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Training in Contrast Detection Improves Motion Perception of Sinewave Gratings in Amblyopia

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Abstract

Purpose: One critical concern about using perceptual learning to treat amblyopia is whether training with one particular stimulus and task generalizes to other stimuli and tasks. Huang, Zhou & Lu examined the issue in the spatial frequency (SF) domain and found that the bandwidth of contrast sensitivity improvement was much broader in amblyopes than in normals. Because previous studies suggested local motion deficits in amblyopia are explained by spatial vision deficits, we hypothesized that training in the spatial domain could benefit motion perception of sinewave gratings.

Methods: Nine adult amblyopes (aged 22.1 ± 5.6) were trained in a contrast detection task in the amblyopic eye for 10 days. Visual acuity, spatial contrast sensitivity functions, and temporal modulation transfer functions (MTF) for sinewave motion detection and discrimination were measured for each eye before and after training. Eight adult amblyopes (aged 22.6 ± 6.7) served as controls.

Results: In the amblyopic eye, training improved (1) contrast sensitivity by 6.6 dB (or 113.8%) across spatial frequencies, with a bandwidth of 4.4 octaves; (2) sensitivity of motion detection and discrimination by 3.2 dB (44.5%) and 3.7 dB (53.1%) across temporal frequencies, with bandwidths of 3.9 and 3.1 octaves, respectively; (3) visual acuity by 3.2 dB (44.5%). The fellow eye also showed small amount of improvement in contrast sensitivities and no significant change in motion perception. Control subjects who received no training demonstrated no obvious improvement in any measure.

Conclusion: Our results demonstrate substantial plasticity in the amblyopic visual system, and provide additional empirical support for perceptual learning as a potential treatment for amblyopia.

Introduction

Amblyopia, resulting from abnormal visual experience in the “sensitive period”, is a visual disorder defined by impaired spatial vision without apparent ocular anomalies that affects about 3% of the general population[1]. In clinical practice, it is widely accepted that amblyopia could be treated for children less than six years old by occluding the affected eye or physiologically punishing (e. g., application of atropine) the fellow eye from months to years, but not for older children and adults because traditional doctrine holds that the visual cortex is hard-wired and no longer subject to therapeutic intervention in older children and adults[2].

However, many recent perceptual learning studies on adults with amblyopia find substantial improvements in visual tasks[3]. For example, Levi et al[4, 5] trained adult amblyopes in a Vernier acuity task and found that some of the novice trainees improved their performance in the Vernier task as well as their Snellen acuity. Li et al[6-8] reported that, after training with a position discrimination task in noise, the amblyopic subjects improved their performance in the task and their visual acuity. Polat et al[9] and Chen et al[10] trained their amblyopic subjects using a Gabor detection task with lateral flankers and found that training significantly improved contrast sensitivity and visual acuity. Zhou et al[11] and Huang et al[12] designed a simple contrast detection task and trained amblyopic subjects at their individual cut-off spatial frequencies. They found that after training, the contrast sensitivity and visual acuity of the amblyopic eye improved by about 5.7 dB (or 92%) and 4.6 dB (or 69.8%), respectively. Most recently, Liu et al[13] found training older amblyopic children in a grating acuity task decreased grating acuity by 2.1% for those who had received patching treatment and increased grating acuity by 36.1% for those who had had no patching treatment, along with a boost of single/crowded E acuities by 0.9/0.7 lines and 1.5/1.2 in the two groups, respectively.

Two very important issues, retention and generalizability, must be considered for perceptual learning to become an effective treatment for adults with amblyopia. Retention refers to the ability to retain the effects of learning over time. For example, Li et al[6] found that the improvement in visual acuity following perceptual learning was stable for at least one year. Polat et al[9] measured the visual acuity of their amblyopic subjects 3, 6, 9 and 12 months after training, and found only a small decrement in visual acuity. Zhou et al[11] reported excellent retention of the training effects for up to one and a half years. Liu et al[13] also found that training-induced improvements in visual acuity persisted for one year.

Generalizability refers to the extent to which learning effects gained in a particular stimulus, task, and context can be transferred to other stimuli, tasks, and contexts. Specificity or lack of generalizability, which is often found in perceptual learning of normal adult subjects[14-20], would render the method less effective --- one would have to do perceptual learning in all the potentially important stimuli, tasks, and contexts. Studies on adults with amblyopia have found generalization of perceptual learning from position judgment[6-8], contrast detection with flankers[9, 10, 21], and contrast detection[11, 12], to visual acuity. Huang et al[12] systematically studied the degree of generalizability of perceptual learning across spatial frequencies. The bandwidth of improvement was estimated from improvements of the contrast sensitivity function (CSF) — the difference between post- and pre-training CSFs (Figure 1a). They found that the full bandwidth (at half height) of the improvement in the spatial frequency domain was 4.04 and 1.40 octaves for amblyopic and normal subjects, respectively, and suggested that the broader bandwidth of perceptual learning in adults with amblyopia provides an important empirical basis for using perceptual learning in amblyopia treatment.

