Mechanisms underlying perceptual learning of contrast detection in adults with anisometropic amblyopia

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What underlies contrast sensitivity improvements in adults with anisometropic amblyopia following perceptual learning in grating contrast detection? In this paper, we adopted the external noise approach (Z.-L. Lu & B. A. Dosher, 1998) to identify the mechanisms underlying perceptual learning in adults with anisometropic amblyopia. By measuring contrast thresholds in a range of external noise conditions at two performance levels (79.3% and 70.7%), we found that a mixture of internal additive noise reduction and external noise exclusion underlay training induced contrast sensitivity improvements in adults with anisometropic amblyopia. In comparison, normal adults exhibited only small amount of external noise exclusion under the same training conditions. The results suggest that neural plasticity may be more robust in amblyopia, lending further support of perceptual learning as a potential treatment for adult amblyopia.

Keywords: perceptual learning, internal noise reduction, external noise exclusion, contrast detection, contrast sensitivity

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Introduction

Amblyopia, also known as "lazy eye," is a spatial vision disorder that affects about 3% of the population (Ciuffreda, Levi, & Selenow, 1991; McKee, Levi, & Movshon, 2003; Simmers, Ledgeway, Hess, & McGraw, 2003). It is characterized by reduced visual acuity in one or both eyes without any organic origin. Although conventional wisdom on visual development suggests that spatial vision becomes hard-wired after the critical period (6–8 yrs of age) and only infant and young child amblyopes are treated in current clinical practice, a number of recent studies suggest that perceptual learning might be a potential treatment for adult amblyopia (Chung, Levi, & Tjan, 2005; Huang, Zhou, & Lu, 2008; Levi & Li, 2009a, 2009b; Levi & Polat, 1996; Levi, Polat, & Hu, 1997; Li & Levi, 2004; Polat, 2009; Polat, Ma-Naim, Belkin, & Sagi, 2004; Zhou et al., 2006). In this study, we investigated the mechanisms of perceptual learning in adults with anisometropic amblyopia.

Mechanisms of amblyopia

Although most researchers agree that amblyopia is a cortical impairment resulted from abnormal visual experience in early childhood, such as misaligned eyes (strabismus) or different refractive powers in the two eyes (anisometropia), the neural basis of amblyopia is still not entirely clear (Barnes, Hess, Dumoulin, Achtman, & Pike, 2001; Daw, 1998; Kiorpes & McKee, 1999). Studies of amblyopic animals have not found a quantitatively causal link between the physiological abnormalities found in primary visual cortex and their behavioral deficits in spatial vision (Kiorpes, Kiper, O'Keefe, Cavanaugh, & Movshon, 1998; Kiorpes & McKee, 1999). For example, the reduced contrast response and spatial resolution of V1 neurons driven by the amblyopic eye underestimated the behavioral deficits in contrast sensitivity and visual acuity in amblyopic monkeys (Kiorpes et al., 1987; Kiorpes et al., 1998; Movshon et al., 1987). The neurophysiological correlates of amblyopia in early visual cortical areas might be amplified and exaggerated at

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higher levels of the visual system (Kiorpes & McKee, 1999; Sharma, Levi, & Klein, 2000).

Mechanisms of amblyopia have also been investigated in psychophysical studies using the external noise approach (Huang, Tao, Zhou, & Lu, 2007; Kersten, Hess, & Plant, 1988; Levi & Klein, 2003; Levi, Klein, & Chen, 2008; Nordmann, Freeman, & Casanova, 1992; Pelli, Levi, & Chung, 2004; Xu, Lu, Qiu, & Zhou, 2006). Several studies based on the linear amplifier model (LAM; Pelli & Farell, 1999) found decreased sampling efficiency and increased additive internal noise in the amblyopic visual system, although the results are not always consistent. Kersten et al. (1988) found that two out of their three amblyopic subjects showed normal sampling efficiency and increased internal noise and the other one had normal internal noise but lower sampling efficiency. Consistent with a notion of reduced sampling efficiency, Nordmann et al. (1992) found that the impact of external noise on grating contrast sensitivity was virtually identical for amblyopes and normal subjects. Pelli et al. (2004) concluded that loss of sampling efficiency was the predominant cause of amblyopic visual deficits. In low spatial frequencies (e.g., 2.3 c/d), the equivalent internal noise of their amblyopes was roughly the same as that of normal subjects. But paradoxically, the equivalent internal noise was *lower* in their subjects with mild amblyopia than in normal subjects in higher spatial frequencies. Levi and Klein (2003) concluded that performance decrements in amblyopia are attributable in part to poorly matched templates, but to a greater degree, to higher internal stimulus-dependent (multiplicative) noise. Based on the perceptual template model (Lu & Dosher, 1999), which is elaborated from the linear amplifier model, Xu et al. (2006) and Huang et al. (2007) found that whereas increased additive internal noise underlay performance deficits in all spatial frequencies in the amblyopic visual system, the degree of perceptual template mismatch increased with the spatial frequency of the stimuli. In a more detailed study, Levi et al. (2008) derived classification images used by normal and amblyopic observers in detecting a discrete frequency pattern (DFP) in both fixed-contrast and visibility-scaled white noise. They concluded that the amblyopes' reduced efficiency for detecting signal in noise is explained in part by reduced template efficiency but to a greater extent by increased random internal noise. The authors pointed out that distinguishing between multiplicative and early vs. late additive noise is model dependent and "remain agnostic on this issue" (page 15, Levi et al., 2008; for a related discussion, see Dosher & Lu, 1999, Appendix A).

Potential mechanisms of amblyopia based on noisy observer models, i.e., deficient templates, increased internal noise and reduced sampling efficiency, are highly related to other explanations of amblyopia in the literature, such as under-sampling (Levi, 1991; Levi & Klein, 1985) and topographical jitter (Hess, 1982; Hess & Field, 1994; Hess & Holliday, 1992), although the precise mapping between these explanations and the constructs of the noisy observer models remains to be worked out. According to the under-sampling theory, the number of high spatial frequency neurons may be reduced in the cortex of strabismic amblyopes (Levi, 1991; Levi & Klein, 1985). The topographical jitter theory hypothesizes that the amblyopic visual cortex has normal number of neurons in all the spatial frequencies but their topological connections are uncalibrated or miswired (Hess & Field, 1994; Hess & Holliday, 1992). Levi et al. (2008) suggests that their finding of increased random internal noise in the amblyopic visual system may reflect a combination of both undersampling and positional jitter.

Finding that the facilitation effect for collinear targets was either markedly lower than normal or even was replaced by inhibition in amblyopic vision, Polat, Sagi, and Norcia (1997) postulated that abnormal long-range spatial interactions may underlie the grouping disorders and perceptual distortions found in amblyopia. The abnormal long-range spatial interactions may lead to deficient perceptual templates and increased internal noise. But more importantly, they may offer explanations of abnormal spatial interactions in amblyopia (Chandna, Pennefather, Kovacs, & Norcia, 2001; Hess, McIlhagga, & Field, 1997; Kovacs, Polat, Pennefather, Chandna, & Norcia, 2000; Wong, Levi, & McGraw, 2005), which have not been investigated in typical external noise studies.

