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Perceptual Learning in Adults with Amblyopia: A Reevaluation of Critical Periods in Human Vision

ABSTRACT: *Critical periods for experience-dependent plasticity are ubiquitous. The idea that experience-dependent plasticity is closely linked with the development of sensory function is still widely held; however, there also is growing evidence for plasticity in the adult nervous system. This article reviews the notion of a critical period for the treatment of amblyopia in light of recent experimental and clinical evidence for neural plasticity. Specifically, adults with amblyopia can improve their perceptual performance via extensive practice on a challenging visual task, and this improvement may transfer to improved visual acuity. Amblyopes achieve this improvement via the mechanisms that have been shown to explain perceptual learning in the normal visual system. It is hypothesized that these same mechanisms account for at least some of the improvement that occurs in the treatment of amblyopia. © 2005 Wiley Periodicals, Inc. Dev Psychobiol 46: 222–232, 2005.*

Keywords: *amblyopia; neural plasticity; perceptual learning; visual acuity*

SPECIFYING PERCEPTUAL SYSTEMS

The perceptual experience of human adults is extremely rich. We hear a wide range of sounds, experience a tactile world that is rich and varied, and we see a large field in living color, dynamic motion, and fine detail. However, perceptual experience is not universal. The sights and sounds are quite different for a child growing up in New York City from those of a child growing up in the Kalahari desert!

It is now clear that the world of the infant is not the “buzzing, blooming confusion” that we once thought (Held, 1984); however, it also is clear that it is not the world of the adult. And while we now know that much of the architecture of the infant nervous system is genetically specified, there is a great deal of refinement

during development (for recent reviews, see Kennedy & Burkhalter, 2004; Kiorpes & Movshon, 2004).

One of the major challenges for the development of perceptual systems is to provide sufficient specification for the development of fundamental properties of seeing, hearing, and touch and simultaneously provide sufficient flexibility to allow for some tailoring (fine-tuning) by the local environment. A second challenge is to provide sufficient flexibility to allow for the physical growth that occurs during development. For example, increases in the distance between the ears and alterations in the size of retina and eyeball along with changes in interpupillary distance over the first 4 years of life may necessitate the plasticity of cortical connections early in life.

The Role of Experience in Perceptual Development

While we are well beyond the early nature-versus-nurture debates of the last century, we are still learning about the role that experience plays in perceptual development. Moreover, it is now clear that the context for thinking about experience has changed dramatically, as our view of the neural mechanisms underlying perception have changed. Since the visual system has been and remains

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a rich test-bed for ideas about development and the role of experience, the remainder of this article is focused on the visual system.

Hubel and Wiesel's (1970) Nobel-prize-winning work showing the importance of sensory experience in shaping neural connections during a critical period early in life was inspired in large measure by the 18th-century notion that early visual deprivation (e.g., blindness at birth) resulted in brain changes that led in turn to defective visual perception (Wiesel, 1982). This remains a topic of great current interest (e.g., Fine et al., 2003). Based in good measure on the work of Hubel and Wiesel and subsequent anatomical and physiological studies, it is now clear that while the visual cortex is by no means a *Tabula Rasa*, there is a good deal of specification at birth; however, it also is clear that there is an important role for maturation and experience.

CRITICAL PERIODS IN PERCEPTUAL DEVELOPMENT

Critical periods for experience-dependent plasticity are ubiquitous. They occur in virtually every species, from *Drosophila* to human (Berardi, Pizzorusso, & Maffei, 2000), and for a wide range of sensory functions. It is now clear that there are different critical periods for different functions (even within the same sensory system; e.g., Harwerth, Smith, Duncan, Crawford, & von Noorden, (1986); Harwerth, Smith, Crawford, & von Noorden (1990)), different critical periods for different parts of the brain, even within different layers of the primary visual cortex (LeVay, Wiesel, & Hubel, 1980), and different critical periods for recovery than for induction of sensory deprivation (Berardi et al., 2000).

It has long been held that there is a close correspondence between sensory development and the critical period, and the idea is illustrated in Figure 1 (adapted from Baumgartner by Teller & Movshon, 1986). The figure shows visual functions (*sehfunktion*) developing at somewhat different rates while the developmental potential (*entwicklungspotenz* in the lower panel) dissipates. The idea that experience-dependent plasticity is closely linked with the development of sensory function is still widely held (Berardi et al., 2000); however, as we shall discuss later, there also is growing evidence for plasticity in the adult nervous system.