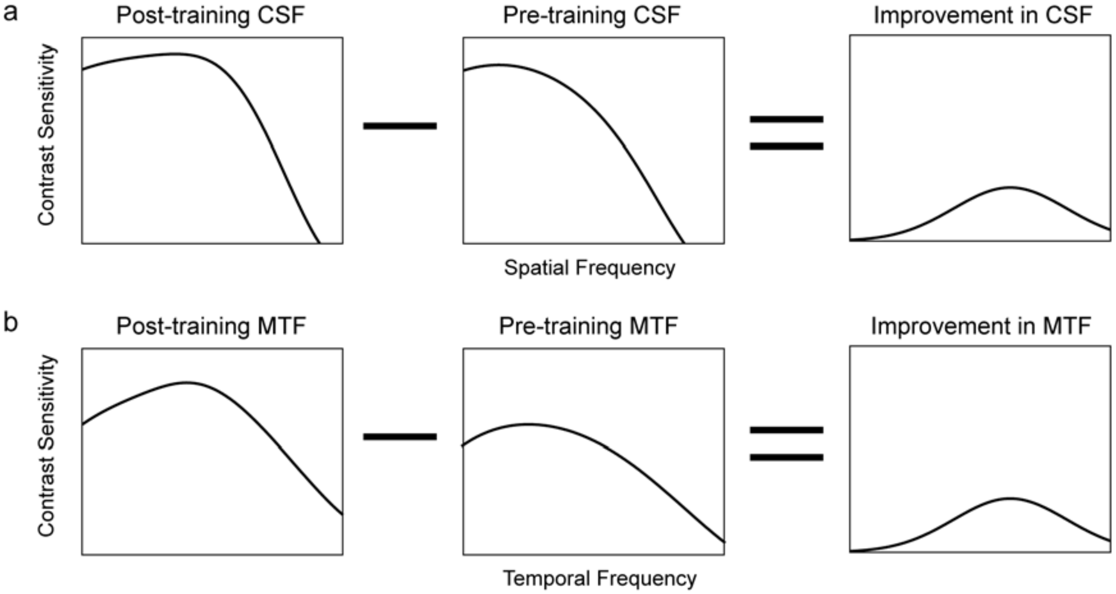

Figure 1. (a) Schematic diagram of the bandwidth of perceptual learning. The bandwidth of perceptual learning can be estimated by subtracting the pre-training contrast sensitivity function from the post-training contrast sensitivity function. (b) In the temporal domain, the bandwidth of perceptual learning can be estimated by subtracting the pre training modulation transfer function from the post-training modulation transfer function.

In the current study, we investigated whether training in spatial vision could generalize to motion perception of sinewave gratings and if so, how broad the effects are in the temporal domain. Previous studies suggested that local motion deficits in both anisometropic[22] and strabismic[23] amblyopia are caused by spatial vision deficits. We hypothesized that perceptual learning in the spatial domain would lead to improved motion perception of sinewave gratings.

Method

Subjects

Seventeen amblyopes, diagnosed by two ophthalmologists (the third and fourth authors) and naïve to the purpose of the experiment participated in the study (for detailed information of all subjects, see Table 1). They were randomly assigned into the training (A1 ~ A9) and control groups (A10 ~ A17). The age of the two groups ranged from 14 to 34 (22.1 ± 5.6) and 14 to 36 (22.6 ± 6.7) years. The research adhered to the tenets of the Declaration of Helsinki and were conducted following the experimental protocol of human subjects approved by the ethics committee of the School of Life Science, University of Science and Technology of China. Written informed consent was obtained from each participant after explanation of the nature and possible consequences of the study.

Table 1 characteristic of each amblyopic participant

	Gender	Age	Eye	Type	Eye alignment	Correction	Visual Acuity	SF of CS training	SF for MTF
A1	M	22	AE	Strab	EXT 25△	-2.25DS:-1.00DC×150°	1.07 (20/237)	4	2
			FE			-2.00DS:-0.50DC×50°	-0.07 (20/17)		
A2	M	25	AE	Aniso	None	-7.00 DS	0.87 (20/150)	15	4
			FE			-1.50 DS	-0.33 (20/9)		
A3	M	25	AE	Aniso	None	+9.25DS:+1.50DC×170°	0.72 (20/106)	2	2
			FE			+5.50DS:+1.50DC×85°	-0.12 (20/15)		
A4	M	22	AE	Aniso	None	+6.50DS:+2.00DC×100°	0.98 (20/189)	10	4
			FE			+3.50DS:+1.50DC×85°	0.07 (20/24)		
A5	M	34	AE	Aniso	None	+7.00DS	0.68 (20/95)	8	4
			FE			-1.00DC×90°	-0.12 (20/15)		
A6	M	14	AE	Aniso	None	-7.50DS	0.87 (20/150)	2	2
			FE			-4.00DS:-1.00DC×175°	0.07 (20/24)		
A7	M	20	AE	Aniso	None	+0.75DS:0.25DC×180°	0.37 (20/27)	24	4
			FE			-1.75DS	-0.03 (20/19)		
A8	F	19	AE	Aniso	None	-11.00DS:-3.00DC×5°	0.40 (20/50)	8	1
			FE			-1.75DS:-0.75DC×175°	0.07 (20/24)		
A9	F	18	AE	Strab	LET 15△	+0.50DS:+0.50DC×90°	0.98 (20/189)	16	4
			FE			Plano	-0.03 (20/19)		
A10	M	18	AE	Aniso	None	+1.50DS:+0.75DC×90°	0.29 (20/39)	none	4
			FE			-1.75DS	0.05 (20/22)		
A11	M	23	AE	Aniso	None	+1.00DS	0.77 (20/119)	none	2
			FE			Plano	-0.22 (20/12)		
A12	M	21	AE	Aniso	None	+4.62DS (RGPCL)	0.95 (20/178)	none	2
			FE			Plano	0.00 (20/20)		
A13	M	14	AE	Aniso	None	+3.50DS	0.19 (20/31)	none	4
			FE			Plano	-0.25 (20/11)		
A14	F	36	AE/LE	Ametropia	None	+16.00DS	0.68 (20/95)	none	2
			AE/RE			+16.00DS	0.67 (20/95)		
A15	M	28	AE	Aniso	None	-9.75DS:-1.00DC×165°	0.18 (20/30)	none	2
			FE			-1.00:-0.50DC×160°	0.14 (20/28)		
A16	M	21	AE	Strab	RXT 10△	+1.25DS:+0.50DC×180°	0.85 (20/142)	none	4
			FE			+1.00DS	-0.21 (20/12)		
A17	M	20	AE	Aniso	None	+1.50DC×90°	0.37 (20/47)	none	2
			FE			-1.50DS:+0.75DC×180°	-0.02 (20/19)		

AE: amblyopic eye, FE: fellow eye; LE: left eye, RE: right eye. Aniso: anisometropia, Strab: strabismus. RGPCL: hard corneal contact lens. Visual acuity is expressed both in logMAR (MAR: minimum angle of resolution in arcmin), fractions were also listed in brackets. SF of CS training: the spatial frequency of grating used in contrast sensitivity training. SF for MTF: the spatial frequency of moving sinewave gratings used in MTF tests. SF is in cycles per degree (cpd).

Apparatus

The stimuli were displayed on a SONY G220 monitor driven by an ATI Radeon^{TM} 9250 video card. The monitor had a display area of 32.8 cm × 24.4 cm, with a resolution of 640 × 480 pixels. The refresh rate of the monitor was set at 85 Hz for the contrast detection tasks and 160 Hz for the motion tasks. The mean luminance of the display was 24 cd/m^2. A special circuit was used to achieve 14-bit grayscale resolution[24]. Stimuli were generated on-the-fly by a PC running Matlab 7.1.0.14 (The Mathworks Corp., Natick, MA) and Psychtoolbox subroutines[25, 26]. Participants viewed the stimuli monocularly, and with their best refractive corrections. A chin/forehead-rest was used to minimize head movements during the experiment. The un-tested eye was occluded with an opaque eye patch.