Perceptual learning in amblyopia

Visual training as a potential therapy for amblyopia has been evaluated since the pioneering work of Campbell, Hess, Watson, and Banks (1978). The results of the early studies have been mixed (Birnbaum, Koslowe, & Sanet, 1977; Ciuffreda, Goldner, & Connelly, 1980; Kupfer, 1957; Mehdorn, Mattheus, Schuppe, Klein, & Kommerell, 1981; Schor & Wick, 1983; Terrell, 1981; Wick, Wingard, Cotter, & Scheiman, 1992). However, unlike most of the studies on perceptual learning in the normal population, these early training studies typically used high contrast stimuli and relatively short training periods (e.g., 7 minutes; except Kupfer, 1957) that were pre-determined irrespective of training progress and subjects' ophthalmological characteristics. Later studies on perceptual learning in the normal visual system showed that it typically requires several hundreds of training trials to significantly improve performance in perceptual tasks.

A number of recent studies (Chung, Li, & Levi, 2006; Huang et al., 2008; Levi & Polat, 1996; Levi et al., 1997; Li & Levi, 2004; Li, Provost, & Levi, 2007; Polat et al., 2004; Simmers & Gray, 1999; Zhou et al., 2006) found that perceptual learning of simple spatial vision tasks led to significant visual acuity improvements in adult amblyopes. For example, Levi and colleagues found that Snellen acuities in two anisometropic amblyopes were significantly improved following intensive training in a vernier acuity task (Levi & Polat, 1996; Levi et al., 1997). In addition, both Li and Levi (2004) and Li et al. (2007) showed transfer of learning of position acuity to Snellen acuity in amblyopes beyond the critical period. Zhou et al. (2006) trained adult and teenager amblyopic subjects in a simple visual detection task and evaluated effects of perceptual learning on visual acuity and contrast sensitivity function (CSF). They found that training at the cutoff spatial frequency improved contrast sensitivity by about 4.9 dB (or 76.5%) and visual acuity by about 4.5 dB (68.4%) in the amblyopic eyes, with excellent retention of the training effects 6 months to 1 1/2 years after training. To evaluate and compare the generalizability of perceptual learning in amblyopic and normal vision, Huang, Zhou, and Lu (2008) estimated the bandwidth of perceptual learning in both normals and amblyopes. Comparing pre- and post-training contrast sensitivity functions in the trained eyes, we found that the average full bandwidth at half height of perceptual learning was 4.04 octaves in the amblyopic group, which is significantly broader than the 1.40 octaves for the normal observers. Polat (2009) suggests that contrast sensitivity is a fundamental function that reflects the output of early visual processing; improvement in contrast sensitivity may facilitate the performance of visual processing during the next stages of the visual cascade.

Given our current understanding of the mechanisms of amblyopia, one very important question is whether the conventional (e.g., patching) and the perceptual learning procedures can address the mechanisms of visual deficits in amblyopia.

Mechanisms of perceptual learning

Motivated by principles in signal processing and neurophysiology, Lu and Dosher (Dosher & Lu, 1998; Lu & Dosher, 1998; for a recent review, see Lu & Dosher, 2008) developed the external noise plus attention/training paradigm and a theoretical framework based on the perceptual template model (PTM) to distinguish mechanisms of attention and perceptual learning. The PTM model describes the input–output relationships of the perceptual and decision process for the observer as a system (Lu & Dosher, 1999; 2008). It characterizes human performance in perceptual tasks in terms of a perceptual template, transducer nonlinearity, internal additive noise, and internal multiplicative noise. The internal additive noise is independent of the contrast of the stimulus; the internal multiplicative noise increases directly with the contrast of the stimulus (signal plus external noise). The PTM characterizes the performance of an observer, d', as:

$$d' = \frac{(\beta c)^{2\gamma}}{\sqrt{N_{\text{ext}}^{2\gamma} + N_{\text{add}}^{2} + N_{\text{mul}}^{2}((\beta c)^{2\gamma} + N_{\text{ext}}^{2\gamma})}}, \tag{1}$$

where c is the signal contrast, β is the gain on a signal-valued stimulus processed through the template, γ characterizes the system's non-linearity, N_{add} is the standard deviation of the internal additive noise, N_{ext} is the standard deviation of external noise, and N_{mul} is the proportional constant of multiplicative noise.

In the PTM-based theoretical framework, perceptual learning impacts performance in one or a combination of three different mechanisms: (1) stimulus enhancement amplifies the stimulus, including both the signal and external noise. This is mathematically equivalent to reducing internal additive noise in learning session t by a factor of $A_a(t)$; (2) retuning the perceptual template to increase the ability to exclude external noise. This is modeled by multiplying the amount of external noise in learning block t by a learning parameter $A_f(t)$; (3) changes in contrast-gain control properties result in a reduction of internal multiplicative noise by $A_m(t)$. Equation 1 can be re-arranged to incorporate the learning parameters as follows:

$$c = \frac{1}{\beta}\left[\frac{(1 + (A_m(t)N_{\text{mul}})^2)(A_f(t)N_{\text{ext}})^{2\gamma} + (A_a(t)N_{\text{add}})^2}{(1/d'^{\,2} - (A_m(t)N_{\text{mul}})^2)}\right]^{\frac{1}{2\gamma}}. \tag{2}$$

Applications of the external noise approach and the PTM framework to the normal population found that two independent mechanisms, tuning of the task relevant perceptual template (external noise exclusion) and enhancing the stimulus (reducing absolute threshold), support perceptual learning across a range of tasks (for a review, see Lu & Dosher, 2009). In this study, we applied both the empirical and theoretical approaches to investigate mechanisms of perceptual learning in amblyopia.

Mechanisms of amblyopia treatments

Mechanisms of the conventional patching procedure have been partially evaluated by Huang et al. (2007). Applying the external noise approach and the PTM-based theoretical framework, Huang et al. evaluated the internal noise and perceptual templates of five treated child amblyopes whose visual acuities had become normal following extensive period of patching. We found that, compared to the fellow eyes, internal noise in the previous amblyopic eyes was still higher at low to medium spatial frequencies, and both the internal noise and the impact of external noise in the amblyopic eyes were higher at high spatial frequencies (Huang et al., 2007). The result suggests that additional training that targets the specific deficits evident at high spatial frequencies and in high external noise should be added to the conventional amblyopia treatment.