Critical Periods and Neural Plasticity in Human Vision

Much of the evidence for critical periods stems from work on the effects of altered sensory input in cat and monkey, in particular, monocular visual deprivation, strabismus,

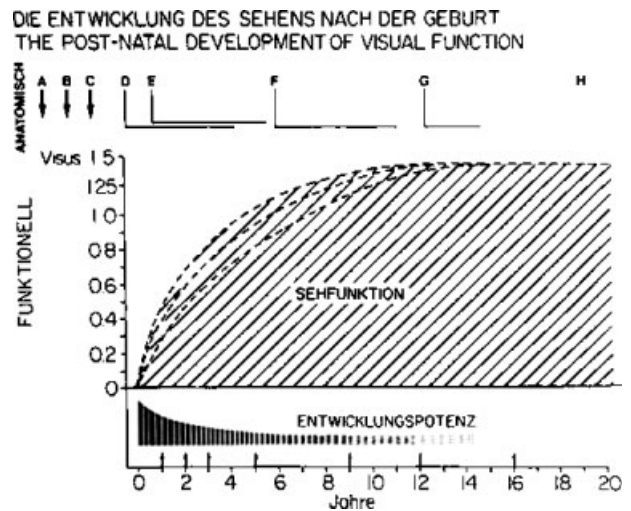


FIGURE 1 Cartoon illustrating visual functions (*sehfunktion*) developing at somewhat different rates while the developmental potential (*entwicklungspotenz* in the lower panel) dissipates. From “Visual development,” by D. Y. Teller & J. A. Movshon, 1986, *Vision Research*, 26, p. 1484. Copyright 1986 by Elsevier Press. Reprinted with permission from the authors.

or unequal refractive error (Wiesel, 1982; for a recent review, see Mitchell, 2004). If the sensory deprivation occurs early, the animal is left with a permanent visual impairment—amblyopia (from the Greek for blunt vision)—and with permanent alterations in primary visual cortex.

In humans, amblyopia occurs naturally in about 2 to 4% of the population (see Ciuffreda, Levi, & Selenow, 1991), and the presence of amblyopia is almost always associated with an early history of abnormal visual experience: binocular misregistration (*strabismus*) or image degradation (high refractive error, *anisometropia*, cataract, or form deprivation). The severity of the amblyopia appears to be associated with the degree of imbalance between the two eyes (e.g., dense unilateral cataract results in severe loss) and to the age at which the amblyogenic factor occurred. Precisely how these factors interact is as yet unknown, but it is now clear that different early visual experiences result in different functional losses in amblyopia (McKee, Levi, & Movshon, 2003), and a clear and significant factor that distinguishes performance among amblyopes is the presence or absence of binocular function.

Critical Periods for the Development of Amblyopia

Clinicians are well aware that amblyopia does not develop after age 6 to 8 years of age (von Noorden, 1981; Worth, 1903), suggesting that there is a “sensitive period” for the development of amblyopia; however, in humans with

naturally occurring amblyopia, the age of onset of the amblyogenic condition(s) is difficult to ascertain, and the effects of intervention combine to make it difficult to obtain a clear picture of the “natural history” of amblyopia development. Thus, much of our current understanding of the development of amblyopia accrues from animal studies (for a review, see Boothe, Dobson, & Teller, 1985) and retrospective studies of clinical records (e.g., von Noorden, 1981). Technological improvements in infant testing also have provided more direct data on the development of naturally occurring amblyopia in humans (Birch, 1983; Jacobson, Mohindra, & Held, 1981; Maurer, Lewis, Brent, & Levin, 1999; Maurer, Lewis, & Tytla, 1983; Mohindra, Jacobson, Thomas, & Held, 1979) and monkeys (Kiorpes & Boothe, 1981; Kiorpes, Boothe, & Carlson, 1984; Kiorpes, Carlson, Alfi, & Boothe, 1989). All of these studies provide strong evidence for amblyopia induced by early deprivation.