Stimuli

The vertical sinusoidal gratings for the spatial contrast sensitivity function (CSF) test were the same as those used in our previous studies[11, 12, 27]. The size of the gratings was 3.0×3.0 deg^2. 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. The viewing distance for the gratings was 2.4 m for all subjects except A7, whose viewing distance was 4.8 m. Seven spatial frequencies (0.5, 1, 2, 4, 8, 12, 16 cycles per degree, cpd) were used in CSF tests for all subjects except A7, for whom the spatial frequencies were doubled.

The vertical sinusoidal gratings were identical for the motion detection and discrimination tests. Each grating subtended 2.5 × 2.5 deg^2. The motion direction was either leftward or rightward. A Gaussian envelope with a 0.5 deg standard deviation was applied to every frame of the moving grating. The moving grating was displayed for 300 ms, including a 25 ms linear onset ramp and a 25 ms offset ramp. Seven temporal frequencies (1, 3, 9, 16, 24, 30, 36 Hz) were used in motion detection and motion direction discrimination. For the training group, the spatial frequency of the moving grating was individually chosen near the spatial frequency at which the contrast threshold estimated from the pre-training CSF test was 0.05. For the control group, the spatial frequency of the moving grating was individually chosen based on individual's performance in practice session. The average spatial frequencies used in the motion tasks for two groups were matched (See Table 1). The spatial frequencies for the MTF tests were lower than that used in contrast sensitivity training so that we could measure MTFs over a wide range of temporal frequencies. The viewing distance for the moving gratings was 1.2 m.

Procedure

A two-interval forced-choice (2IFC) grating detection task was used to measure the CSFs of each subject. In each trial, a sinusoidal grating was randomly presented in one of two successive intervals, each lasting 118 ms and preceded by a 259-ms fixation display, in which two vertical and two horizontal line segments outside the stimulus area were used to indicate the center of the display. The two intervals, one with a grating and the other blank, were separated by 500 ms, and a brief tone signaled each interval's onset. Participants were asked to indicate which interval contained the grating via two keys on the computer keyboard. A new trial started 500 ms after each response. No feedback was provided.

To measure the contrast threshold for motion detection, a 2IFC moving grating detection task was used. In each trial, two 300-ms intervals, each signaled by a brief tone and preceded by a 256-ms fixation display, were presented successively. A moving grating was randomly displayed in one of the two intervals. Subjects were asked to indicate which interval contained the moving grating via two different keys. A new trial started 256 ms after each response. No feedback was provided.

To measure the contrast threshold for motion direction discrimination, a 2AFC motion direction discrimination task was used. In each trial, a fixation frame was first shown for 256 ms. A moving grating, either moving to the left or right, was then presented for 300 ms. A brief tone signaled the onset of the stimuli. Subjects were asked to indicate the direction of the motion via two different keys. A new trial started 256 ms after each response. No feedback was provided.

A 3-down-1-up staircase[28] that converges to 79.3% correct was used to measure contrast thresholds in all tests. The signal contrast was decreased by 10% (multiplied by 0.9) after every three consecutive correct responses, and increase by 10% (multiplied by 1.1) after every incorrect response.

The same 2IFC sinusoidal grating detection task was also used in the training phase. Each subject was trained near his/her own cut-off spatial frequency, defined as the spatial frequency at which the contrast threshold from the pre-training CSF measurement of the amblyopic eye was 0.5. During training, feedback was provided following each correct response. The 3-down-1-up staircase method was also used to track the contrast threshold through the whole training session.

Experimental design

Subjects in the training group went through three phases: pre-training tests, training and post-training re-tests. In the pre- and post-training tests, visual acuities and CSFs of both eyes were measured first, and then the modulation transfer functions (MTF) of motion detection and discrimination in both eyes. The order of motion detection and discrimination measurements was counter-balanced across subjects. In the training phase, participants practiced on grating detection in 10 sessions. Participants in the control group took the same set of tests and re-tests of visual acuity, and MTFs of motion detection and discrimination with a 10-day interval between them, but no CSF measurements and grating detection training.

CSFs were measured in seven spatial frequencies, each with one staircase of 100 trials. MTFs for motion detection and motion direction discrimination were measured in seven temporal frequencies, each with one staircase of 100 trials. All spatial or temporal frequency conditions and therefore staircases were intermixed in a given task.

Subjects were given 100 practice trials in the amblyopic eye before each pre-training test. The results of these trials were used to provide rough estimates of the thresholds and set the starting contrasts of the staircases.

In the training phase, subjects were trained to detect gratings near the cutoff spatial frequencies in their amblyopic eyes. A training session contained 9 blocks with 120 trials in each block. Subjects took one training session per day. A session usually took 40 to 60 minutes. Subjects in the training group took 12 measurement sessions and 10 training sessions in 22 days. Subjects in the control group had 8 measurement sessions and a 10-day break.

Statistical analysis

For each observer, the magnitude of improvement for each measure, e.g., spatial contrast sensitivity, average CSFs, was calculated as:

$$I_{individual} = 20\log_{10}\left(\frac{Measure_{post-training}}{Measure_{pre-training}}\right) dB .$$

Because better visual acuity means smaller MAR, the improvement of visual acuity was calculated as:

$$I_{individual} = 20\log_{10}\left(\frac{MAR_{pre-training}}{MAR_{post-training}}\right) dB .$$

We report $I_{group} = \frac{\sum I_{individual}}{N}$, where N is the total number of participants in a group, as the average magnitude of improvement for each group.

The percent improvement was calculated as: $P_{group} = (10^{I_{group}/20} - 1)\cdot 100\%$.

To estimate the area under the CSF and MTF (for detection and direction discrimination), the log truncated parabolic model (TP model)[29-31] was used to fit the measured CSFs and MTFs:

$$\log_{10}(CSF \text{ or } MTF) = \begin{cases} \log_{10}(\gamma_{\max}) - \delta, & \log_{10}(sf) < \log_{10}(f_{\max}) - \beta/2\sqrt{-\delta/\log_{10}(0.5)} \\ \log_{10}(\gamma_{\max}) + \log_{10}(0.5)\left(\frac{\log_{10}(sf) - \log_{10}(f_{\max})}{\beta/2}\right)^2, & otherwise \end{cases}$$

where $\gamma_{\max}$ is the peak gain (sensitivity), $f_{\max}$ is the peak spatial or temporal frequency, β represents the bandwidth which describes the function's full-width at half-maximum (in octaves), and δ represents the low-frequency truncation level.

