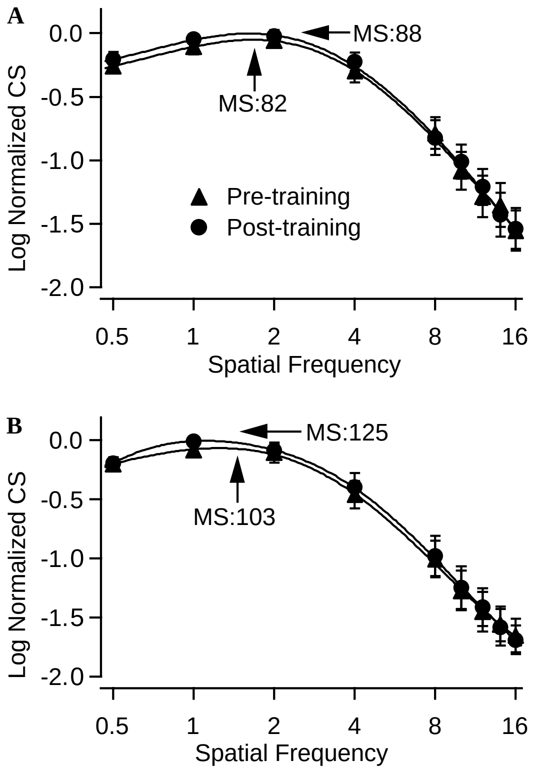

Fig. 5. Average contrast-sensitivity functions in the amblyopic eyes (A) and the fellow eyes (B) for observers in Group III. Triangles, pre-training; circles, post-training. For each observer, the maximum contrast sensitivity (of all the data points on the pre- and post-training CSF's) was set to 1.0. The CSF's were normalized to the maximum contrast sensitivity. Errors indicate SEM. MS = maximum sensitivity. The smooth curves represent the best fitting DOG models.

off spatial frequency decreased 0.24 dB (or 2.7%; $t(4) = 0.05$, $p > 0.10$), from 28 to 27 c/deg.

After two CSF's measurements (no training), visual acuity in the amblyopic eyes and fellow eyes improved 0.1 dB (or 0.9%; $t(5) = 0.43$, $p > 0.10$; SE, 0.3 dB; range, −1.1 to 1.0 dB; median, 0 dB) and 0.7 dB (or 8.1%; $t(5) = 1.40$, $p > 0.10$; SE, 0.5 dB; range, 0–2.9 dB; median, 0 dB), respectively (Table 2). The improvement was not significant for both eyes. No statistical significance between them ($t(5) = 1.13$, $p > 0.10$) can be detected.

3.4. Comparisons of the training protocols

The magnitudes of improvements, measured in terms of percent change of average CSF, maximum contrast sensitivity, cut-off spatial frequency, and visual acuity, are summarized in Fig. 6 for the three groups.

Treating spatial frequency as a within-subject factor and training protocol as the between-subject factor, we performed an analysis of variance test to compare the efficacies of the training protocols on CSF. In the trained amblyopic eyes, the training protocols produced significantly different improvements on CSF ($F(2,24) = 4.748$, $p < 0.05$). Tukey HSD post hoc tests found that CSF improvements in Group I are significantly greater than those in Group III ($p < 0.05$, as shown in Fig. 6), while no significant difference was found between Groups I and II ($p > 0.40$), and between Groups II and III ($p > 0.10$). In the untrained fellow eyes, no statistical difference was found among the three groups ($F(2,18) = 1.061$, $p > 0.10$).

The efficacy of the training protocols on visual acuity was compared using an analysis of variance test with observer as the random factor. We found that the different training protocols produced significantly different improvements of visual acuity in the trained amblyopic eyes ($F(2,20) = 16.79$, $p < 0.001$) and in the untrained fellow eyes ($F(2,20) = 3.98$, $p < 0.05$). Tukey HSD post hoc tests found that (Fig. 6), in the amblyopic eyes, both Group I and Group II improved more than Group III (both $p < 0.001$), while there was no significant difference between Group I and Group II ($p > 0.10$); in the untrained fellow eye, Group I improved significantly more than Group II ($p < 0.05$) and marginally significantly more than Group III ($p = 0.08$), while there was no significant difference between Group II and Group III ($p > 0.99$).

