

Perceptual Learning Improves Visual Performance in Juvenile Amblyopia

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PURPOSE. To determine whether practicing a position-discrimination task improves visual performance in children with amblyopia and to determine the mechanism(s) of improvement.

METHODS. Five children (age range, 7–10 years) with amblyopia practiced a positional acuity task in which they had to judge which of three pairs of lines was misaligned. Positional noise was produced by distributing the individual patches of each line segment according to a Gaussian probability function. Observers were trained at three noise levels (including 0), with each observer performing between 3000 and 4000 responses in 7 to 10 sessions. Trial-by-trial feedback was provided.

RESULTS. Four of the five observers showed significant improvement in positional acuity. In those four observers, on average, positional acuity with no noise improved by approximately 32% and with high noise by approximately 26%. A position-averaging model was used to parse the improvement into an increase in efficiency or a decrease in equivalent input noise. Two observers showed increased efficiency (51% and 117% improvements) with no significant change in equivalent input noise across sessions. The other two observers showed both a decrease in equivalent input noise (18% and 29%) and an increase in efficiency (17% and 71%). All five observers showed substantial improvement in Snellen acuity (approximately 26%) after practice.

CONCLUSIONS. Perceptual learning can improve visual performance in amblyopic children. The improvement can be parsed into two important factors: decreased equivalent input noise and increased efficiency. Perceptual learning techniques may add an effective new method to the armamentarium of amblyopia treatments. (*Invest Ophthalmol Vis Sci.* 2005;46:3161–3168) DOI:10.1167/iovs.05-0286

Amblyopia is a developmental disorder of spatial vision that affects approximately 3% of the population worldwide.^{1,2} It occurs at an early age as a result of abnormal visual experience. The common causes are refractive imbalance (anisometropia),³ misalignment of the visual axis (strabismus),⁴ asymmetric meridian power (astigmatism),⁵ high refractive error,⁶ and/or form deprivation resulting from congenital cataract⁷ or ptosis.⁸ The key clinical characteristic is reduced visual acuity in the amblyopic eye without any manifest ocular disease. The

amblyope's line visual acuity is often worse than the isolated single-letter acuity—a difference known as crowding.⁹ The loss of acuity can be attributed in part to the loss of contrast sensitivity in medium and high spatial frequency (SF) mechanisms.^{10,11} The degree of binocular imbalance strongly influences the depth of amblyopia.^{3,12} In addition, amblyopes show deficits in a range of visual tasks. These include hyperacuity,^{13–16} shape perception,¹⁷ contour integration,¹⁸ spatial interaction of surrounding visual objects,^{19,20} phase sensitivity,²¹ visual counting,²² pattern vision,²³ stereopsis,²⁴ and motion-processing²⁵ deficits. Several psychophysical theories have been proposed to explain the abnormal visual perception in the amblyopic brain: (1) an increase in the size of cortical receptive fields,¹³ with the peak of the SF tuning shifted to lower spatial frequencies; (2) a decrease in the contrast sensitivity of small cortical filters^{10,11}; (3) a decrease in the density of cortical neurons (i.e., undersampling)²⁶; and (4) an increase in spatial uncertainty or distortion, with the neural representation of the visual image being somewhat distorted at the cortical level.^{26–29} Recent studies have shown that the loss of binocular vision may be critical in the development of amblyopia.^{30,31}

Amblyopia is often said to be irreversible beyond the critical age. Thus, treatment for amblyopia is commonly undertaken only in children younger than 10 years (usually younger than 6).³² However, recent studies have shown that occlusion therapy can be successful, even when initiated between 9 and 15 years of age.^{33,34} There is now considerable evidence that the mature amblyopic brain retains a certain degree of plasticity.^{35–39} The standard amblyopia therapy over the past four centuries has consisted of penalizing the preferred eye with an eye patch or atropine,⁴⁰ thus forcing the brain to use visual signals from the amblyopic eye. The response to occlusion therapy is related to the type and the depth of amblyopia.^{41,42} As visual acuity improves, all aspects of amblyopia, such as contrast sensitivity,⁴³ hyperacuity,⁴⁴ lateral interaction,⁴³ contour integration,⁴⁵ visual counting,⁴⁶ stereoacuity,⁴⁷ and eye movement⁴⁴ deficits normalize to a certain extent during the treatment. The recovery of acuity has been shown to be associated with an overall increase in cortical activity,⁴⁸ and the visual acuity gained in the amblyopic eye can frequently be retained for a period.^{49,50} Most recent studies attempt to standardize the time course of patching and to maximize the treatment efficacy.⁵¹ Drug treatment for amblyopia is currently being evaluated. However, the use of a neurotransmitter (levodopa) to increase the plasticity of the amblyopic brain is still controversial.^{52,53}

In a recent study, we demonstrated that perceptual learning may be a useful approach to improving visual performance in adult amblyopia.⁴⁶ We asked seven adult observers with amblyopia to practice a repetitive position-discrimination task. The observers' task was to identify the misaligned stimulus out of three stimuli (three-alternative forced choice; 3AFC). The stimulus comprised two line segments, each of eight discrete Gabor patches. Trial-by-trial feedback was provided. After practice, the participants showed substantial improvement in the trained visual task. To explore the underlying learning mechanisms, we added positional noise to the individual discrete

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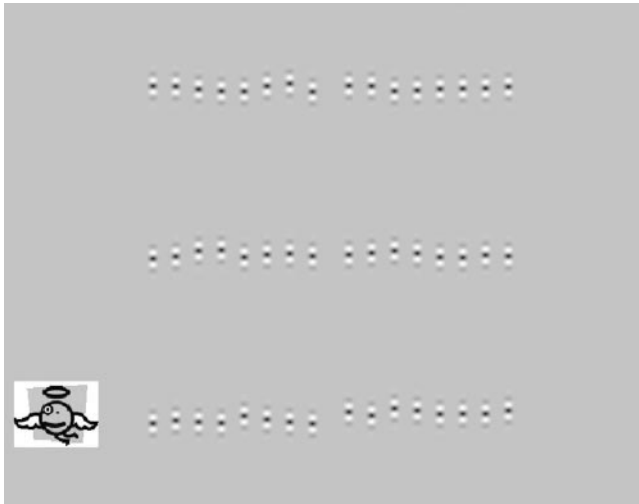


FIGURE 1. Visual stimuli with positional noise. The top stimulus is misaligned, in that the mean offset of the right segment is higher than that of the left segment. Trial-by-trial feedback was provided audiovisually. If the response was incorrect, the cartoon angel shown pointed to the correct choice with different sounds.

parts of the stimuli. We found that learning boosted the brain's ability to sample the stimulus information (i.e., improved efficiency) and lowered the equivalent internal noise levels, (i.e., decreased the internal jitter of the neural representation of the visual stimuli). The learning effects transferred to visual acuity and other higher-level visual tasks, such as counting and stereopsis. On average, the adult amblyopes showed approximately two letter lines (30% in minimum angle of resolution [MAR]) improvement in uncrowded single-letter acuity.