Results

Training effects in spatial vision

Training near individuals' cut-off spatial frequencies led to significant improvements of contrast sensitivity (one-tailed paired *t*-test, $t(8)= -4.02$, $p < 0.005$) in the amblyopic eye. Averaged across subjects, contrast sensitivity at the training frequency improved 9.2 dB (Standard error, SE = 2.4 dB) or 188.4% (SE = 31.8%). The average learning curve, including data in both test and training sessions, plotted as log (sensitivity) vs. log (training days), is shown in Figure 2. The slope of the learning curve is 0.30 ($r^2 = 0.69$, $p < 0.005$).

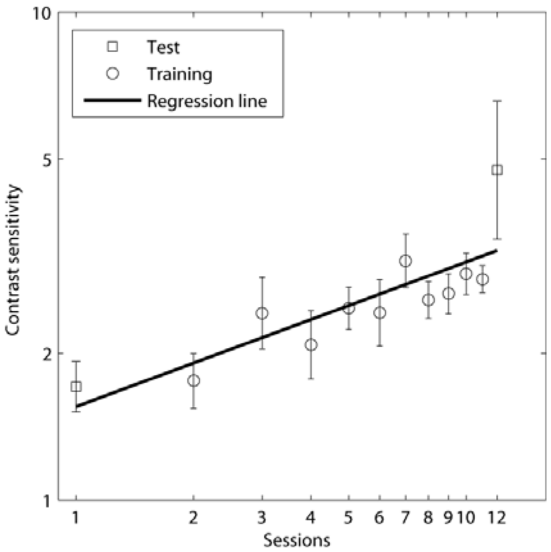

Figure 2. Average learning curve of the training group. The squares stand for contrast sensitivities measured in the pre- and post-test phases. The circles represent contrast sensitivities in the training sessions. Error bars represent standard errors. Regression was performed on the data from the test and training sessions.

Training also led to significant improvements of contrast sensitivity in other spatial frequencies in the amblyopic eye (See Figure 3a). A two-way ANOVA was performed on the data in the four lowest spatial frequency conditions: 0.5, 1, 2 and 4 cpd, because thresholds were not measurable for some participants in higher spatial frequencies. The result showed that the training effect was significant ($F(1,7) = 16.53$, $p < 0.01$). Contrast sensitivity improvement varied significantly with spatial frequency ($F(3,21) = 3.37$, $p < 0.05$), but there was no significant interaction between training and spatial frequency ($F(3,21) = 0.70$, $p > 0.5$). Averaged over subjects and spatial frequencies, contrast sensitivity improved 6.6 (SE = 0.9) dB or 113.8% (SE = 10.9%).

Training in the amblyopic eye also improved contrast sensitivity in the fellow eye. At the training frequency, contrast sensitivity improved 3.4 (SE = 1.7) dB or 47.9% (SE = 21.6%) on average after training (one-tailed paired *t*-test, $t(8) = -2.03$, $p < 0.05$). The magnitude of improvement in the fellow eye was significantly smaller than that in the amblyopic eye (paired *t*-test, $t(8) = 2.83$, $p < 0.05$ (one-tailed)). A two-way ANOVA showed that contrast sensitivities in other spatial frequencies also improved ($F(1,7) = 6.48$, $p < 0.05$). Averaged across frequencies and subjects, the magnitude of improvement was 1.1 (SE = 0.4) dB or 13.5% (SE = 4.7%) for the fellow eye (See Figure 3b).

After training, visual acuity in the amblyopic eyes improved 3.2 (SE = 0.7) dB or 44.5% (SE = 8.4%) (paired *t*-test, $t(8) = 3.82$, $p < 0.01$, Figure 4). There was no significant difference between the visual acuities before and after training in the fellow eye (paired t-test, $t(8) = 1.22$, $p > 0.10$). For the control group, there was no significant change in the amblyopic (paired t-test, $t(8)= 0.45$, $p > 0.50$) and fellow eyes (paired t-test, $t(8)= 1.46$, $p > 0.15$).

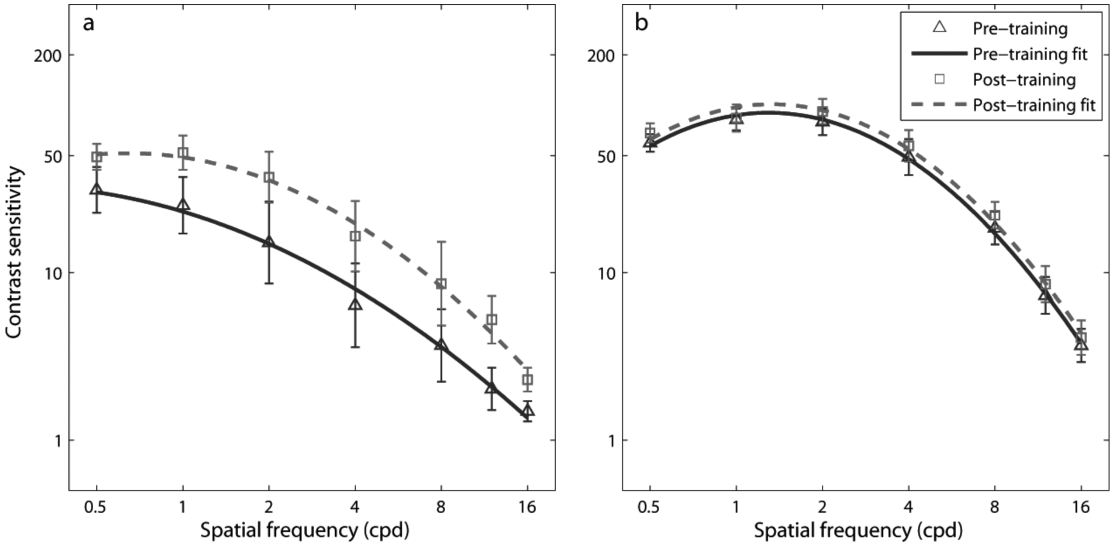

Figure 3. Pre- and post- training spatial contrast sensitivity functions of the amblyopic (a) and fellow eyes (b) in the training group. Triangles: pre-training. Squares: post-training. The continuous and dashed curves are the best fitting TP model for pre- and post-training CSFs, separately.