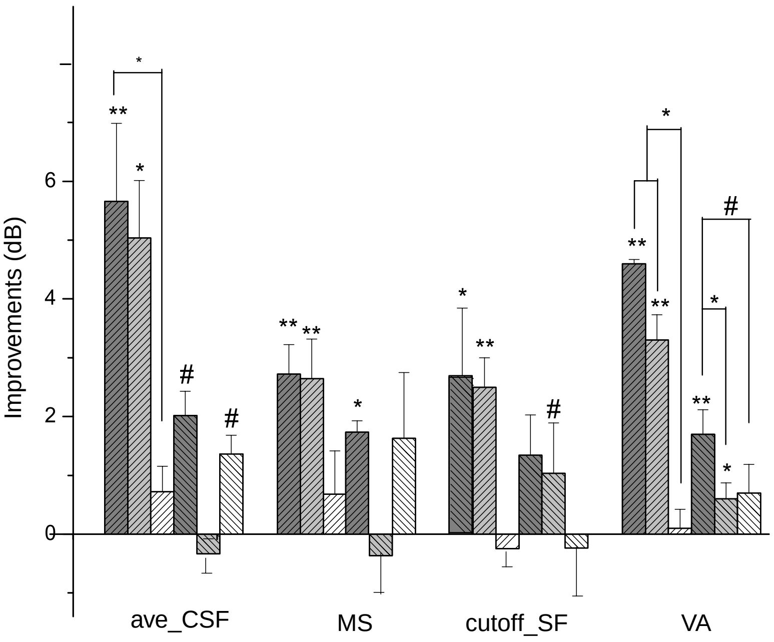

Fig. 6. Summary of training effects. The three groups are represented by three different shades of gray: gray (Group I), light gray (Group II), and white (Group III). The fellow and amblyopic eyes are represented by right-oriented and left-oriented grid lines. Average percent improvements in contrast-sensitivity function (avg_CSF), maximum contrast sensitivity (MS), cut-off spatial frequency (cut-off_SF), and visual acuity (VA) are plotted for each group and both eyes. Error bars represent SEM. $^*p < 0.05$; $^{**}p < 0.01$; $^{\#}0.05 < p < 0.10$.

We noted that total number of trials prescribed in Groups I and II is slightly different (on average 13,068 and 11,070 trials for Group I and II, respectively), but we do not think the difference is critical when we compare the efficacies of the training protocols because all subjects had reached their asymptotic performance level during training for at least three sessions.

We can calculate the "net effects" of training in Groups I and II by subtracting the "baseline" improvements in Group III between the two CSF and visual acuity measurements. For Group I, the net effects of training on average CSF, maximum sensitivity, cut-off spatial frequency, and visual acuity are 4.9 dB (76.5%), 2.0 dB (26.5%), 2.9 dB (39.9%), and 4.5 dB (68.4%) in the amblyopic eye, and 0.7 dB (7.8%), 0.1 dB (1.2%), 1.6 dB (19.9%), and 1.0 dB (12.5%) in the fellow eye. For Group II, the net training effects are 4.3 dB (64.4%), 2.0 dB (25.3%), 2.7 dB (37.2%), and 3.2 dB (45.1%) in the amblyopic eye, and −1.7 dB (−17.8%), −2.0 dB (−20.5%), 1.3 dB (15.8%), and 0 dB (−0.5%) in the fellow eye.

3.5. Retention

We define retention coefficient of visual acuity as $\frac{\mathrm{VA}_{\mathrm{retested}}-\mathrm{VA}_{\mathrm{pre-training}}}{\mathrm{VA}_{\mathrm{post-training}}-\mathrm{VA}_{\mathrm{pre-training}}} \times 100\%$, and retention coefficient of contrast sensitivity as $\frac{\mathrm{CS}_{\mathrm{retested}}(f)-\mathrm{CS}_{\mathrm{pre-training}(f)}}{\mathrm{CS}_{\mathrm{post-training}}(f)-\mathrm{CS}_{\mathrm{pre-training}}(f)} \times 100\%$. A retention coefficient of 100% indicates a full retention of the effects of training, while a retention coefficient less or greater than 100% indicates degradation or further amelioration after cessation of the training. A retention coefficient of 0 indicates no retention.

Retention of training effects on contrast sensitivity was evaluated for eight observers. At the training spatial frequency, the retention coefficients for one observer in Group I were 246%, 147%, and 63%, tested 3, 9, and 12 months post-training; the average retention coefficients for other two observers in Group I were 223% and 672%, tested 1 month and 9 months post-training. Another patient from Group II demonstrated 125% retention 12 months later (we measured full CSF here). In general, the retention of the effects of perceptual learning was fairly robust, consistent with previous Reports (Sagi & Tanne, 1994; Sowden, Rose, & Davies, 2002).