In the present study, we sought to determine whether positional discrimination could be improved in patients with juvenile amblyopia (between the ages of 7 and 10 years) with perceptual learning. Positional noise was used to mimic the positional noise inside the human visual system and to learn about the underlying neural mechanisms. Our purpose was to

characterize the limits of improvement for a range of noise levels and the time course of learning. To determine whether perceptual learning of a position task transfers to visual acuity, we monitored the change in visual acuity during the course of training. Our ultimate goal is to develop more effective and efficient techniques for amblyopia treatment, which is currently based almost entirely on passive occlusion of the preferred eye, in clinical settings.

METHODS

Visual Stimuli

In this study, we used an experimental setup similar to that in our previous studies⁴⁶ to measure the positional-discrimination threshold. The stimulus comprised two line segments with a 34-arcmin gap between the two segments (Fig. 1). Each segment consisted of eight Gabor patches (carrier SF, 5 cyc/deg), and the patch separation was 21.3 arcmin. The Gaussian envelope standard deviation of each Gabor patch was 2.5 and 7.5 arcmin for the horizontal and vertical orientations, respectively. The mean luminance of the stimuli was 55 cd/m², and the contrast of each Gabor patch was 99%. Light shielding was used to block stray light from the monitor screen. Positional noise was produced by distributing the position of each Gabor patch in the vertical direction according to a Gaussian probability function. The average offset of each jittered segment was forced to be zero by uniformly shifting the eight patches. An offset was produced by randomly shifting the right segment up or down.

Observers and Procedures

Five young amblyopes, aged from 7 to 10 years (mean age, 8.5 years), were tested with full optical corrections. Table 1 shows the clinical data of individual observers. Note that all had previously undergone occlusion therapy. Viewing was monocular; the eye not being tested was occluded with a standard black eye patch. The observer's head was not constrained by a headrest, but careful attention was paid to keeping the head straight. The data collection for each observer was completed in approximately 4 weeks. Each session took approximately 2 hours (including breaks). None of the observers had any prior experience in psychophysical experiments. The research adhered to the tenets of the Declaration of Helsinki. The experiments were un-

TABLE 1. Clinical Data

Observer	Age (y)	Gender	Type	Strabismus (Dist)	Eye	Refractive Error	Line Letter Acuity (Single Letter Acuity)	Prior Treatment
BB	8.25	M	Strab	L 12 ^Δ EsoT	R L	+5.00/−0.50 × 180 +6.00/−0.50 × 180	20/20 ⁺² 20/40 (20/40 ⁺²)	Occlusion therapy for 4 months, then fusional and antisuppression training for another 4 months. VA 20/40 (linear Lea); no improvement.
JN	7.13	M	Strab, Aniso	R 16 ^Δ EsoT	R L	+7.00/−1.50 × 165 +4.00/−0.50 × 180	20/100 (20/63 ⁺²) 20/25	Occlusion therapy for a year. VA (linear Lea): 20/100 → 20/50 VA (single Lea): 20/50 → 20/25.
MO	8.5	M	Strab	L 35 ^Δ EsoT	R L	+3.50 +3.50	20/20 20/32 (20/25)	Occlusion therapy for 6 weeks. VA 20/25 (linear Lea); no improvement.
AH	8.63	F	Strab	R 20 ^Δ EsoT R 5 ^Δ HyperT	R L	+6.00/−1.00 × 90 +6.00/−0.50 × 90	20/100 ⁺² (20/40 ^{−2}) 20/20 ⁺²	Occlusion therapy.
CL	10	F	Aniso	None	R L	−0.12/−1.50 × 180 +3.25/−1.12 × 165	20/20 ⁺² 20/40 ^{−1}	Occlusion therapy.

In the present study, the Bailey-Lovie chart was used for visual acuity measurement. The visual acuity data of the prior treatments were based on the Lea chart. Strab, strabismus; aniso, anisometropia; eso, esotropia; hyper, hyperopia.

dertaken with the understanding and written consents of all juvenile observers and their parents, and all procedures were approved by institutional review.

When testing and training the amblyopic eye, we chose the viewing distance to be approximately proportional to the observer's visual acuity. Three observers (CL, MO, and BB) were tested at 2 m (carrier SF, 5 cyc/deg; Gaussian SD, 2.5 [H] and 7.5 [V] arcmin; gap 34 arcmin). The other two observers (JN and AH) were tested at 1 m, so that the angular dimensions of the stimuli were proportionally larger (carrier SF, 2.5 cyc/deg; Gaussian SD, 5 [H] and 15 [V] arcmin; gap 68 arcmin). When testing the nonamblyopic eye, we maintained the same viewing distance as for the amblyopic eye, except for the testing of observer CL in whom the nonamblyopic eye was tested at 4 m (carrier SF, 10 cyc/deg; Gaussian SD, 1.25 [H] and 3.75 [V] arcmin; gap, 17 arcmin). To take into account the different viewing distances, we specified the noise and the threshold in units of the patch carrier SF (i.e., λ units).