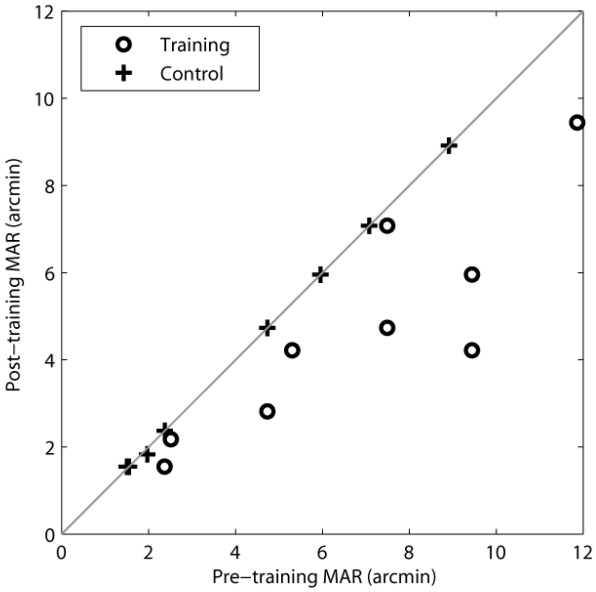

Figure 4. Visual acuities of the amblyopic eye in the training and control group.

Effects of training on motion perception

In the training group, perceptual learning in grating detection in the amblyopic eye significantly improved contrast sensitivity of motion detection in the amblyopic eye (two-way ANOVA, $F(1,8) = 9.26$, $p < 0.05$; Figure 5a). Averaged across temporal frequencies and subjects, contrast sensitivity in motion detection improved 3.2 (SE = 0.5) dB or 44.5% (SE = 5.9%). Although contrast threshold in motion detection varied significantly with temporal frequency ($F(4,32) = 71.98$, $p < 0.0001$), there was no significant interaction between training and temporal frequency (*F*(4,32) = 1.54, $p > 0.20$).There was no significant improvement of contrast sensitivity of motion detection in the fellow eyes (two-way ANOVA, training effect, *F*(1,8) = 0.17, $p > 0.50$; Figure 5b).

Perceptual learning in grating detection in the amblyopic eye also improved contrast sensitivity of motion direction discrimination in the amblyopic eyes (two-way ANOVA, *F*(1,8) = 9.92, $p < 0.05$; Figure 6a). Averaged across temporal frequencies and subjects, contrast sensitivity in motion direction discrimination improved 3.7 (SE = 0.7) dB or 53.1% (SE = 8.4%). Although contrast threshold in motion direction discrimination varied significantly with temporal frequency (*F*(3,24) = 13.11, $p < 0.0001$), there was no significant interaction between training and temporal frequency (F(3,24) = 0.70, $p > 0.50$). There was no significant improvement of contrast sensitivity of motion direction discrimination in the fellow eyes (two-way ANOVA, training effect, *F*(1,8) = 0.10, $p > 0.50$; Figure 6b).

In the control group, there was no significant difference between the modulation transfer functions for motion detection and discrimination in pre- and post-training tests in both the amblyopic and fellow eyes (Figures 5c, d and 6c, d).

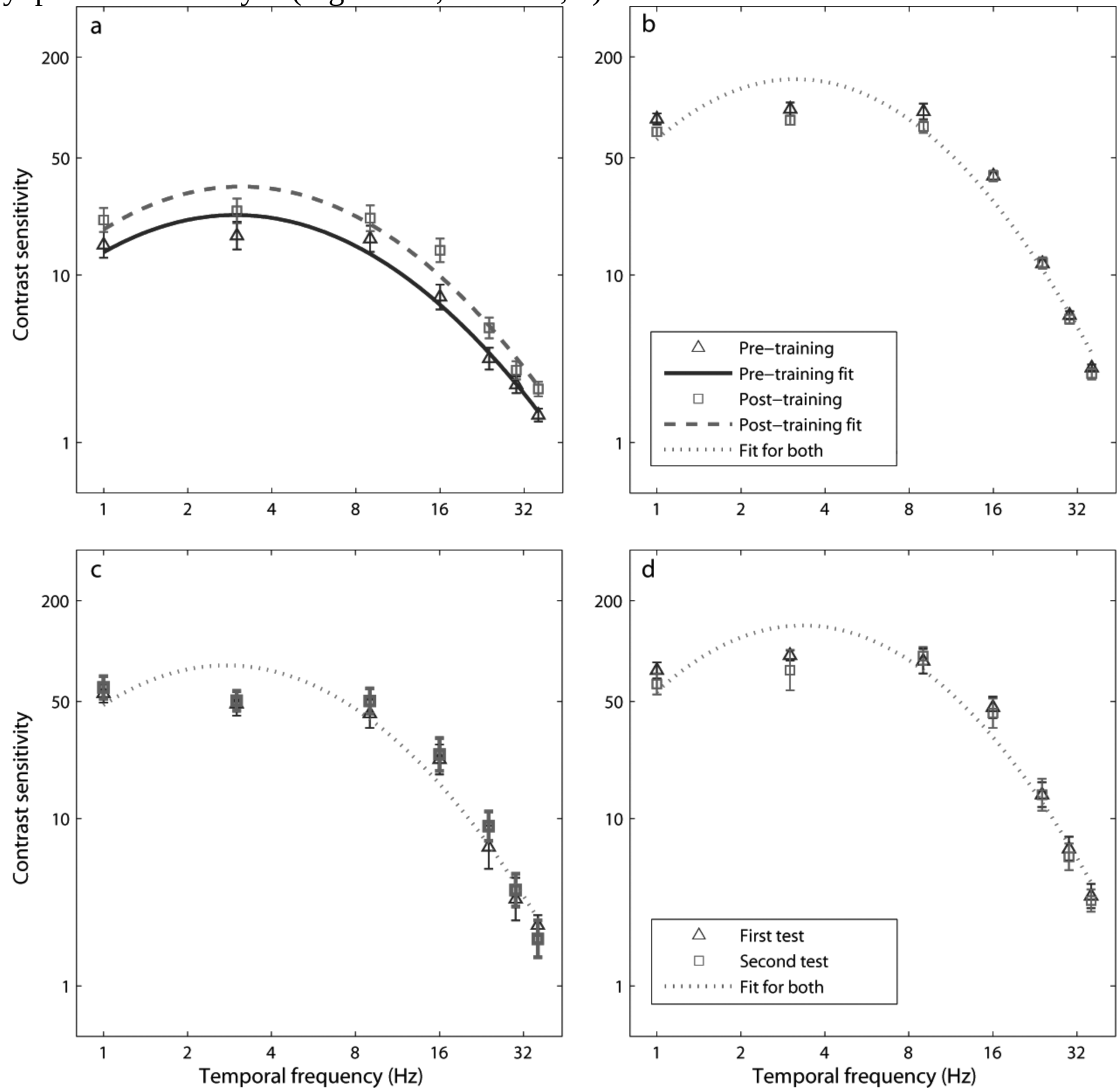

Figure 5. (a) Pre- and post- training temporal MTFs for motion detection of the amblyopic eye in