Mechanisms of perceptual learning in amblyopia have also been studied by Li and Levi (2004), Levi (2005), Li, Young, Hoenig, and Levi (2005), and Chung et al. (2005) using the external noise approach. Using a letter identification task with stimuli embedded in luminance noise, Levi (2005) found that perceptual learning improved sampling efficiency in all four amblyopic subjects (Levi, 2005). Using a position judgment task with random jittering of the component elements of the stimuli, Li et al. (2005) and Li and Levi (2004) found that perceptual learning enhanced sampling efficiency and/or decreased internal equivalent noise in both juvenile and adult amblyopia. The results were later confirmed by Li et al. (2007) and by Li, Klein, and Levi (2008) using the classification image technique.

Polat and colleagues developed a perceptual learning procedure that was designed to improve the abnormal lateral interactions in adult amblyopia by stimulating the deficient neuronal populations and effectively promoting their collinear interactions (Polat, 1999, 2008, 2009; Polat et al., 1997, 2004). The training program was tailored and specifically designed to target each individual's deficiencies. Although the lateral interaction function of the amblyopes in the beginning of the treatment showed no facilitation and in fact increased amount of suppression, training reduced the amount of suppression to a normal level (Polat, 2008; Polat et al., 2004).

Overview

In this study, we evaluated the mechanisms of perceptual learning in adults with anisometropic amblyopia in a grating detection task using the external noise approach and a theoretical framework based on the PTM model (Lu & Dosher, 2008). We trained adult amblyopes in a contrast detection task under varying amounts of external noise and evaluated the mechanisms of perceptual learning in this task. Grating contrast detection thresholds in eight external noise conditions were measured at two criterion performance levels. We found that performance improved in all external noise conditions. The improvement can be characterized as a result of decreased internal additive noise and improved external noise exclusion. In comparison, normal subjects showed smaller amount of perceptual learning only in the high external noise conditions. Training also greatly improved the visual acuity of the amblyopic eye of the amblyopic observers.

Methods

Subjects

Seven adults (A1–A7) with unilateral naturally occurring anisometropic amplyopia (21.1 ± 2.3 years; visual acuity: 20/200 to 30/50; see Table 1 for details) and five adults (N1–N5) with normal or corrected-to-normal vision (20 to 24 years) participated in the study with informed consent. All amblyopic subjects were screened with the cover test, synoptophore, and four-diopter prism tests (to exclude small-angle strabismus). The refractions of their eyes were determined under cycloplegia. All subjects, naïve to psychophysical experiments, were prescribed corrective glasses (if necessary) and wore them during the entire experiment.

Stimuli

Signal stimuli were windowed vertical sinusoidal gratings with a mean luminance of 27 cd/m^2. The stimuli was rendered on a 240 × 240 pixel grid, subtending 3.06 × 3.06 degrees at a viewing distance of 2.28 m. The flat

Subjects	Sex	Age	Eye	Refractive	Acuity[a]	SF(c/d)
A1	M	19	AE	+4.75DS/+0.75DC × 80	0.699	4
			DE	+1.00DS	0	
A2	F	24	AE	+3.50DS	0.602	8
			DE	Plano	−0.176	
A3	F	20	AE	+3.00DS	0.222	12
			AE	+1.25DS	0.222	
A4	M	18	AE	+3.25DS/−0.50DC × 120	0.523	8
			DE	+0.25DS	−0.301	
A5	F	21	AE	+4.50DS	0.921	4
			DE	−3.25DS/−0.75DC × 175	0	
A6	M	22	AE	+4.50DS/+1.25 × 90	0.301	8
			DE	Plano	−0.176	
A7	F	25	AE	+5.75DS/+0.37DC × 40	0.602	4
			DE	+0.75DS	−0.079	

Table 1. Amblyopic observers' characteristics. *Note*: [a]Visual acuity in LogMAR unit was assessed with the Chinese Tumbling E Chart (Mou, 1966) and defined as the score associated with 75% correct judgments. SF, spatial frequency.

portion of the circular window had a radius of 1.03 degrees. A 0.5 degree half-Gaussian ramp was added to the flat part of the circular window to blend the stimuli to the background. For each amblyopic subject, the spatial frequency of the training stimuli was chosen such that the estimated 79.3% correct contrast threshold from pre-training CSF measurements was 0.15 at the training frequency (Table 1). The mean training frequency was 6.9 c/d; the median training frequency was 8 c/d. The median training spatial frequency of the amplyopia group (8 c/d) was used in training the normal observers.[1]

External noise frames were made of 5 × 5 pixel patches each subtending 0.064 × 0.064 deg^2. Each noise patch's contrast level was drawn independently from one identical Gaussian distribution with mean 0 and standard deviation that ranged from 0 to 0.33 in different trials. Because the maximum achievable contrast is ±1.0 on the display, a noise sample with standard deviation of 0.33 conforms reasonably well to a Gaussian distribution. In a given trial, external noise images were made of elements with jointly independent, identically distributed contrasts. Eight external noise levels (0.0, 0.021, 0.042, 0.083, 0.125, 0.167, 0.250, and 0.333) were used in the experiment. External noise images were windowed in the same way as the signal stimuli.

Apparatus

All the signal and external noise frames were generated and displayed in real time using Matlab programs based on Psychotoolbox extensions (Brainard, 1997; Pelli, 1997) using a PC computer. The stimuli were presented on a Sony G220 Triniton monitor with a resolution of 640 × 480 pixels and a refresh rate of 85 Hz. Using a special circuit that combines two 8-bit output channels of the graphics card, the display system produced 14-bit gray-level resolution and was gamma-corrected using a psychophysics procedure (Li, Lu, Xu, Jin, & Zhou, 2003). All displays were viewed monocularly with natural pupil at a viewing distance of approximately 2.28 m in a dimly lighted room.

Procedure

Figure 1 depicts a typical trial. Each trial started with a 83-ms fixation cross in the center of the display, followed by two intervals of 175 ms each, separated by a 500-ms blank screen. Demarcated by a brief tone in the beginning, each interval consisted of five images: two external noise images, one signal or blank image and another two external noise images, each lasting 35 ms. All external noise images were independently sampled. Observers were asked to indicate which interval contained the signal by pressing a key on the computer keyboard. A correct response was followed immediately by a brief tone. The response also initiated the next trial.

Design

Subjects performed a two-interval forced-choice (2IFC) detection task in eight external noise conditions. Threshold versus external noise contrast (TvC) functions at two target performance levels were measured with two staircase procedures in each training session. TvC functions at two performance levels were measured to provide data to constrain the PTM (Dosher & Lu, 1999). The 3-down/1-up (three consecutive correct responses resulted in a reduction of contrast, $C_{n+1} = 0.9C_n$; one wrong response resulted in an increase in contrast, $C_{n+1} = 1.1C_n$) and 2-down/1-up staircases (two consecutive correct responses resulted in a reduction of contrast, $C_{n+1} = 0.9C_n$; one wrong response resulted in an increase in contrast, $C_{n+1} = 1.1C_n$) converged to 79.3% and 70.7% correct performance levels, respectively (Levitt, 1971). For each staircase, the threshold for grating detection in each external noise condition was estimated from the reversals of the corresponding staircase. 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 of the remaining reversals was taken as the contrast threshold for grating detection. Typically 10 or more reversals per staircase were averaged.