Psychophysical Methods

A 3AFC paradigm was used to measure position discrimination. The observer's task was to indicate the position of the misaligned stimulus (top, middle, or bottom). Stimuli remained on the monitor screen until the observer had responded. Trial-by-trial feedback was provided audiovisually. If the response was correct, a popup box with a check (\checkmark) would appear on the computer screen accompanied by a verbal response (e.g., "excellent," "good job") and a sound (e.g., "clapping"), to keep the child engaged. For an incorrect response, a cartoon angel (see Fig. 1) would point to the correct choice with different sounds (e.g., "oops," "sorry"). A modified interleaved staircase method was used to control the offset level and to track the individual thresholds.⁴⁶ A Weibull analysis was performed to fit the psychometric curve to the response data. The position-discrimination threshold was defined as the offset at which 66% correct responses were obtained (detectability $d' = 1.1^{54}$). A session consisted of 396 responses (132 responses for each noise setting).

Noise Modeling

A positional averaging model⁵⁵ was used to quantify the effects of external positional noise (σ_c) on the threshold (σ_{th}):

$$\sigma_{th}^2 = 2d'^2 \left(\frac{1}{k} - \frac{1}{n} \right) (\sigma_c^2 + \sigma_i^2) \quad (1)$$

where k denotes the number of samples extracted per segment, n is the number of samples (i.e., eight) in each segment, and σ_i is the equivalent input noise. By measuring the thresholds in different external noise settings, both σ_i and k can be estimated by fitting a threshold versus noise (TvN) curve on the basis of a least-squares computation.

Equivalent input noise is the noise that must be added to the stimulus to mimic the limiting noise in the visual system. It largely reflects the amount of noise the observer's visual system adds to the stimulus and quantifies the spatial distortion of the visual space. When external stimulus noise is small compared with equivalent input noise, threshold is determined mainly by equivalent input noise. As the stimulus noise increases and equals the equivalent input noise in magnitude, the threshold begins to rise in proportion to stimulus noise level. Sampling efficiency (E) reflects the computation underlying the use of the information (samples) of the stimulus. In other words, it is a measure of how many samples are extracted from the stimulus for positional averaging, and was defined as:

$$E = \frac{k}{n} \cdot 100\% \quad (2)$$

RESULTS

Figure 2 shows that the pretraining positional thresholds of the amblyopic eye, especially for zero and intermediate noise lev-

els (blue solid line), were significantly and substantially elevated when compared with the fellow nonamblyopic eye (blue dashed line). For all observers, the amblyopic eye approached the nonamblyopic eye when the noise level was high. Our observers were tested with different spatial scales according to their visual acuity levels. Therefore, the threshold is plotted in λ units (wavelength of Gabor patches), to facilitate the comparison between individual observers.

Our primary interest was to quantify the effect of perceptual learning in the amblyopic eyes. We found that, with practice, four of the five observers (JN, CL, AH, and MO) showed marked improvement in positional acuity; however one observer (BB) showed no improvement across sessions (Fig. 2). Note that the number of sessions varied among the observers. For clarity, we divided the threshold data of the amblyopic eye into four session groups. For the four observers who improved, positional acuity with no noise improved on average by approximately 32% and with intermediate and high noise by approximately 25% and 26%, respectively. The mean data of those four observers is shown in Figure 2 (bottom right). At the highest noise level, the improved posttraining performance of the amblyopic eye was almost comparable with that of the fellow preferred eye. Figure 3A shows a summary of pre- versus posttraining performance for all noise levels (zero, intermediate, and high). The posttraining threshold was defined as the mean threshold of the last two to four sessions (after performance became asymptotic). The data of amblyopic adults (gray symbols) is plotted in the figure (and in the subsequent figures) for comparison. The area below the dashed grey 1:1 line represents posttraining performance being better than the pretraining performance. The overall means of the individual improvements across all three noise levels were $19.2\% \pm 5.5\%$ (solid black line) and $23.4\% \pm 2.7\%$ (solid gray line) for juvenile and adult amblyopes, respectively. The mean improvement was approximately the same in both observer groups, suggesting similar limits of learning. We noted that the largest improvement was as high as 50%, and it is important to note that one observer did not show any learning effect.

To explore the neural mechanisms underlying perceptual learning, we used a position averaging model (equation 1) to fit the threshold data in Figure 2 and to parse the improvement into an increase in efficiency or a decrease in equivalent input noise. The reduced performance in the amblyopic eye (before perceptual learning) can be explained by the elevated internal positional noise and/or the reduced sampling efficiency (Figs. 4A, 4B). The mean equivalent input noise was 0.027 and 0.083 λ for the preferred and amblyopic eyes, respectively. The mean efficiency was almost the same (approximately 3.5%) in both the preferred and the amblyopic eyes; however, one observer (AH) showed markedly reduced sampling efficiency in the amblyopic eye (2.09%) compared with the fellow preferred eye (3.13%). The data of adult amblyopes⁴⁶ (gray open circles) are included in the figure; the large black open circles shows the mean data of all juvenile and adult observers.

There were important individual differences in the pattern of perceptual learning. With training, two observers (JN and CL) showed increased efficiency (51% and 117% improvement) with no significant change in equivalent input noise across sessions (Figs. 4C, 4D). Their TvN curves gradually shifted downward across sessions (Fig. 2). This improvement is seen in Figure 4C, as no change in pre- versus posttraining internal noise (data near 1:1 line) and in Figure 4D as a substantial increase in efficiency (above 1:1 line). We note that for observer CL the posttraining performance approached the performance levels of the fellow nonamblyopic eye. Two observers (MO and AH) showed both a decrease in equivalent input noise (18% and 29%) and an increase in efficiency (17% and