the training group are plotted. (b) Pre- and post- training temporal MTFs for motion detection of the fellow eye in the training group are plotted. For the control group, MTFs for motion detection measured in two tests of the amblyopic eye are plotted in (c), and those of the fellow eye are plotted in (d). In (a) and (b), Triangles: pre-training. Squares: post-training. In (c) and (d), triangles and squares represent the data measured in the first and second tests respectively. In (a), the continuous and dashed curves are the best fitting TP models for pre- and post-training MTFs, separately. There was no significant difference between the two MTFs in (b), (c) and (d). The dotted curve is the best fitting TP model for pre- and post- training or the first and second MTFs.

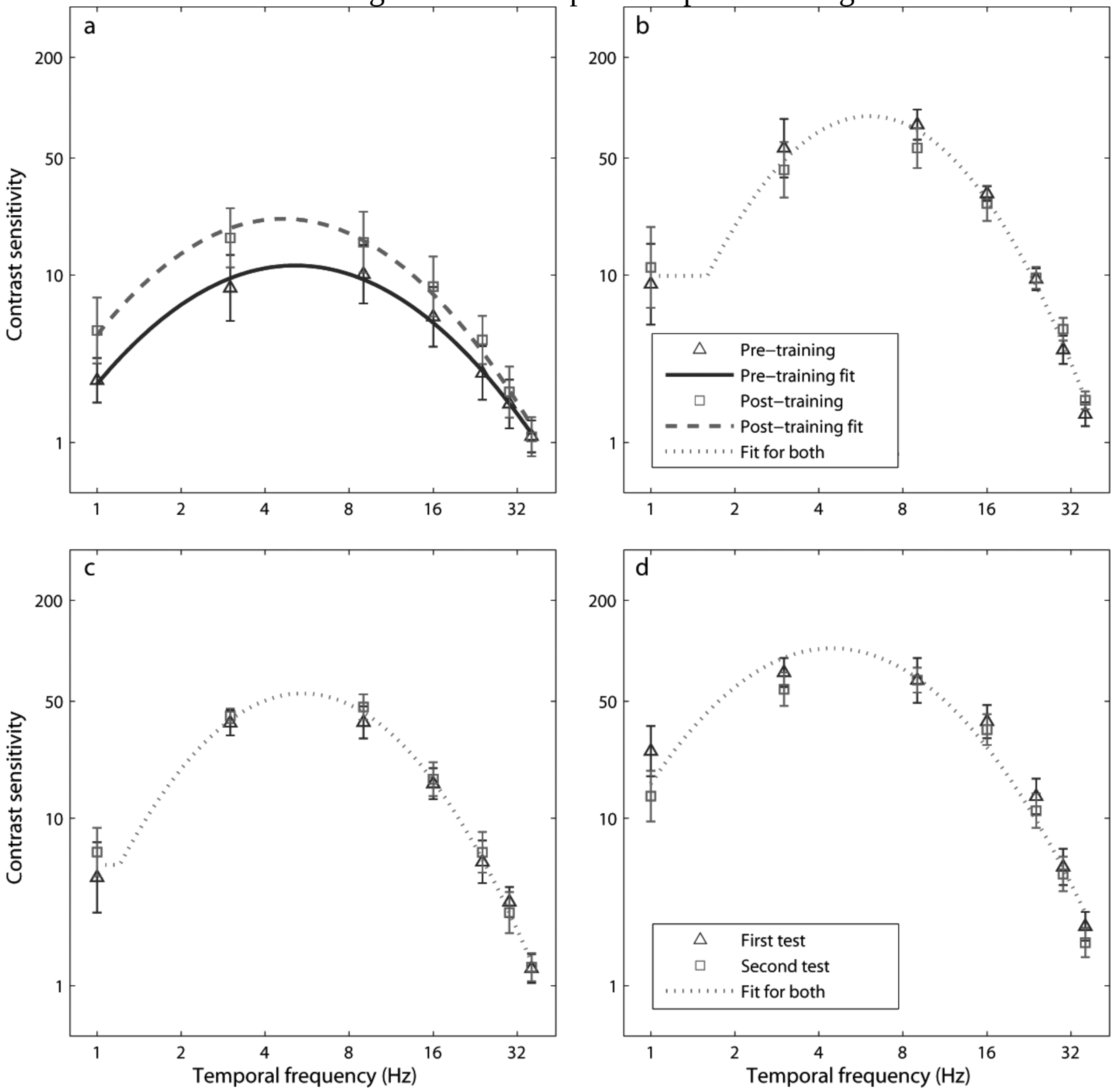

Figure 6. Pre- and post- training temporal MTFs for motion direction discrimination of the training group are plotted in (a) and (b). (a), amblyopic eye; (b) fellow eye. MTFs for motion direction discrimination measured in two tests of the control group are plotted in (c) and (d). (c), amblyopic eye; (d), fellow eye. In (a) and (b), triangles and squares represent the MTFs measured pre- and post-training respectively. In (c) and (d), triangles and squares represent the data measured in the first and second tests, respectively. In (a), the continuous and dashed curves are the best fitting TP models for pre- and post-training MTFs, separately. In (b), (c) and (d), the dotted curves are the best fitting TP model for pre- and post- training or the first and second MTFs, because there was no significant difference between pre- and post- training MTFs, or

between the first and second MTFs.

Bandwidth analysis

For the training group, we computed the bandwidth of perceptual learning in both the spatial and motion perception domain[12]. Specifically, we computed the difference (improvement) between the post-training and pre-training contrast sensitivity functions (Figure 1a) and modulation transfer functions (Figure 1b) and estimated the bandwidth of the improvements.

Following Huang et al[12], we calculated the bandwidth of the improvement of the spatial contrast sensitivity function. The magnitudes of improvement were normalized to the observed improvement at the training frequency, and the spatial frequencies were normalized to the training frequency. The normalized improvements of each participant were pooled together. The spatial frequencies were divided into seven bins: [-5, -4), [-4, -3), [-3, -2), [-2, -1), [-1, 0), 0, and (0, 2]. The data within each bin were averaged, weighted by the standard deviation of each bin, and fitted by a Gaussian function: $a \cdot \exp\left(-\left(\frac{\log(sf) - \log(sf_0)}{\sigma}\right)^2\right)$. The bandwidth of the improvement was defined as: $2\sqrt{\ln(2)} \cdot \sigma$. A bootstrap procedure was adopted to estimate the standard deviation of the bandwidth. The bandwidth of the contrast sensitivity improvement of the amblyopic eye was 4.4 (SE = 0.05) octaves, comparable to Huang et al[12].