Subjects ran 1152 trials in each session, consisting of 144 trials per external noise level with 80 trials per 3-down/1-up staircase and 64 trials per 2-down/1-up staircase. These 16 staircases were intermixed. Data were collected from at least 6 sessions for the amblyopic group and 8 sessions for the normal subjects. Observers were given instruction trials before data collection. Each session took about 45 minutes.

Fitting Procedure

A least square procedure was used to fit the PTM to the TvC functions (Equation 2). Following Dosher and Lu (1998, 1999), the empirical TvC functions from each of two training sessions were averaged and fit by the model. $A_a(1)$, $A_f(1)$, and $A_m(1)$ were all set to 1.0. For those subjects who participated in six sessions of training, the full model had a total of ten parameters: N_a, N_m, β, γ, $A_a(2)$, $A_a(3)$, $A_f(2)$, $A_f(3)$, $A_m(2)$, and $A_m(3)$. For those who participated in eight sessions of training, the full model had three additional parameters: $A_a(4)$, $A_f(4)$, and $A_m(4)$. The additional parameters are necessary to model the data from the two additional training sessions.

Four forms of the PTM-based models were considered: (1) one model with no change of any learning parameter with training (all $A_a = A_f = A_m = 1$), (2) two models with single mechanisms of learning (change of A_a or A_f), (3) one model with a mixture of two mechanisms (change of

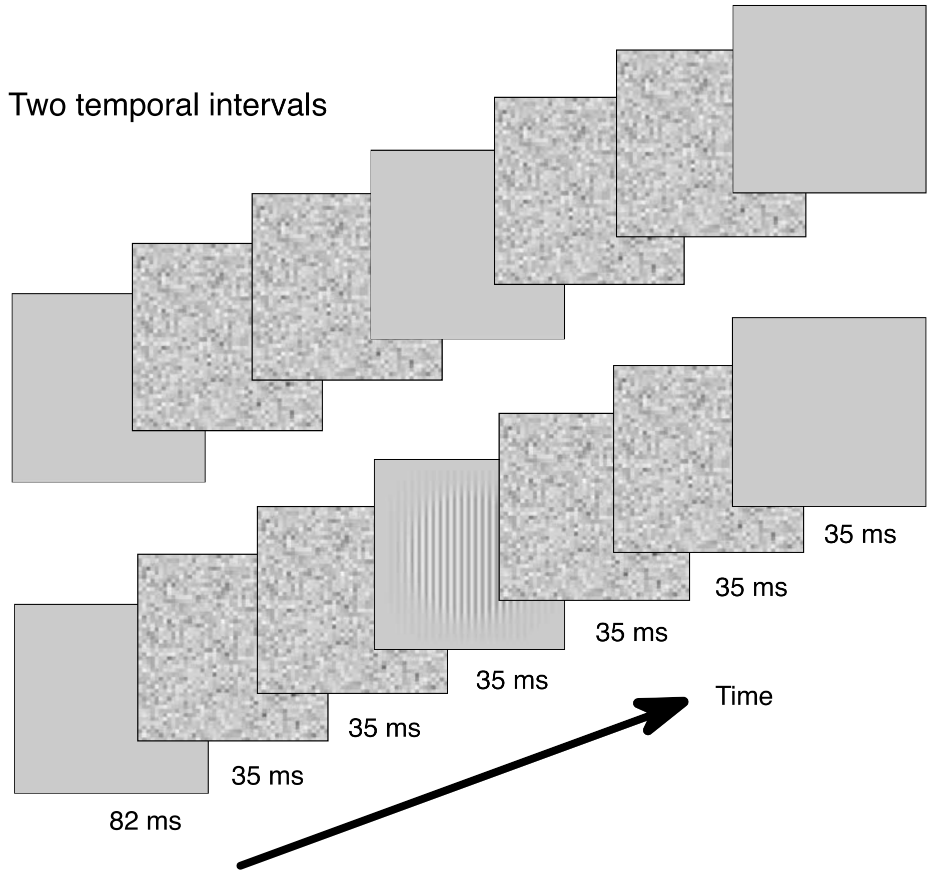

Figure 1. A typical trial sequence. Each trial began with an 83-ms fixation cross in the center of the display, followed by two intervals of 175 ms each, separated by a 500-ms blank screen. Both intervals consisted of five 35-ms images: two external noise frames, one signal or blank frame and another two noise frames. All external noise frames were independently sampled.

both A_a and A_f), and (4) one full model in which all three mechanisms are involved in learning. We did not consider A_m-related versions of the PTM and treated A_a and A_f mixture model as the fullest model because the threshold ratio between two criterion performance levels is essentially constant across eight noise levels and training sessions (see below), indicating that practice did not alter multiplicative noise or contrast gain-control properties of the perceptual system (Dosher & Lu, 1998; Lu & Dosher, 1999).

For each model form, the fitting procedure minimized the least square difference between the log of the measured threshold contrasts (c_t) and the log of the model-predicted thresholds (c_t^{therory}). The log approximately equates the standard error over the large range of contrast thresholds, corresponding to weighted least squares and equivalent to the maximum likelihood solution for continuous data. The goodness of fit is gauged by the r^2 statistic:

$$r^2 = 1.0 - \frac{\sum[\log(c_t^{\text{theory}}) - \log(c_t)]^2}{\sum[\log(c_t) - \text{mean}(\log(c_t))]^2}. \tag{3}$$

Different variants of the models were compared using an F-test for nested models (Hays, 1988):

$$F(\mathrm{d}f_1, \mathrm{d}f_2) = \frac{(r^2_{\text{full}} - r^2_{\text{reduced}})/\mathrm{d}f_1}{(1 - r_{\text{full}}{}^2)/\mathrm{d}f_2}, \tag{4}$$

where $\mathrm{d}f_1 = k_{\text{full}} - k_{\text{reduced}}$ and $\mathrm{d}f_2 = N - k_{\text{full}}$. The k's are the number of parameters in each model, and N is the number of data points.

Results

TVC functions

Contrast thresholds at two criterion performance levels (Pc = 79.3% and Pc = 70.7%) were measured in eight external noise conditions. TvC functions of individual amblyopic subjects, averaged over every two training sessions, are shown in Figure 2. Average TvC functions across all observers in the amplyopia and normal groups are shown in Figure 3, also pooled over every two training sessions.