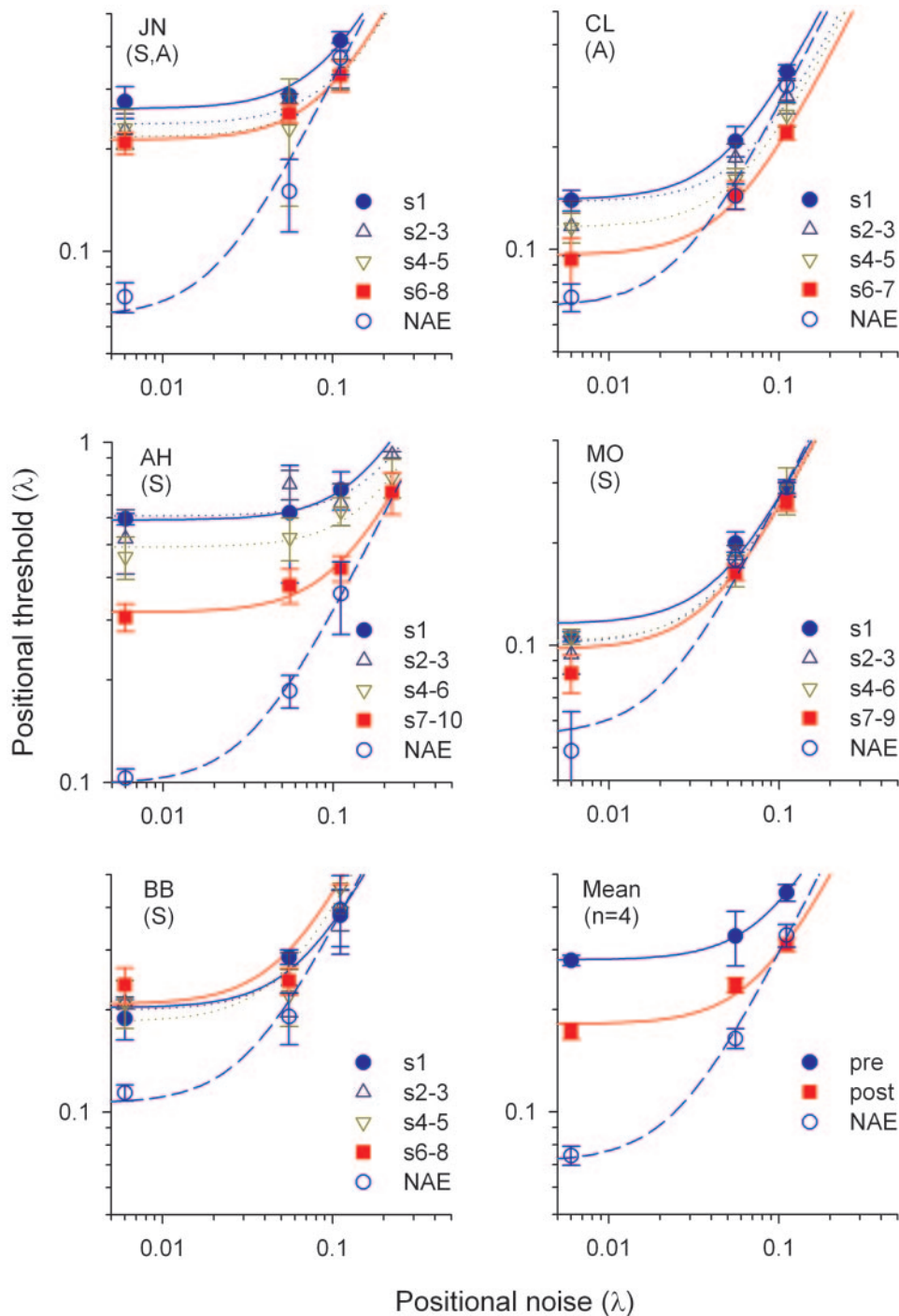


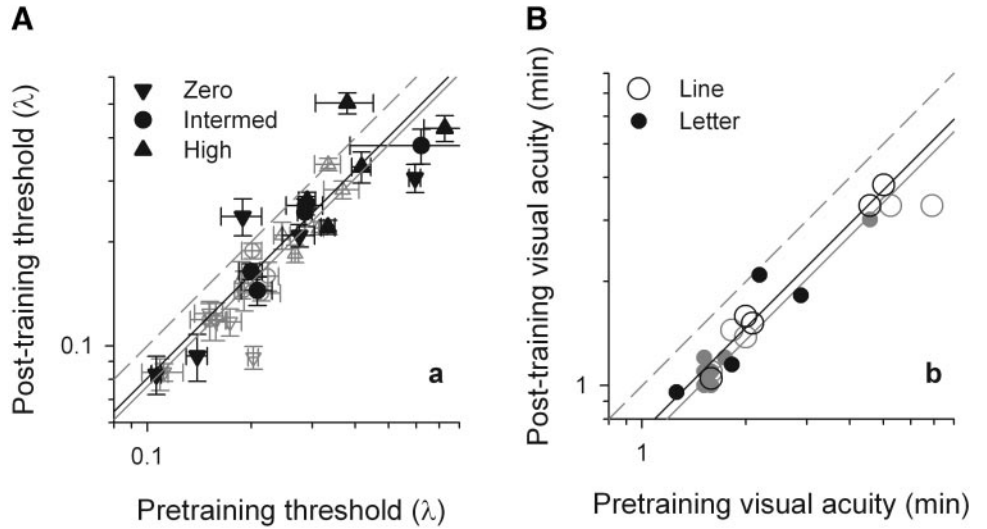
FIGURE 2. The positional discrimination thresholds in λ units for different positional noise settings across training sessions. The number of sessions varied among the observers. For clarity, the threshold data of the amblyopic eye were divided into four session groups. Each data point, except those for session 1, represents the threshold averaged across two to four sessions. Error bar, SE of the mean threshold. *Blue open circle*: data for the nonamblyopic eye (NAE). The type of amblyopia is indicated in parenthesis below the observer's initials: S, strabismic; A, anisometropic. Three observers (CL, MO, and BB) were tested at 2 m, and the other two observers (JN, and AH) were tested at 1 m.

71%; Figs. 4C, 4D). The TvN curves gradually shifted downward, and the knee points of the curves gradually shifted leftward across sessions (Fig. 2). The adult amblyope data⁴⁶ are also replotted in Figures 4C and 4D (gray open circles), and the large black open circles show the mean data of all juvenile and adult observers. On average, the equivalent input noise decreased from 0.078 to 0.066 λ (16%), and the efficiency increased from 7% to 9% (28%).