An attractive hypothesis, foreshadowed in Figure 1, is that structures and functions which develop earliest are most robust to the effects of abnormal visual input while those that develop more slowly seem most susceptible. Levi and Carkeet (1993) called this the “Detroit model” a biological analogue of the “last hired, first fired” philosophy. This hypothesis suggests that different structures and/or functions may be susceptible to the effects of visual deprivation at different times during development. As noted earlier, there is clear evidence from anatomical and physiological studies that the sensitive period in Layer IVc (the input layer) of the cortex of monkeys is considerably shorter than that of other layers (LeVay et al., 1980). Behavioral studies of lid-sutured monkeys (Harwerth et al., 1986, 1990) provide strong evidence that different psychophysical functions are affected by lid suture at different times. For example, they found that early lid suture (age 3–6 months) had a marked influence upon scotopic and photopic spectral sensitivity, and essentially abolished pattern and binocular vision. A later onset of deprivation (up to about 25 months) had no influence upon spectral sensitivity, but resulted in reduced contrast sensitivity at high spatial frequencies, and reduced binocular summation. Lid suture beyond 25 months had no effect on contrast sensitivity, but still disrupted binocular functioning. There are several points worth noting: First, to extrapolate these results to monocular pattern deprivation in humans, the 1:4 rule should be applied (i.e., 1 monkey year is equivalent to about 4 human years; Boothe et al., 1985). Second, the effects of deprivation seem to be the “mirror image” of the developmental sequence. Thus, as noted earlier, different visual functions (and presumably their underlying anatomical and physiological structures) develop at different rates. Those which develop earliest seem most robust to the influences of pattern deprivation while those that develop

last are most at risk and remain susceptible for the longest time.

While the upper limit for susceptibility of excitatory binocular interactions is not yet certain, it appears to be later than that for acuity or contrast sensitivity in monkeys, and may extend to at least 7 or 8 years (and possibly more) in humans. Psychophysical studies of interocular transfer in humans with a history of strabismus (Banks, Aslin, & Letson, 1975; Hohmann & Creutzfeldt, 1975) provide an indirect estimate of the period of susceptibility of binocular connections. The results of both studies suggest that binocular connections are highly vulnerable during the first 18 months of life, and remain susceptible to the effects of strabismus until at least age 7 years.

Is there a critical period for treatment of amblyopia? The notion that there is a critical period(s) for the development of amblyopia has often been taken to indicate that there also is a critical period for the treatment of amblyopia. This concept grew out of the work of Claude Worth (1903). Worth suggested that the presence of a “sensory obstacle” (e.g., unilateral strabismus) arrested the development of visual acuity (“amblyopia of arrest”), so that the patient’s acuity remained at the level achieved at the time of onset of strabismus. In this view, the depth of amblyopia is a direct function of the age of onset of the “sensory obstacle.” Worth further suggested that if amblyopia of arrest were allowed to persist, that “amblyopia of extinction” could occur as a result of binocular inhibition. In Worth’s view, only this “extra” loss of sensory function (i.e., the amblyopia of extinction) could be recovered by treatment. Although this latter notion is open to question in the light of present knowledge, the ideas of Worth have had a powerful influence upon both clinicians and basic scientists. Thus, many of our currently held concepts of amblyopia, such as plasticity, sensitive periods, and abnormal binocular interaction, were already described more than a century ago, and gained currency with the work of Hubel and Wiesel (1970) and the many anatomical and physiological studies that followed. Thus, while amblyopia can often be reversed when treated early, treatment is generally not undertaken in older children and adults. Next, we consider both experimental and clinical evidence for plasticity in the adult visual system that calls into question the notion of a critical period for treatment.

LEARNING AND PLASTICITY IN THE “MATURE” VISUAL SYSTEM

Recent work suggests that there is a good deal more plasticity in the adult sensory nervous system than previously suspected. Sensory cortex is topographically