For the amblyopia group, manipulating the contrast of external noise resulted in significant changes in contrast threshold. Averaged across subjects and training sessions, contrast thresholds ranged from 0.11 at the lowest external noise level to 0.29 at the highest external noise level. As expected, the more stringent criterion performance level (79.3%) required higher thresholds than the less stringent criterion performance (70.7%). Threshold ratio between the two criterion performance levels is essentially constant across eight external noise levels and training sessions (mean = 1.35, *SE* = 0.025): Using a repeated measure ANOVA with both training sessions and external noise levels as within-subject factors, we found that the threshold ratio between the two performance levels was not significantly affected by external noise level ($F(7,42) = 0.899$, $p > 0.50$), training session ($F(2,12) = 1.029$, $p > 0.35$), and only marginally affected by their interaction ($F(14,84) = 1.609$, $p = 0.09$). Ratio constancy across external noise and practice levels indicates that training did not alter the multiplicative noise or the contrast gain-control properties of the perceptual system (Dosher & Lu, 1998; Lu & Dosher, 1999).

For the average observer of the amblyopia group, significant threshold reduction was observed across all

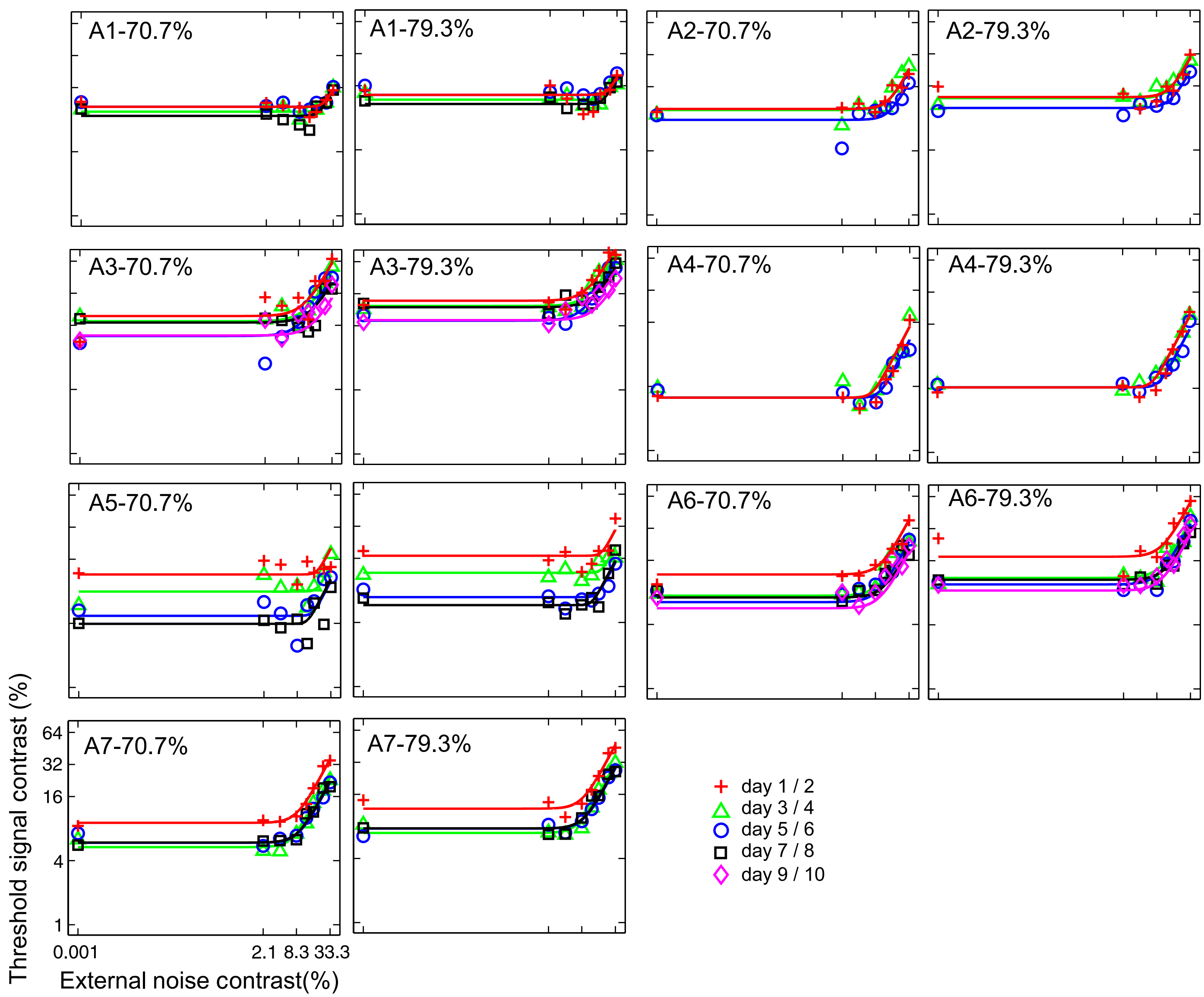

Figure 2. Threshold contrast vs. external noise contrast functions (TvC) of individual amblyopic subjects (A1–A7). Each curve represents data averaged from 2 training sessions. The 3/1 staircase corresponds to 79.3% correct; 2/1 staircase corresponds to 70.7% correct. Smooth curves represent TvC functions generated by the best-fitting PTM model.

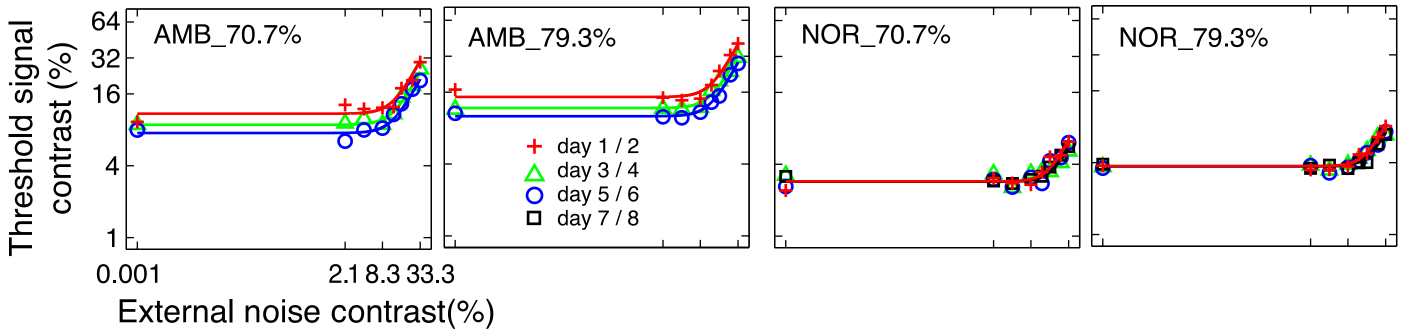

Figure 3. Threshold contrast vs. external noise contrast functions (TvC) for the average observer in Group I (amblyopia) and Group II (normal). Each curve represents data averaged from 2 training sessions. The 3/1 staircase corresponds to 79.3% correct; 2/1 staircase corresponds to 70.7% correct. Smooth curves represent TvC functions generated by the best-fitting PTM model. For Group I (amblyopia), data from the first six sessions are included. For Group II (normal), data from eight training sessions are included.

the external noise conditions over six training sessions. Averaged over observers, criterion performance level and external noise levels, contrast thresholds decreased 29.1% (range: 13.5–50.4%) from the first day to the sixth day of training. The pattern was found in five out of the seven subjects. Significant threshold reduction was only found in the low external noise conditions for subject A1 and high external noise levels for subject A4. Significant performance improvement in all noise levels signifies a combined mechanism (changes in both additive noise and the ability to exclude external noise) while improvement only in low noise or high noise conditions provided an empirical demonstration of single mechanism of perceptual learning that operates only in the presence of small or large amounts of external noise.