After the practice of position discrimination, there was an important generalized transfer of learning effects to an untrained letter-recognition task. Figures 5A and 5B show the line and single-letter acuities across training sessions. We recorded the session-to-session visual acuity in three observers (JN, AH,

and CL) and found that, in general, their visual acuity normalized gradually with training sessions. To avoid the potential training effects of repeatedly recognizing the letters on the chart, we measured visual acuity only before and after the entire learning experiment was completed by the other two observers (BB and MO). There were important individual variations. Observers JN, BB, and MO showed as much as a 35% improvement (about two letter lines on the Bailey-Lovie chart). In contrast, observer AH showed only enhancement (28%) in line acuity, but not in single-letter acuity, indicating that although the resolution was unchanged, the crowding effect was reduced. On average, our observers showed a $27\% \pm 2\%$ and $26\% \pm 6\%$ improvement in line and single-letter acuities, re-

FIGURE 3. (A) Summary of pre- and posttraining positional discrimination threshold. Data points show the threshold data for zero, intermediate, and high noise levels. The data of adult amblyopes⁴⁶ (gray symbols) is included in the figure. *Black and gray lines*: the overall means of the individual improvements across all three noise levels, for juvenile and adult amblyopes, respectively. *Gray dashed line*: 1:1 line. (B) Summary of pre- and posttraining visual acuity. The data points represent line and single-letter acuities. Single-letter acuity data were not obtained for observer CL.



spectively. Asymptotic performance was obtained in approximately 7 to 10 sessions. We did not obtain single-letter acuity data for observer CL.

It is worth noting that even though single-letter acuity improved gradually with practice, most observers still showed crowding (i.e., their line letter acuity was still worse than their

single-letter acuity). After practice, observer MO obtained 20/20 acuity (line and letter acuities) in both the amblyopic and preferred eyes; however, the positional discrimination threshold in his trained amblyopic eye was still much worse than that in the fellow preferred eye. We note that MO was a mild amblyope (visual acuity 20/25–20/32) to begin with. Sim-

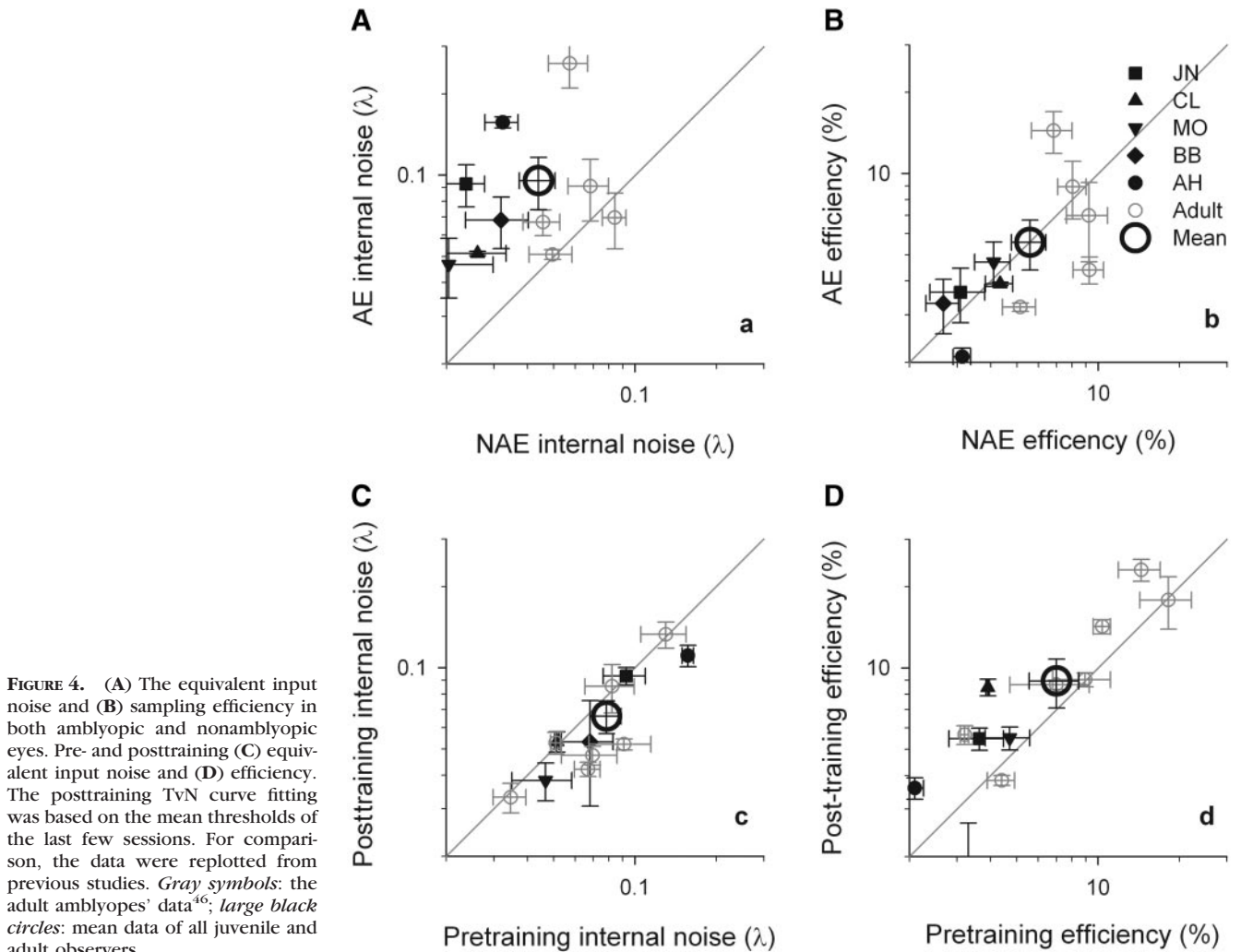


FIGURE 4. (A) The equivalent input noise and (B) sampling efficiency in both amblyopic and nonamblyopic eyes. Pre- and posttraining (C) equivalent input noise and (D) efficiency. The posttraining TvN curve fitting was based on the mean thresholds of the last few sessions. For comparison, the data were replotted from previous studies. *Gray symbols*: the adult amblyopes' data⁴⁶; *large black circles*: mean data of all juvenile and adult observers.