organized: In visual cortex, the world is mapped retinotopically, in auditory cortex tonotopically, and in somatosensory cortex the skin surface is mapped somatotopically. What we have learned over the past 20 years or so is that in the adult, these sensory maps are plastic—reorganizing within limits in response to injury and experience. While we still do not fully understand the mechanisms, it is clear that there is plasticity at the synaptic and cellular level and at the level of cortical representation. When the somatosensory, auditory, or visual cortex is deprived of its normal sensory input, the area reorganizes (for a review, see Buonomano & Merzenich, 1998). In the visual system, for example, Chino Kaas, Smith, Langston, and Cheng (1992) made a small lesion in the retina of an adult cat, depriving the primary visual cortex of activating input. After enucleating the nonlesioned eye, they found substantial and rapid reorganization of receptive field around the cortical area corresponding to the lesion. Similar reorganization occurs in primate cortex following bilateral lesions (Heinen & Skavenski, 1991). This reorganization is interesting because the new receptive fields support visual function, and therefore act to “fill in” the blind spots in the perceptual world. They also provide some important clues about the mechanisms of adult neural plasticity that have important implications for understanding amblyopia. Chino et al. actually measured function immediately before as well as after enucleating the fellow eye. They found that the reorganization occurred only after enucleation, and then occurred within hours. This suggests that the reorganization may have involved adaptive alterations in the effectiveness of existing connections that were suppressed by the fellow eye. In this scenario, removing the intact fellow eye may have “unmasked” these existing (but perhaps weak) connections. Later, we will discuss the implications of this for understanding plasticity in amblyopia.

Adults are capable of improving performance on sensory tasks through repeated practice or perceptual learning (Yes, you can teach old dogs new tricks!) (for a recent review, see Fine & Jacobs, 2002), and this learning also has consequences in the cortex (Buonomano & Merzenich, 1998). The strong interest in visual learning stems from the possibility that the learning takes place in early stages of visual processing. Indeed, the finding that learning with simple patterns shows non-transfer to different locations, different orientations, or the untrained eye has been taken as evidence that the learning might take place in early stages of processing; however, as noted by Mollon and Danilova (1996), nontransfer of learning, often thought to be early, can sometimes be explained by central mechanisms, and the massive interconnectedness of cortex makes it difficult to separate early and late stages of processing. Evidence directly linking perceptual learning to neural plasticity at an early

stage has not been conclusive. Schoups, Vogels, Qian, and Orban (2001) reported that after practicing orientation discrimination, neurons in area V1 of monkeys had sharper orientation tuning functions, but Ghose, Yang, and Maunsell (2002)^{Q11} failed to find evidence for similar physiological correlates of orientation discrimination learning in V1 and referred the behavioral performance improvement to processes downstream of V1. Interestingly, sharpening of orientation tuning functions of neurons does occur in area V4 after learning (Yang & Maunsell, 2004), suggesting that perceptual learning may result in neural changes in higher, but not lower, visual areas.

LEARNING AND PLASTICITY IN THE “MATURE” AMBLYOPIC VISUAL SYSTEM

What are the limits and mechanisms of improvement in visual performance in adults with amblyopia? As noted earlier, in adults with normal vision, practice can improve performance on a variety of visual tasks, and this learning can be quite specific. The perceptual learning which follows practice is considered to be a form of neural plasticity. Interestingly, similar neural plasticity exists in the visual system of adults with naturally occurring amblyopia due to anisometropia, strabismus, or both. For example, adults with amblyopia demonstrate substantial and significant perceptual learning of Vernier acuity (Levi & Polat, 1996; Levi, Polat, & Hu, 1997; see Figure 2, top panel). All observers showed significant improvement after practicing Vernier acuity at one orientation. The improvement was most marked at the trained orientation, with little improvement at the untrained orientation. In some (anisometric amblyopes), there was substantial transfer to the untrained eye at the trained orientation—and much less transfer at the untrained orientation. In contrast to the marked improvement in the trained (Vernier) task, there was very little improvement in an untrained (line detection) task. Thus, perceptual learning in amblyopia is task specific. At least in some observers, the improvement in performance appears to reflect neural learning beyond the site of binocular convergence. Interestingly, in that study, 2 observers showed improvements in Snellen acuity that were comparable to their Vernier improvement. The Snellen acuity results of 1 observer are shown in the lower panel of Figure 2. For this observer, Snellen acuity improved from its initial value of 20/42, reaching 20/20 after practicing the Vernier task.