For the normal group, contrast thresholds increased 1-fold or so as external noise increased, from about 0.033 to 0.065 averaged over training sessions. Again, the more stringent performance criterion (79.3%) required higher thresholds than the less stringent one (70.7%). Threshold ratio between the two criterion levels is also constant across the eight external noise levels and training sessions (mean = 1.31, *SE* = 0.028): Using a repeated measure ANOVA with both training sessions and external noise levels as within-subject factors, we found that the threshold ratio between the two performance levels was not significantly affected by external noise level ($F(7,28) = 1.478$, $p > 0.20$), training session ($F(3,12) = 0.989$, $p > 0.40$), and their interaction ($F(21,84) = 1.335$, $p > 0.10$). The result indicates that training did not alter the multiplicative noise or the contrast gain-control properties of the perceptual system (Dosher & Lu, 1998; Lu & Dosher, 1999).

For normal observers, no significant threshold reduction was observed in the low external noise conditions over 8 days of practice. The average threshold in the lowest four external noise conditions reduced only about 5.8%. On the other hand, small yet significant threshold reduction was observed in the high external noise conditions over 8 days of practice: The average threshold in the highest four external noise conditions reduced about 11.6% (range: −0.1% to 17.8%). Two subjects showed no learning following 8 days of practice; the other 3 exhibited a pattern that is similar to the average observer, i.e. significant learning was found only in high external noise conditions.

The thresholds were significantly higher in the amblyopic group than in the normal group before training at both the more stringent performance level (79.3%; $F(1,10) = 9.828$, $p < 0.025$) and the less stringent performance level (70.7%; $F(1,10) = 7.846$, $p < 0.025$). This remains after training: $F(1,10) = 10.061$, $p < 0.01$ at 79.3% correct, and $F(1,10) = 8.014$, $p < 0.025$ at 70.7%. Averaged over two performance levels and noise conditions, the average threshold ratio between the amblyopic group and the normal group is 3.96 before training, and 3.17 after training. These results indicated that there were uncured deficits in the amblyopic visual system after 6–8 days of training.

PTM modeling

In the amblyopia group, a mixture of stimulus enhancement and external noise exclusion was identified as the mechanism of perceptual learning underlying the observed performance improvements for five out of the seven subjects and the average observer. Accounting for 97.8% of the variance of the average observer, this model is superior to all its reduced forms (one $0.05 < p < 0.10$; one $p < 0.05$; all other $p < 0.001$). Stimulus enhancement was identified as the mechanism of perceptual learning for subject A1: the model provided statistically equivalent fit to the fullest model ($p > 0.10$) and is superior to the model that assumed no perceptual learning at all ($p < 0.01$). External noise exclusion was identified as the mechanism of perceptual learning for subject A4: the model is statistically equivalent to the fullest model ($p > 0.10$)

	A1	A2	A3	A4	A5	A6	A7	Average
N_a	0.011 ± .004	0.039 ± .005	0.068 ± .079	0.001 ± .003	0.001 ± .002	0.039 ± .045	0.021 ± .003	0.053 ± .006
N_m	0.47 ± 0.06	0.00 ± 0.01	0.00 ± 0.01	0.47 ± 0.07	0.59 ± 0.07	0.39 ± 0.04	.00 ± 0.01	0.00 ± 0.01
β	2.44 ± 0.28	1.55 ± 0.19	0.59 ± 0.07	2.58 ± 0.41	1.87 ± 0.24	1.04 ± 0.14	0.98 ± 0.11	1.20 ± 0.10
γ	3.16 ± 0.40	1.68 ± 0.21	1.21 ± 0.27	2.65 ± 0.31	4.06 ± 0.58	1.46 ± 0.19	1.56 ± 0.15	1.40 ± 0.14
$A_f(2)$		1.04 ± 0.15	0.83 ± 0.15	0.99 ± 0.12	0.69 ± 0.09	0.68 ± 0.08	0.68 ± 0.08	0.81 ± 0.09
$A_f(3)$		0.75 ± 0.09	0.76 ± 0.10	0.75 ± 0.09	0.50 ± 0.06	0.63 ± 0.08	0.60 ± 0.07	0.71 ± 0.08
$A_f(4)$			0.64 ± 0.08		0.51 ± 0.06	0.53 ± 0.06	0.62 ± 0.08	
$A_a(2)$	0.72 ± 0.07	0.96 ± 0.10	0.87 ± 0.07		0.22 ± 0.03	0.51 ± 0.06	0.44 ± 0.05	0.74 ± 0.08
$A_a(3)$	1.05 ± 0.15	0.67 ± 0.07	0.59 ± 0.08		0.03 ± 0.04	0.42 ± 0.05	0.51 ± 0.06	0.59 ± 0.07
$A_a(4)$	0.54 ± 0.05		0.84 ± 0.10		0.01 ± 0.01	0.48 ± 0.05	0.51 ± 0.06	
r^2_full	0.874	0.900	0.898	0.935	0.829	0.935	0.973	0.978
r^2_red	0.800	0.802	0.798	0.893	0.357	0.724	0.809	0.859
$r^2\_A_a$	0.866	0.847	0.841	0.893	0.760	0.837	0.863	0.920
$r^2\_A_f$	0.815	0.879	0.883	0.935	0.578	0.906	0.959	0.954
*F*_full red	2.873*	9.550‡	8.647*	6.331‡	24.30‡	28.52‡	54.68‡	53.09‡
*F*_full A_a	0.637	10.35‡	9.801‡	12.66‡	7.054‡	26.34‡	73.57‡	51.78‡
*F*_full A_f	4.592†	4.032*	2.603$^{\#}$	0.001	25.87‡	7.762‡	9.932‡	21.45‡
F_A_a red	5.210†	6.007†	5.092‡	0	31.38‡	13.03‡	7.323‡	15.64‡
F_A_f red	0.968	13.13‡	13.53‡	13.31‡	9.750‡	36.19‡	67.25‡	42.41‡

Table 2. Parameters of the best-fitted PTM model for amblyopic subjects. *Note*: A_a, changes in internal additive noise; A_f, changes in the impact of external noise; full model: changes in both A_a and A_f. $A_a(1) = 1$, $A_f(1) = 1$. *$p < 0.05$; $^{\dagger}p < 0.01$; $^{\ddagger}p < 0.001$; $^{\#}0.05 < p < 0.10$.

and superior to the model that assumes no learning at all ($p < 0.01$). The parameters of the best fitting model are shown in Table 2. For the average amblyopic observer (Figure 3), perceptual learning reduced internal noise by about 40.6% and improved external noise exclusion by about 29.5% across six sessions of training. Additional practice after six training sessions did not lead to further learning in all but one subject, indicating that most of the learning effects occurred during the first six training sessions.