A similar bandwidth analysis was conducted on the improvement of contrast sensitivity in motion detection and motion direction discrimination. For each participant, the improvements of contrast sensitivities in the motion tasks were normalized to his/her maximum magnitude of improvements. The data were averaged at each temporal frequency and weighted by the corresponding standard deviation. The same Gaussian function was used to fit the data (Figure 1b). The standard deviation of the fitted bandwidth was estimated through a bootstrap procedure. For the motion detection task, the bandwidth of learning improvement was 3.9 (SE = 0.1) octaves. For the motion direction discrimination task, the bandwidth of learning was 3.1 (SE = 0.1) octaves.

A multivariate analysis

To identify factors that are important for the improvements following perceptual learning, we carried a multivariate linear regression analysis on our data, using age, pre-training visual acuity (VA, MAR in unit of arcmin is used), pre-training cut-off spatial frequency, and improvement at training frequency as independent variables (Table 2), and improvement of VA, improvement of cut-off frequency, improvement of the total area under the CSF, improvement of total area under the MTF in motion detection, and improvement of the total area under the MTF in motion direction discrimination as dependent variables (Table 3). Improvements in dB were used in the analysis. The total area under the sensitivity functions provides a window of visibility[32]. A log truncated parabolic function was used to fit to the CSFs [29-31, 33] and MTFs. The cut-off frequencies and areas under CSFs/MTFs were then derived from the best fitting TP model. The regression model we used can be expressed as:

$$y_{predicted} = \beta_0 + \beta_1 \cdot age + \beta_2 \cdot VA_{pre} + \beta_3 \cdot cut\text{-}off_{pre} + \beta_4 \cdot improvement_{training\_frequency} \cdot$$

We found that the linear model provided a good account of the improvement of the total area under the CSF ($F(4,8) = 6.50$, $p < 0.05$). The improvement of the total area under the CSF was significantly correlated with pre-training cut-off frequency (coefficient $\beta_3 = -0.71$, $p < 0.05$), and marginally correlated with age (coefficient $\beta_1 = -0.65$, $p = 0.056$), suggesting more improvements for subjects with lower pre-training cut-off spatial frequency and younger age (see Figure 7). The model also provided a good account of the improvement of the total area under the MTF in motion direction discrimination ($F(4,8) = 17.91$, $p < 0.01$): age, pre-training VA and pre-training cut-off frequency ($\beta_1 = -0.68$, $\beta_2 = -0.75$, $\beta_3 = -0.61$, all $p < 0.05$) are all significantly correlated with the improvement.

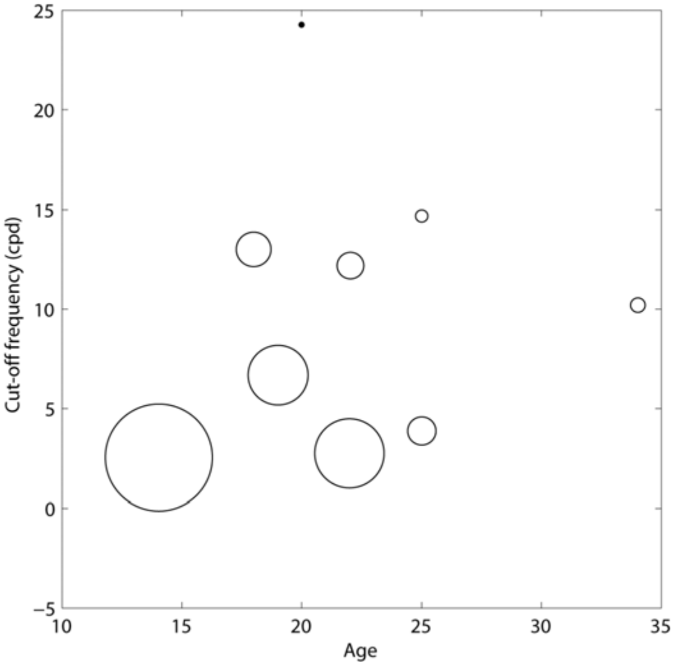

Figure 7. The markers represent the improvements of the area under CSF of different subjects. Abscissa: Age; Ordinate: Pre-training cut-off frequency. The size of markers indicates the magnitude of improvements.

To further explore the relationships between the various improvements, we computed pair-wise correlations. The improvement of cut-off frequency was positively correlated to the improvement of the area under CSF, and the areas under MTFs in motion detection and motion direction discrimination. The improvement of the area under CSF was positively correlated to the areas under MTFs in motion detection and motion direction discrimination. The correlation between improvement of the area under MTF in motion detection and improvement of the area under MTF in motion direction discrimination was marginally significant ($p = 0.063$). See Table 4 for details.

Table 2. Independent variables used in multivariate regression. Improvements are in unit of dB.

Subject	Age	Pre-training VA (arcmin)	Pre-training CSF cut-off (cpd)	Contrast sensitivity improvement at training SF (dB)
A1	22	11.86	2.76	11.85
A2	25	7.50	14.69	3.84
A3	25	5.31	3.82	8.63
A4	22	9.44	12.19	21.81
A5	34	4.73	10.17	2.36
A6	14	7.50	2.49	14.24
A7	20	2.37	24.28	2.67
A8	19	2.51	6.69	14.48
A9	18	9.44	13.00	2.96

Table 3. Dependent variables considered in multivariate regression. Improvements are in unit of dB, and the actual improvements of VA (changes of MAR in arcmin) and cut-off frequency (in cpd) are also listed in the brackets. * indicates that the variable was well predicted by our model.