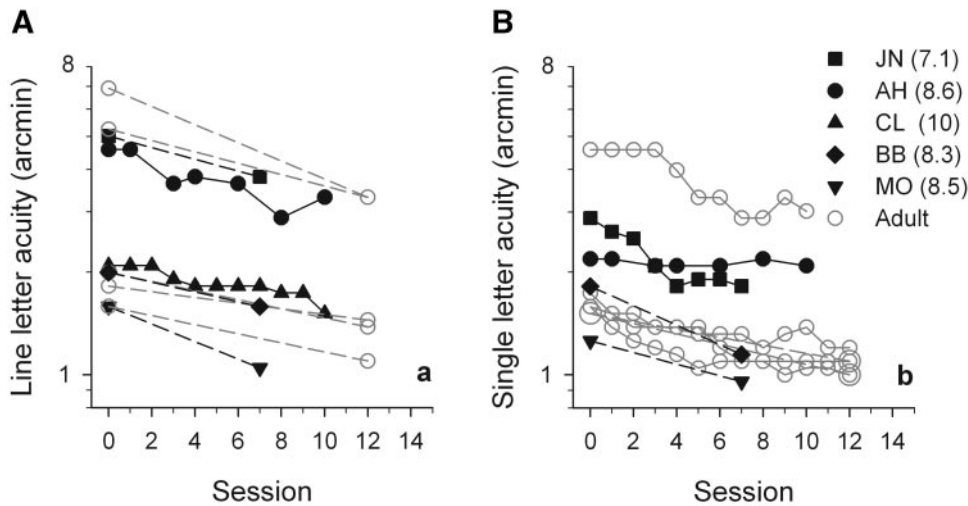


FIGURE 5. (A) Line and (B) single-letter acuities across training sessions. The acuity data of adult amblyopes from a recent study⁴⁶ (gray open symbols) are shown. The ages of the observers are shown in parentheses. For several observers, the measurement of visual acuity was performed only before and after the entire learning experiment.

ilarly, in a previous study⁵⁶ several older observers had visual acuity of 20/20 or better, but significantly reduced positional acuity.

To summarize, when we compared the visual acuity data of adult amblyopes from our earlier study⁴⁶ as included in Figures 3B and 5 with the visual acuity data of the juvenile amblyopes, we found that the limit of improvement in juvenile amblyopes was about the same as we had observed in adult amblyopes. The overall mean improvement of all juvenile and adult observers in letter acuity (both line and single) was approximately 30%. Figures 3A and 3B reveal that there is a close connection between positional acuity and visual acuity.^{57,58} This suggests that these visual functions possibly share the same early visual mechanisms. In an exception, one subject in the present study, and in our study of adults, showed no improvement in positional acuity but a significant improvement in visual acuity. In our previous report,⁴⁶ the adult observer had very good positional acuity (at a ceiling); however, that was not the case in the present study.

DISCUSSION

Our results show that, in general, the visual performance in children with amblyopia can be substantially improved through practicing a positional discrimination visual task repetitiously. Our use of positional noise, combined with a simple noise model, enables us to identify the underlying neural mechanisms for perceptual learning. Four of the five observers showed enhancement of sampling ability after practice, allowing the amblyopic brain to extract more relevant stimulus information for position processing. Two observers also showed a reduction of equivalent internal noise, contributing to the recalibration of the spatially distorted visual system. There was a generalized transfer of learning effects to an untrained letter-recognition task, resulting in as much as a 2-line improvement. We note that there were individual differences in learning. One of the five juvenile observers did not show any change in positional acuity across sessions. Although he was highly motivated, his pretraining positional threshold could not be lowered through practice. It is not clear why this observer did not show any learning effect. We note that he had a very high level of internal noise. We suspect that the nonresponsiveness may be due to some physiological limitations, such as less malleable synaptic connections. It may be that the higher the level of internal noise, the more practice is needed to trigger neuronal changes.

Our initial speculation was that the developing brain in children may be more plastic and more malleable than that of adults. The extent to which visual acuity improves in juvenile amblyopes was unexpectedly about the same as we found in adult amblyopes in our previous study.⁴⁶ There are some differences between these two studies. In our recent study, adult observers performed 750 trials (almost twice as many as juvenile observers in the present study) in longer sessions (approximately 2.5 hours). Because it is difficult for children to maintain attention in a demanding task for such a long time, we asked the children to perform only 400 trials per session. The minimum amount of practice needed to trigger the learning-related neural changes is not clear. To apply this technique clinically to treat amblyopia, it will be necessary to determine the dose-response for perceptual learning.

In this study, all observers had completed occlusion therapy before starting the experiments (Table 1). Their amblyopic vision had already improved to a certain extent after the preferred eye was patched for a long period. It is possible that the improvement would have been much greater for "fresh" (previously untreated) amblyopes. Of note, the observers BB and MO did not show any improvement in the amblyopic eye with the prior occlusion therapy, but their visual acuity improved with the practice of the position-discrimination task. Our juvenile observers showed as much as two letter lines of enhancement in visual acuity after just 20 hours of practice. Asymptotic improvement was obtained in 14 to 20 hours. Previous work with adult amblyopes also resulted in a 30% to 50% improvement in visual acuity with perceptual learning.^{43,46} We speculate that younger children of the normal treatment age (<6 years of age) may show greater perceptual learning effect.

Unlike conventional passive patching, perceptual learning is more active and intensive. Observers must attend to the fine details of the visual stimuli very carefully before making perceptual responses. Immediate feedback to the observers' responses was provided on each trial. Whenever they gave the wrong answer, they were provided enough time to inspect and determine the correct choice. Traditional orthoptics involves less active participation from the patient, and it rarely involves the element of direct feedback or a "computer game" situation of "competing for better scores." We postulate that practice with feedback allows some sort of recalibration or reweighing of disordered visual mechanisms, enabling observers to sample the stimulus information more efficiently and to reduce the uncalibrated internal position jitter. It has been suggested that learning is mediated by synaptic plasticity,⁵⁹⁻⁶¹ and perhaps

this forms the basis of cortical reweighing. However, these changes may be due in part to higher-level processes in which the observer learns to attend to the most salient information with the amblyopic eye.

Perceptual learning may be a very useful approach for treatment of amblyopia. Levi et al.^{62,63} first showed that practicing a Vernier task repetitiously can improve visual performance in adult amblyopes. One of their observers even showed a strong improvement (50%) in visual acuity after six sessions of practice. It appears that practicing other visual tasks, such as contrast detection, may also lead to the improvement of visual perception in the amblyopic eye.^{37,43} Previous studies have shown that the gained improvement in acuity with perceptual learning can be substantially maintained for a period.^{43,46} With practicing position discrimination, we found that there is a generalized improvement in performance of other untrained, higher level visual tasks.⁴⁶ The period of training is relatively brief (only 7–10 sessions) and may therefore be more practical than prolonged occlusion. All these studies support the notion that perceptual learning is a potentially useful technique to be applied in clinical situations. In future studies, the use of a combination of different visual tasks for amblyopia treatment should be considered.