In the normal group, external noise exclusion was identified as the mechanism of perceptual learning for three out of the five subjects and the average observer. The model accounted for 94.1% of the variance of the

	N1	N2	N3	N4	N5	Average
N_a	0.019 ± .003	0.033 ± .005	0.038 ± .004	0.050 ± .006	0.074 ± .082	0.057 ± .007
N_m	0.48 ± 0.06	0.00 ± 0.01	0.00 ± 0.02	0.00 ± 0.01	0.00 ± 0.01	0.00 ± 0.01
β	6.36 ± 0.91	5.27 ± 0.69	5.68 ± 0.66	6.90 ± 0.81	5.36 ± 0.63	5.72 ± 0.63
γ	2.46 ± 0.30	1.74 ± 0.21	1.97 ± 0.21	1.47 ± 0.16	1.26 ± 0.16	1.54 ± 0.20
$A_f(2)$	1	0.96 ± 0.10	0.79 ± 0.08	1	0.72 ± 0.10	0.86 ± 0.10
$A_f(3)$	1	0.77 ± 0.08	0.95 ± 0.10	1	0.85 ± 0.10	0.90 ± 0.10
$A_f(4)$	1	0.88 ± 0.11	0.68 ± 0.08	1	0.86 ± 0.09	0.85 ± 0.08
$A_a(2)$	1	1	1	1	1	1
$A_a(3)$	1	1	1	1	1	1
$A_a(4)$	1	1	1	1	1	1
r^2_full	0.760	0.854	0.688	0.875	0.872	0.943
r^2_red	0.745	0.817	0.600	0.859	0.819	0.923
$r^2\_A_a$	0.760	0.819	0.615	0.861	0.845	0.925
$r^2\_A_f$	0.754	0.854	0.684	0.874	0.858	0.941
*F*_full red	0.549	2.253*	2.506*	1.116	3.627†	3.066*
*F*_full A_a		4.240†	4.133†	2.036	3.644*	5.303†
*F*_full A_f	0.434		0.239	0.239	1.881	0.449
F_A_a red	1.341	0.227	0.753	0.186	3.161*	0.673
F_A_f red	0.685	4.761†	4.977†	2.078	5.129†	5.856†

Table 3. Parameters of the best-fitting model for the normal subjects. *Note*: A_a, changes in internal additive noise; A_f, changes in the impact of external noise; full model: changes in both A_a and A_f. $A_a(1) = 1$, $A_f(1) = 1$. *$p < 0.05$; $^{\dagger}p < 0.01$.

average observer: It is statistically equivalent to the full model ($p > 0.10$) and superior to the most reduced model ($p < 0.01$). No significant learning was found in the other two subjects. The most reduced model is statistically equivalent to the fullest model ($p > 0.10$). The parameters of the best fitting model are shown in Table 3. For the average normal observer (Figure 3), perceptual learning improved external noise exclusion by about 14.9% across eight sessions of training, which is significantly less than the amount of external noise exclusion in the amblyopia group ($z = 2.91$, $p < 0.01$).

Visual acuity

For the amblyopic subjects, visual acuity in the amblyopic eyes and the fellow eyes increased 32.3% ($t(6) = 4.07$, $p < 0.01$) and 7.7% ($t(6) = 2.40$, $p < 0.05$), respectively, following 6–8 days of training on grating detection. Significant visual acuity improvement was found in the amblyopic eye of all the subjects. The magnitude of improvement in the amblyopic eye was significantly higher than that in the fellow eyes ($t(6) = 4.53$, $p < 0.01$). Visual acuity did not improve significantly for normal subjects ($t(4) = 1.50$, $p > 0.10$).

In Figure 4, we plotted visual acuity (LogMAR) in the amblyopic eye after training against that prior to training for the seven amblyopes. The best fitting linear regression line has a slope of 0.69, suggesting more visual acuity improvement for observers with worse initial acuities. The result is consistent with Li et al. (2008).

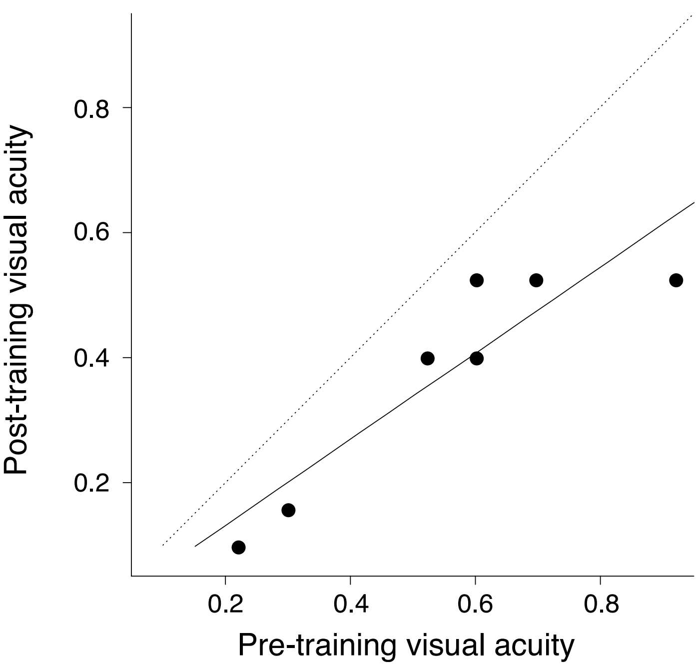

Figure 4. Post- versus pre-training LogMAR visual acuity for amblyopic subjects (Group I). The best fitting linear regression line ($r^2 = 0.91$, $p < 0.01$) has a slope of 0.69, suggesting greater improvements for subjects with initially worse visual acuities. The dashed line is the identity line with a slope of 1.

Discussion

Five out of seven amblyopic subjects improved their performance in both low and high external noise conditions, indicating a combined mechanism of internal additive noise reduction and external noise exclusion. Subject A1 learned only in low external noise conditions, signifying a pure internal noise reduction mechanism; subject A4 learned only in high external noise conditions, indicating a single mechanism of external noise exclusion. For the average amblyopic observer, the internal noise and the impact of external noise was reduced by about 40% and 30%, respectively. In the normal group, significant but modest learning was found for 3 out of 5 subjects in high external noise conditions. External noise exclusion was identified as the mechanism underlying the improvement following eight sessions of practice. The other two normal subjects exhibited no significant learning. For the average normal observer, the impact of external noise was reduced by about 15%, which was mostly accomplished during the first two training sessions. Perceptual learning also significantly improved the visual acuity of the amblyopic eyes.