These results suggest that some adults with amblyopia retain at least some cortical plasticity. Repetitive training leads to substantial improvement on Vernier acuity that is task and orientation specific. This result is consistent with recent evidence for a remarkable degree of plasticity in the

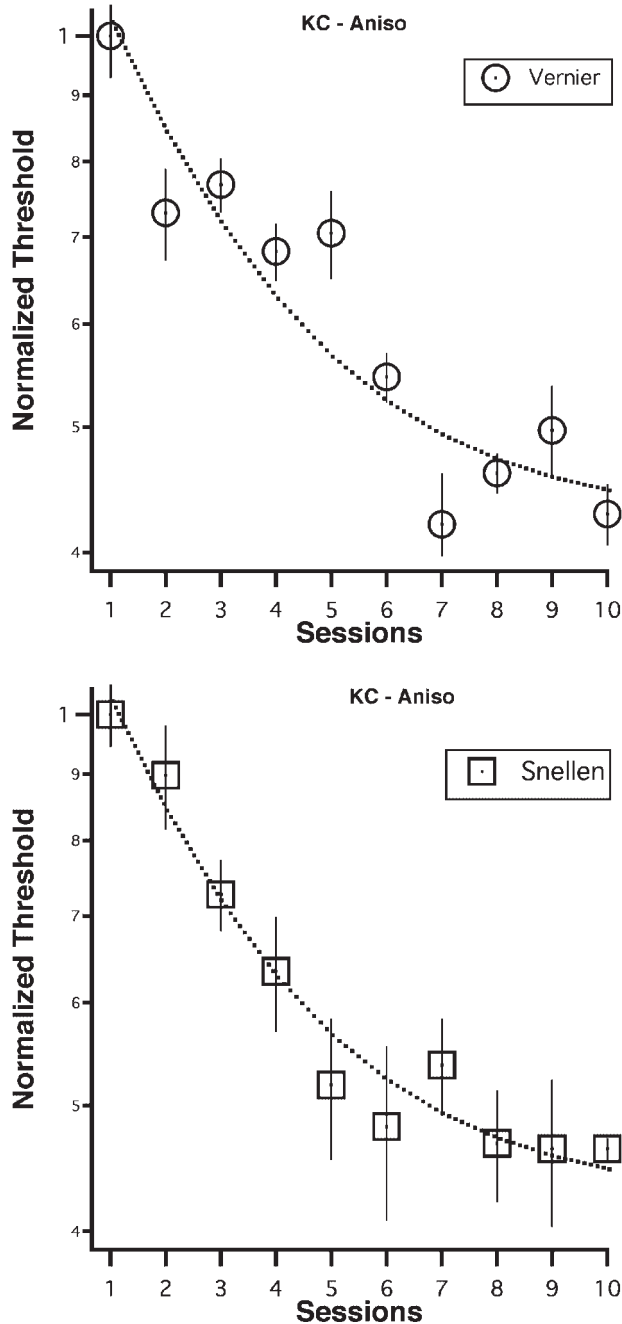


FIGURE 2 Improvement in Vernier acuity (top) and Snellen acuity (bottom). For both figures, thresholds have been normalized to the prelearning value (i.e., they were set to 1 at Session 1). Each session represents about 1,000 trials of Vernier acuity. After “Improvement in Vernier acuity in adults with amblyopia. Practice makes better,” by D. M. Levi, U. Polat, & Y. S. Hu, 1997, *Investigative Ophthalmology & Visual Science*, 38, pp. 1497 and 1504. Adapted with permission from the authors.

visual cortex of adult cats with experimentally induced retinal lesions (Chino et al., 1992; Gilbert & Wiesel, 1992); however, it is surprising because the physiological effects of strabismus or lid suture on the cortex are

generally thought to be irreversible after some critical period (typically 3–4 months in cats and monkeys).

Why Does Practice Improve Performance?

There have been many attempts to explain why training or practice results in lower thresholds in normal foveal vision, and a full discussion is beyond the scope of this article. One point of view is that perceptual learning reflects alterations of neural response rather early in the visual pathway, where neurons are sensitive to local features (for a review, see Karni & Bertini, 1997). An alternative point of view is that improvement in performance is based on high-level (or cognitive) processes (e.g., Mollon & Danilova, 1996). Perceptual learning of Vernier acuity of normal adults is accompanied by a narrowing of the orientation tuning (Saarinen & Levi, 1995) and a retuning of the observer’s perceptual template (i.e., an alteration of the weightings of inputs from basic visual mechanisms; Li, Levi, & Klein, 2004). Although it is possible that this reflects alterations in the orientation tuning properties of low-level cortical neurons, we note the point made forcefully by Mollon and Danilova (1996) that the learning may be central, and the specificity may lie in what is learned. In this view, the narrowing of orientation tuning or template retuning may reflect the observer learning to attend to and rely on the signals from a more sensitive (and more narrowly tuned) subset of all neurons that respond to the stimulus. If this is the case, perceptual learning in amblyopes may reflect the brain learning to attend to and use the most salient or reliable information when viewing with the amblyopic eye.