Questions remain about how amblyopes improve the ability to extract stimulus information with learning. We previously reported that, in normal observers, a retuning of the behavioral receptive field or “decision” template can fully account for the improvement in visual performance.⁶⁴ This template retuning may also explain the improved efficiency of our amblyopic observers; however, we note that in contrast to normal observers, some of our amblyopes (both children and adults) also showed a reduction in internal noise.

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References

- Brown SA, Weih LM, Fu CL, Dimitrov P, Taylor HR, McCarty CA. Prevalence of amblyopia and associated refractive errors in an adult population in Victoria, Australia. *Ophthalmic Epidemiol.* 2000;7:249–258.
- Newman DK, East MM. Prevalence of amblyopia among defaulters of preschool vision screening. *Ophthalmic Epidemiol.* 2000;7:67–71.
- Weakley DR. The association between anisometropia, amblyopia, and binocularity in the absence of strabismus. *Trans Am Ophthalmol Soc.* 1999;97:987–1024.
- Adams GGW. Update on squint and amblyopia. *J R Soc Med.* 2003;96:3–6.
- Dobson V, Miller JM, Harvey EM, Mohan KM. Amblyopia in astigmatic preschool children. *Vision Res.* 2003;43:1081–1090.
- Klimek DL, Cruz OA, Scott WE, Davitt BV. Isoametropic amblyopia due to high hyperopia in children. *J AAPOS.* 2004;8:310–313.
- Thakur J, Reddy H, Wilson MEJ, et al. Pediatric cataract surgery in Nepal. *J Cataract Refract Surg.* 2004;30:1629–1635.
- Hornbliss A, Kass LG, Ziffer AJ. Amblyopia in congenital ptosis. *Ophthalmic Surg.* 1995;26:334–337.
- Simmers AJ, Gray LS, McGraw PV, Winn B. Contour interaction for high and low contrast optotypes in normal and amblyopic observers. *Ophthalmic Physiol Opt.* 1999;19:253–260.
- Levi DM, Harwerth RS. Spatio-temporal interactions in anisometropic and strabismic amblyopia. *Invest Ophthalmol Vis Sci.* 1977;16:90–95.
- Hess RF, Howell ER. The threshold contrast sensitivity function in strabismic amblyopia: evidence for a two type classification. *Vision Res.* 1977;17:1049–1055.
- Smith EL, Hung LF, Harwerth RS. The degree of image degradation and the depth of amblyopia. *Invest Ophthalmol Vis Sci.* 2000;41:3775–3781.
- Levi DM, Waugh SJ, Beard BL. Spatial scale shifts in amblyopia. *Vision Res.* 1994;34:3315–3333.
- Fronius M, Sireteanu R, Zubcov A. Deficits of spatial localization in children with strabismic amblyopia. *Graefes Arch Clin Exp Ophthalmol.* 2004;242:827–839.
- Kelly SL, Buckingham TJ. Movement hyperacuity in childhood amblyopia. *Br J Ophthalmol.* 1998;82:991–995.
- Levi DM, Klein S. Differences in vernier discrimination for gratings between strabismic and anisometropic amblyopes. *Invest Ophthalmol Vis Sci.* 1982;23:398–407.
- Levi DM, Li RW, Klein SA. “Phase capture” in amblyopia: the influence function for sampled shape. *Vision Res.* 2005;45:1793–1805.
- Hess RF, McIlhagga W, Field DJ. Contour integration in strabismic amblyopia: the sufficiency of an explanation based on positional uncertainty. *Invest Ophthalmol Vis Sci.* 1997;37:3145–3161.
- Bonneh YS, Sagi D, Polat U. Local and non-local deficits in amblyopia: acuity and spatial interactions. *Vision Res.* 2004;44:3099–3110.
- Levi DM, Hariharan S, Klein SA. Suppressive and facilitatory spatial interactions in amblyopic vision. *Vision Res.* 2002;42:1379–1394.
- Popple AV, Levi DM. Amblyopes see true alignment where normal observers see illusory tilt. *Proc Natl Acad Sci USA.* 2000;97:11667–11672.
- Sharma V, Levi DM, Klein SA. Undercounting features and missing features: evidence for a high-level deficit in strabismic amblyopia. *Nat Neurosci.* 2000;3:496–501.
- Levi D, Saarinen J. Perception of mirror symmetry in amblyopic vision. *Vision Res.* 2004;44:2475–2482.
- Walraven J, Janzen P. TNO stereopsis test as an aid to the prevention of amblyopia. *Ophthalmic Physiol Opt.* 1993;13:350–356.
- Simmers AJ, Ledgeway T, Hess RF. The influences of visibility and anomalous integration processes on the perception of global spatial form versus motion in human amblyopia. *Vision Res.* 2004;45:449–460.
- Wang H, Levi DM, Klein SA. Spatial uncertainty and sampling efficiency in amblyopic position acuity. *Vision Res.* 1998;38:1239–1251.
- Hess RF, Field DJ. Is the spatial deficit in strabismic amblyopia due to loss of cells or an uncalibrated disarray of cells? *Vision Res.* 1994;3397–3406.
- Barrett BT, Pacey IE, Bradley A, Thibos LN, Morrill P. Nonveridical visual perception in human amblyopia. *Invest Ophthalmol Vis Sci.* 2003;44:1555–1567.
- Lagreze WD, Sireteanu R. Two-dimensional spatial distortions in human strabismic amblyopia. *Vision Res.* 1991;31:1271–1288.
- McKee SP, Levi DM, Movshon JA. The pattern of visual deficits in amblyopia. *J Vis.* 2003;3:380–405.
- Murphy KM, Duffy KR, Jones DG. Experience-dependent changes in NMDAR1 expression in the visual cortex of an animal model for amblyopia. *Vis Neurosci.* 2004;21:653–670.
- Mintz-Hittner HA, Fernandez KM. Successful amblyopia therapy initiated after age 7 years: compliance cures. *Arch Ophthalmol.* 2000;118:1535–1541.
- Park KH, Hwang JM, Ahn JK. Efficacy of amblyopia therapy initiated after 9 years of age. *Eye.* 2004;18:571–574.
- Mohan K, Saroha V, Sharma A. Successful occlusion therapy for amblyopia in 11- to 15-year-old children. *J Pediatr Ophthalmol Strabismus.* 2004;41:89–95.
- Kaarniranta K, Kontkanen M. Visual recovery of the amblyopic eye in an adult patient after loss of the dominant eye. *Acta Ophthalmol Scand.* 2003;81:539.
- Simmers AJ, Gray LS. Improvement of visual function in an adult amblyope. *Optom Vis Sci.* 1999;76:82–87.
- Fronius M, Cirina L, Cordey A, Ohrloff C. Visual improvement during psychophysical training in an adult amblyopic eye following visual loss in the contralateral eye. *Graefes Arch Clin Exp Ophthalmol.* 2005;243:278–280.