The improvement on visual acuity also retained well. Retention coefficients for Group I were measured at several intervals post-training. The average retention coefficients of the group is listed in Table 3. The improvements were almost fully retained for five

Table 3
Retention (with SD) of improvements in visual acuity (%)

Time interval (months)	AE	DE	Numbers
1	99.6 ± 17.6	100 ± 20	2
3	100 ± 14.1	50 ± 19.6	2
5	100 ± 33.4	100 ± 21.6	2
9	72.3 ± 16.3	71 ± 21.3	2
12	89.6 ± 10.1	100 ± 18	3
18	111 ± 15.6	75 ± 35.4	2

months, close to 90% for one year and more than 100% for one and a half year. The degree and duration of retention seem to be better than those observed in a vernier training task (Levi & Polat, 1996).

4. Discussion

In the amblyopic eyes, training at a single spatial frequency improved contrast sensitivity by about 4.9 dB (or 76.5%), averaged across all the spatial frequencies, and visual acuity by about 4.5 dB (68.4%; Group I). Repeated training over the entire range of spatial frequency used in CSF test improved the average contrast sensitivity by about 4.3 (64.4%), and visual acuity by about 3.2 dB (45.1%; Group II). No significant training effects were found in the control group (Group III). Both training protocols generated significantly more improvements in CSF and visual acuity than the passive control procedure. Even though on average larger amount of improvements was generated by training in one single spatial frequency, the magnitudes of improvements produced by the two procedures were not statistically different.

Training at a single spatial frequency in the amblyopic eyes improved contrast sensitivity (0.7 dB or 7.8%, averaged across spatial frequencies) and visual acuity (1.0 dB or 12.5%) in the untrained, fellow eyes. Repeated training over the entire range of spatial frequencies used in CSF test and the control procedure did not significantly improve CSF or visual acuity in the fellow eyes for most observers.

Compared to the control group, both training protocols produced significant improvements in CSF and visual acuity, indicating significant performance improvements due to training rather than re-testing. Group I improved most in terms of CSF and visual acuity in both the amblyopic and the fellow eyes, even though the magnitudes of improvements produced by the two training protocols are not statistically different. Among the three training protocols tested, the most effective training protocol was therefore practice of sine-wave grating detection near the cut-off frequency.

We chose to investigate the effects of perceptual learning on both contrast-sensitivity function and visual acuity because contrast sensitivity is believed to be a fundamental characteristic of the visual system and the most important measure in spatial vision (Nicholas, Heywood, & Cowey, 1996). Our results complement those of Levi and Polat (1996) and Levi et al. (1997) who trained adult amblyopes in a vernier task and showed a 50% performance (~3.5 dB) improvements after eight (or so) sessions of training, and those of Polat et al. (2004), that documented a 2-fold (~9.5 dB) contrast sensitivity improvement in adult amblyopes following training in Gabor detection (with and without flankers). In the two previous and the current studies, training in some basic psychophysical task also improved visual acuity. On the other hand, "direct" training in a letter acuity task did not produce considerable improvements in peripheral visual acuity (Westheimer, 2001). Perhaps training in basic psychophysical tasks improved processing/coding of basic visual features that in turn facilitated performance in the high-level visual acuity task, while training of visual acuity may not have allowed direct access to some of the basic visual features (Ahissar & Hochstein, 1996; Dosher & Lu, 1998).

For Group I, training at a single spatial frequency near the initial cut-off of the contrast-sensitivity function improved contrast sensitivity over a wide range of spatial frequencies. The range of spatial frequency over which learning generalized in the amblyopic eyes seemed to be much wider than that documented in para-fovea of normal observers (Sowden et al., 2002). This potentially interesting aspect of perceptual learning in amblyopes is discussed in detail in another manuscript (Lu, Huang, & Zhou, in preparation).

Different patterns of inter-occular transfer of perceptual learning from the trained amplyopic eyes to the untrained fellow eyes were found in Group I and Group II, following different training schemes. While significant performance improvements were observed in the fellow eyes in Group I after training at a single spatial frequency in the amblyopic eyes, no significant inter-occular transfer was found in Group II, who participated in repeated CSF measurements. Why the two training protocols generated these different results is beyond the scope of the current study. Nevertheless the effect is interesting and worth further investigation.

Retention of the training effects was excellent for the few observers tested: improvements on visual acuity were fully retained for at least 5 months and were close to 90% 1 year post-training. It can also be fully retained for one and a half years in two subjects tested. The considerable degree of improvements on CSF and visual acuity as well as the excellent retention suggests that perceptual learning might be of great clinical value in treating adult amblyopes (Polat et al., 2004), and the age-boundary for amblyopia treatment may not be so hard-wired as is maintained in the current literature on the topic (Levi et al., 1997). For child amblyopes, combining the active, intensified perceptual learning method with the conventional occlusion procedures may also potentially increase the efficacy of the conventional procedures. A large-scale, carefully controlled clinical study is necessary to further evaluate perceptual learning as a clinical tool for treating child and adult amblyopia.

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