Subject	Improvement of VA	Improvement of CSF cutoff	Improvement of CSF Area*	Improvement of MTF (detection) Area	Improvement of MTF (discrimination) Area*
A1	1.98 (-2.42)	6.39 (3.00)	13.82	8.29	7.06
A2	0.50 (-0.42)	1.92 (3.63)	1.72	2.21	2.94
A3	2.00 (-1.09)	1.89 (0.93)	5.60	2.79	7.29
A4	7.00 (-5.23)	4.79 (8.98)	5.54	2.72	-0.04
A5	4.50 (-1.91)	1.09 (1.36)	3.08	5.20	1.89
A6	3.99 (-2.76)	11.44 (6.82)	21.90	16.55	16.42
A7	3.70 (-0.82)	1.25 (3.77)	-0.03	0.92	4.10
A8	1.25 (-0.34)	6.80 (7.95)	11.65	2.26	12.32
A9	4.00 (-3.49)	1.66 (2.73)	6.41	-1.21	4.99

Table 4. Coefficients of pairwise correlations. Statistical significance is denoted by different symbols, *** for $p < 0.001$, ** for $p < 0.005$, * for $p < 0.05$, † for $p < 0.1$

	Improvement of VA	Improvement of CSF cutoff	Improvement of CSF Area	Improvement of MTF (detection) Area	Improvement of MTF (discrimination) Area
Improvement of VA	1	0.029	-0.040	0.063	-0.346
Improvement of CSF cutoff		1	0.944^{***}	0.812^{*}	0.786^{*}
Improvement of CSF Area			1	0.819^{*}	0.842^{**}
Improvement of MTF (detection) Area				1	$0.641^{\dagger}$
Improvement of MTF (discrimination) Area					1

Discussion

Our result showed that training in the amblyopic eye in a contrast detection task using stimuli at individuals' cutoff spatial frequencies improved the contrast sensitivity and visual acuity of the amblyopic eye by 6.6 dB (113.8%) and 3.2 dB (44.5%) , respectively. Moreover, such training led to 3.2 dB (44.5%) and 3.7 dB (53.1%) improvements in motion detection and discrimination following training. In comparison, amblyopic participants who received no training had no significant changes in motion perception. The result in the control group ruled out the possibility that the improved motion perception of the training group was due to learning effect in the motion tests themselves. Taken together, we conclude that training in contrast detection task can improve both spatial CSFs and motion perception of sinewave gratings. This result confirmed our hypothesis based on the analysis of the nature of local motion deficits in amblyopia [22, 23].

Physiological and psychophysical evidences suggested that amblyopia impairs global motion perception [34-37]. Two stages are involved in global motion processing: a local motion stage in V1, and a global integration stage in extra-striate cortical areas, such as MT and MST [38-41]. Global motion deficits in the amblyopic visual system could result from the deficits from either stage or both. For example, Simmers and his colleagues[35, 36] found that there are independent global motion processing deficits in addition to contrast sensitivity deficit in amblyopic vision. Constantinescu et al [37] reported a case of bilateral deprivation amblyopia caused by congenital cataracts. They found that there was a selective deficit for global motion processing despite of the recovery of visual acuity (20/20). We expect that training in contrast detection task could improve global motion perception in amblyopia because it improved local motion perceptual. On the other hand, training on motion integration is necessary to improve the second stage of global motion processing.

In the motion tasks, we used stimuli at spatial frequencies that corresponded to the 0.05 threshold on the contrast sensitivity functions because the motion task with gratings at the training spatial frequency, i.e., the cut-off spatial frequency (threshold=0.5) in pre-training CSF, was too difficult for the amblyopic participants. Because the maximum contrast sensitivity improvement was at the training spatial frequency, we believe that the improvement of motion perception at cut-off frequency would have been greater than what we have observed at the lower spatial frequencies. This is probably why the average improvement in CSF was larger than those in motion detection and direction discrimination (6.6 dB vs. 3.2 dB and 3.7 dB).

We found no significant interaction between training and spatial and temporal frequencies in CSF and MTFs. The result suggests that the improvements were general across different spatial and temporal frequencies. The bandwidth of the improvement in CSF was 4.4 (SE = 0.1) octaves, similar to Huang et al[12] . The broad bandwidth revealed broad generalization of perceptual learning in spatial vision[12]. The bandwidths of the improvement in the temporal domain were 3.9 (SE = 0.1) and 3.1 (SE = 0.05) octaves for motion detection and discrimination, respectively, essentially spanning the entire range of temporal frequencies in our experiment. Our results suggest that training at one spatial frequency could lead to improvements of the MTFs in motion perception. Further experiments are necessary to assess whether the bandwidth in the temporal domain for amblyopia is broader than that for normal observers.

A more comprehensive examination of the effect of perceptual learning in amblyopia requires measurements of the entire spatio-temporal sensitivity surface before and after perceptual learning. The amount of data collection with the traditional psychophysical procedures is insurmountable. The new generation of adaptive methods for the spatio-temporal contrast sensitivity surface[42] might allow us to do that in the near future.

We did not find significant correlations between VA improvement and other parameters. The multivariate regression and pairwise correlation didn't reveal any connections between VA and other factors. VA and CSF reflect different aspects of vision: VA reflects the spatial discrimination limits in high contrast conditions, while CSF describes the performance of the visual system at threshold level across different spatial frequencies. In a large sample study of amblyopia, McKee et al [43]found that optotype acuity and contrast sensitivity are two different dimensions of visual deficits in amblyopia. Because the VA task depends on a variety of spatial frequency channels, it may not necessarily correlate with cutoff SF; Contrast sensitivity at high spatial frequencies is still abnormal in amblyopes who are deemed "treated" based on the criterion of remediated visual acuity [27].

In a related study, Huang, Lu et al. [44] investigated the mechanism underlying contrast sensitivity improvements in adults with anisometropic amblyopia following perceptual learning in grating contrast detection. Using the external noise approach[45], they measured contrast thresholds in a range of external noise conditions at two performance levels (79.3% and 70.7%) in a grating contrast detection task through six to eight sessions of training. They found that a mixture of internal additive noise reduction and external noise exclusion underlay training induced contrast sensitivity improvements in adults with anisometropic amblyopia. We believe the same mechanisms of perceptual learning worked in the current study.

Early psychophysical studies on normal adults have demonstrated that performance improvements remain specific to basic attributes of the trained stimulus, including spatial location[14], orientation[16, 18, 46, 47], spatial frequency [15], eye [16, 17], and task [18-20]. Several recent studies suggest that perceptual learning could transfer to untrained stimuli or tasks [48-51]. Amblyopia impairs many visual functions. It is not feasible to recover each impaired visual function by training with a corresponding task. An efficient treatment requires large degree of generalizability to untrained stimuli or tasks. Spatial information processing is the first processing stage of motion analysis [52]. Here we demonstrated that the training in spatial vision led to improvements of first processing stage of motion perception in amblyopia. Our results provide additional evidence of generalization of perceptual learning in amblypia and empirical support for perceptual learning as a potential treatment for amblyopia.

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