38. Rahi JS, Logan S, Borja MC, Timms C, Russell-Eggitt I, Taylor D. Prediction of improved vision in the amblyopic eye after visual loss in the non-amblyopic eye. *Lancet*. 2002;360:621-622.
39. Liao DS, Krahe TE, Prusky GT, Medina AE, Ramoa AS. Recovery of cortical binocularity and orientation selectivity after the critical period for ocular dominance plasticity. *J Neurophysiol*. 2004;92:2113-2121.
40. Pediatric Eye Disease Investigator Group. The course of moderate amblyopia treated with atropine in children: experience of the amblyopia treatment study. *Am J Ophthalmol*. 2003;134:630-639.
41. Levartovsky S, Oliver M, Gottesman N, Shimshoni M. Factors affecting long term results of successfully treated amblyopia: initial visual acuity and type of amblyopia. *Br J Ophthalmol*. 1995;79:225-228.
42. Cobb CJ, Russell K, Cox A, MacEwen CJ. Factors influencing visual outcome in anisometropic amblyopes. *Br J Ophthalmol*. 2002;86:1278-1281.
43. Polat U, Ma-Naim T, Belkin M, Sagi D. Improving vision in adult amblyopia by perceptual learning. *Proc Natl Acad Sci USA*. 2004;101:6692-6697.
44. Simmers AJ, Gray LS, McGraw PV, Winn B. Functional visual loss in amblyopia and the effect of occlusion therapy. *Invest Ophthalmol Vis Sci*. 1999;40:2859-2871.
45. Chandna A, Gonzalez-Martin JA, Norcia AM. Recovery of contour integration in relation to logMAR visual acuity during treatment of amblyopia in children. *Invest Ophthalmol Vis Sci*. 2004;45:4016-4022.
46. Li RW, Levi DM. Characterizing the mechanisms of improvement for position discrimination in adult amblyopia. *J Vis*. 2004;6:476-487.
47. Richardson SR, Wright CM, Hrisos S, Buck D, Clarke MP. Stereoacuity in unilateral visual impairment detected at preschool screening: outcomes from a randomized controlled trial. *Invest Ophthalmol Vis Sci*. 2005;46:150-154.
48. Weiss AH, Kelly JP. Spatial-frequency-dependent changes in cortical activation before and after patching in amblyopic children. *Invest Ophthalmol Vis Sci*. 2004;45:3531-3537.
49. Rutstein RP, Corliss DA. Long-term changes in visual acuity and refractive error in amblyopes. *Optom Vis Sci*. 2004;81:510-515.
50. Holmes JM, Beck RW, Kraker RT, et al. Risk of amblyopia recurrence after cessation of treatment. *J AAPOS*. 2004;8:420-428.
51. Stewart CE, Moseley MJ, Stephens DA, Fielder AR. Treatment dose-response in amblyopia therapy: the Monitored Occlusion Treatment of Amblyopia Study (MOTAS). *Invest Ophthalmol Vis Sci*. 2004;45:3048-3054.
52. Bhartiya P, Sharma P, Biswas NR, Tandon R, Khokhar SK. Levodopa-carbidopa with occlusion in older children with amblyopia. *J AAPOS*. 2002;6:368-372.
53. Pandey PK, Chaudhuri Z, Kumar M, Satyabala K, Sharma P. Effect of levodopa and carbidopa in human amblyopia. *J Pediatr Ophthalmol Strabismus*. 2002;39:81-89.
54. Wickens TD. *Elementary Signal Detection Theory*. Oxford, UK: Oxford University Press; 2002
55. Zeevi YY, Mangoubi SS. Vernier acuity with noisy lines: estimation of relative position uncertainty. *Biol Cybern*. 1984;50:371-376.
56. Li RW, Edwards MH, Brown B. Variation in vernier acuity with age. *Vision Res*. 2000;40:3775-3781.
57. Levi DM, Klein SA. Hyperacuity and amblyopia. *Nature*. 1982;298:268-270.
58. Levi DM, Klein SA. Vernier acuity, crowding and amblyopia. *Vision Res*. 1985;25:979-991.
59. Ahissar E, Vaadia E, Ahissar M, Bergman H, Arieli A, Abeles M. Dependence of cortical plasticity on correlated activity of single neurons and on behavioral context. *Science*. 1992;257:1412-1415.
60. Zohary E, Celebrini S, Brittn KH, Newsome WT. Neuronal plasticity that underlies improvement in perceptual performance. *Science*. 1994;263:1289-1292.
61. Brown TH, Kairiss EW, Keenan CL. Hebbian synapses: biophysical mechanisms and algorithms. *Annu Rev Neurosci*. 1990;13:475-511.
62. Levi DM, Polat U. Neural plasticity in adults with amblyopia. *Proc Natl Acad Sci USA*. 1996;93:6830-6834.
63. Levi DM, Polat U, Hu YS. Improvement in vernier acuity in adults with amblyopia: practice makes better. *Invest Ophthalmol Vis Sci*. 1997;38:1493-1510.
64. Li RW, Levi DM, Klein SA. Perceptual learning improves efficiency by re-tuning the "template" for position discrimination. *Nat Neurosci*. 2004;7:178-183.