The finding that perceptual learning improves contrast sensitivity and visual acuity in the amblyopic visual system via a combination of internal additive noise reduction and external noise exclusion is consistent with Li and Levi (2004) and Li et al. (2005, 2008), who found that perceptual learning enhances sampling efficiency and/or decreases internal equivalent noise in both juvenile and adult amblyopia. Xu et al. (2006) and Huang et al. (2007) found that increased additive noise and mismatched perceptual template underlay performance deficits in the amblyopic visual system, although the degree of perceptual template mismatch increased with the spatial frequency of the test stimuli. That perceptual learning reduced internal noise and improved external noise exclusion suggests that the training scheme can address both mechanisms underlying amblyopic deficits. Whereas performance improvements in high external noise conditions are potentially related to improved forward and backward masking, improved performance in all the external noise conditions may be related to improved temporal integration (Polat, 2009). On the other hand, our results also showed that 6 to 8 training sessions (1152 trials/session) is not sufficient to eliminate all the deficits in the amblyopic visual system. Recent studies by Levi et al suggest that longer training protocols may lead to larger amount of improvements (Li et al., 2007, 2008). We are conducting new experiments to improve the training protocols.

The finding that normal subjects exhibited very small amount of learning at 8 c/d in the current study is consistent with Huang et al. (2008). We found in that study that training normal subjects in a grating detection task at 10 c/d generated no performance improvements in clear displays, and training at cutoff spatial frequencies generalized more to other spatial frequencies in amblyopic than in normal adults. In the current study, we show that different mechanisms of perceptual learning underlie performance improvements in amblyopic and normal adults, and the magnitudes of internal noise reduction and external noise exclusion are more pronounced in amblyopic (40% and 30%) than normal adults (0% and 15%). Typically, learning was not observed under low external noise level (clear display) for normal subjects. These findings all point to the notion that the amblyopic visual system maybe more plastic than its normal counterpart.

Often regarded as task-independent early neural limitations, internal additive noise limits all kinds of neural processing (Pelli & Farell, 1999). Our previous studies showed that internal additive noise is highly elevated in the adult amblyopic visual system (Xu et al., 2006) and even in treated amblyopia (Huang et al., 2007). A pronounced reduction in internal additive noise enhances the signal-to-noise ratios for broadly in a wide range of channels following training. Consequently, there may be much more "room" in the amblyopic visual system that remained to be "exploited" through practice. Under this scenario, the learning effects related to decreased internal additive noise may generalize. Training at a single spatial frequency could thus benefit performance in other spatial frequencies. On the contrary, template retuning may have limited effects in relatively narrow settings. Consequently, improvements gained via perceptual template re-tuning might be more specific. In the current study, most amblyopic subjects demonstrated both internal additive noise reduction and external noise exclusion, but normal observers only exhibited external noise exclusion. This may partially explain the finding in Huang et al. (2008) that the bandwidth of perceptual learning is broader in amblyopia (4.04 octaves) than in normals (1.40 ocataves). Plasticity may be more robust in amblyopia, lending further support to the statement that perceptual learning can be used to treat amblyopia (Huang et al., 2008; Levi & Li, 2009b).

The external noise approach and the associated observer models provide a conceptual framework to analyze perceptual deficiencies and perceptual learning in the amblyopic visual system (Lu, Liu, & Dosher, in press). The theoretical constructs in the external noise approach are related to other explanations of amblyopia. The perceptual template in the PTM represents the "receptive field" at the observer level. Increased deficits in high external noise in high spatial frequency conditions suggest deficient perceptual templates in those conditions, potentially associated with miswiring of cortical neurons ("topographical jitter") in any (or all) of the stages of visual processing (Hess & Field, 1994). It is also possible that deficient perceptual templates result from subsampling of the high spatial frequency channels in the amblyopic visual system (Levi, 1991; Levi & Klein, 1985). Perceptual learning may rewire connections between neurons and therefore reduce the effect of topographic jitter (Hess & Holliday, 1992), as reflected in improved performance in high external noise. Learning may also increase sampling in amblyopic vision or reduce the lateral inhibition between neurons (Polat, 2009). All these changes may reduce the internal noise level and/or retune the perceptual template and thus improve subjects' performance. A more detailed model of the amblyopic visual system is necessary to directly relate all these potential theories of amblyopia and perceptual learning in amblyopia.

Polat (2009) proposed that contrast sensitivity is a fundamental function that reflects the output of early visual processing, representing the performance of neurons in the primary visual cortex; improvement in contrast sensitivity may facilitate visual processing in later stages. Several recent studies found that training on contrast detection can indeed lead to improved contrast sensitivity and visual acuity (Huang et al., 2008; Polat, 2008, 2009; Polat et al., 2004; Zhou et al., 2006), although Levi and Li (2009b) concluded that practicing on a variety of different tasks and stimuli seems to transfer to improved visual acuity. Whether improvements in contrast sensitivity is the bottleneck for the other visual functions is a very interesting question.

In this study, 32% visual acuity improvement was found in the trained amblyopic eyes. The magnitude of improvement is much lower than what we obtained in two previous studies that trained amblyopic subjects in clear displays near their cutoff spatial frequencies (68.4%; Huang et al., 2008; Zhou et al., 2006), although the magnitude is comparable to that obtained by other groups (Levi & Li, 2009b). The smaller magnitude of acuity improvement may have stemmed from (1) the use of a training frequency that is much lower than the cutoff spatial frequency (defined as the spatial frequency at which threshold contrast is 50%; Huang et al., 2008; Zhou et al., 2006), and/or (2) the use of external noise in the training process. Because spatial vision in amblyopia is more affected at high spatial frequencies, training at or near the cutoff spatial frequency might be more effective (Levi & Li, 2009b). Both Dosher and Lu (2005) and Lu, Chu, and Dosher (2006) showed that training in clear displays is more effective in perceptual learning.

Huang et al. (2007) found that contrast sensitivity functions in the amblyopic visual system were still abnormal 3 years after the amblyopes' visual acuities became normal. Compared to the fellow eyes, the previous amblyopic eyes still exhibited increased internal noise at low to medium spatial frequency and increases in both internal noise and impact of external noise at high spatial frequencies. It would be very interesting to train these clinically "treated" amblyopes at both clear and noisy displays to see whether the amblyopic visual system could be fully recovered.

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Footnote

[1]Our aim was to compare mechanisms of perceptual learning in the normal visual system in comparable stimulus conditions with identical training procedures. Another interesting comparison can be made by training the normal observers near their cutoff frequencies (Huang et al., 2008).

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