Using “Noise” to Understand the Mechanisms Underlying Learning

Recent empirical and theoretical advances have given us important new insights into the mechanisms of perceptual learning (Doshier & Lu, 1998, 1999; Gold, Bennett, & Sekuler, 1999). These studies used external noise to titrate the level of noise in the visual nervous system (internal noise) while observers practiced a discrimination task. The basic idea is simple: We measure performance (threshold) with and without external noise added to the stimulus while the observer performs a visual task. When the external noise is small relative to the observer’s internal noise, performance is limited by the internal noise. When the external noise is large relative to the internal noise (illustrated by the inflection point in Figure 3), it will dominate and thresholds will rise. Using this external noise approach, sometimes referred to as the Equivalent Noise or Linear Amplifier Model (Pelli, 1990), we can attribute any changes during learning to two

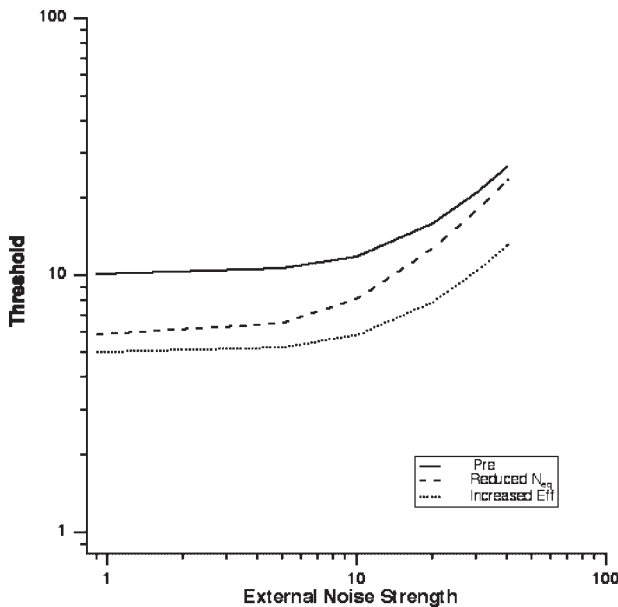


FIGURE 3 Threshold versus noise (TvN) curves based on the Equivalent Noise model. This figure illustrates two of the possible posttraining outcomes. The “pretraining” TvN curve is shown as the solid curve. The dotted curve illustrates a pure improvement in efficiency. The dashed curve shows a pure decrease in equivalent input noise (which shifts the “knee” point of curve down and to the left).

important factors: a change in equivalent input noise and/or an increase in the efficiency with which the stimulus information is used. Equivalent input noise is the noise that must be added to the stimulus to act like the limiting noise in the visual system. Efficiency reflects the computation underlying the use of the information (samples) of the stimulus (Pelli, 1990).

Figure 3 illustrates two of the possible posttraining outcomes (threshold vs. noise, TvN, curves) based on the Equivalent Noise model (The “pretraining” TvN curve is shown by the solid curve.): (a) A pure improvement in efficiency would shift the curve uniformly downward (dotted curve). This type of improvement has been reported for learning faces and complex patterns (Gold et al., 1999). A mostly downward shift also occurs for learning orientation discrimination in peripheral vision (Doshier & Lu, 1998, 1999). (b) A pure decrease in equivalent input noise would shift the “knee” point of the curve down and to the left (dashed curve). Another pattern of learning that has been found (but not shown here) for learning simple foveal discrimination tasks is a rightward shift of the curve, produced by a combination of improved efficiency and increased equivalent input noise. This type of learning also has been modeled in terms of improved exclusion of external noise with fixed equivalent late noise (Lu & Doshier, 2004).

We have used this approach to ask how amblyopes learn in several tasks. In one experiment, we repeatedly measured letter identification thresholds in a group of amblyopes in white pixel (luminance) noise (i.e., adding dark and bright pixels, like snow on a television screen, to the picture). Relative to normal observers, amblyopes show reduced efficiency for letter identification (Pelli, Levi, & Chung, 2004). Following practice (approximately 5,000 trials), amblyopes show substantial improvement in thresholds both with no noise (the leftmost datum in each graph, and at high noise levels). The curves in Figure 4 are the fits of the equivalent noise model, and it is clear that all 4 observers showed substantial improvement (lowering) of thresholds over the entire noise range.

The equivalent noise approach allows us to parse the improvement into two factors: reduced equivalent input noise or increased efficiency. This model is likely an oversimplification; nonetheless, Figure 5 shows that the improvement (specified as percent change to facilitate comparison) was primarily a consequence of increased efficiency (black bars with diagonal stripes) with much smaller (or no) changes in equivalent input noise (gray bars). Interestingly, after practice, the amblyopic eye thresholds had improved to a level similar to those of the preferred eye (gray symbols in Figure 4: Open gray symbols were prior to practice, and solid gray symbols are following practice.) It also is interesting to note that there was little or no transfer of learning from the amblyopic to the preferred eye (compare open and filled gray symbols). The improvement in amblyopic performance via increased efficiency is similar to the improvement in letter identification that occurs in peripheral vision following practice (Chung, Tjan, & Levi, 2005). We note that there is little evidence that practice improves letter recognition in the normal fovea, at least for first order letters like ours (Doshier & Lu, 2004), probably because the normal fovea is so overpracticed in this task.

We also have applied the equivalent noise approach to studying the effects of learning on positional acuity, using positional noise (i.e., perturbation of the positions of parts of the stimulus) rather than luminance noise (Li & Levi, 2004). Previous studies have shown that the amblyopic visual system has high levels of equivalent input positional noise and that it fails to extract useful information efficiently (Hess & Field, 1994; Levi & Klein, 2003; Wang, Levi, & Klein, 1998; Watt & Hess, 1987). Li and Levi (2004) showed that repetitive practice can lower the noise levels and/or boost the amblyopic brain’s ability to use relevant information more efficiently. It is possible that practice with feedback allows recalibration or reweighing of disordered visual mechanisms, enabling observers to sample and use the stimulus information more efficiently as well as to reduce uncalibrated internal position jitter or spatial distortions. In addition, practicing

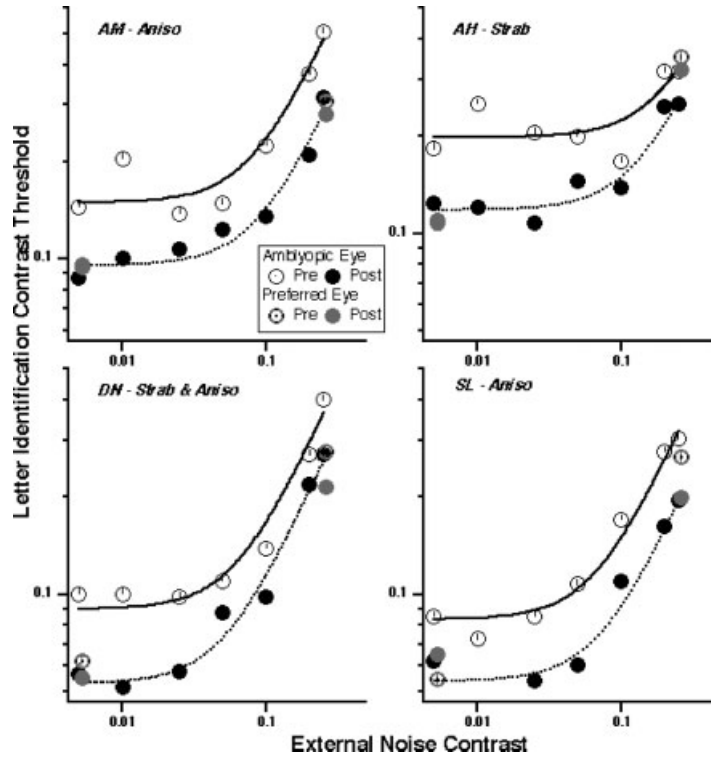


FIGURE 4 Threshold versus noise (TvN) curves for 4 amblyopes. Black symbols and curves are for the amblyopic eyes, pre- (open) and post- (solid) training. The training consisted of practicing approximately 5,000 letter identifications in noise trials. The gray symbols are the pre- (open) and post- (solid) practice thresholds for the nonamblyopic eyes.

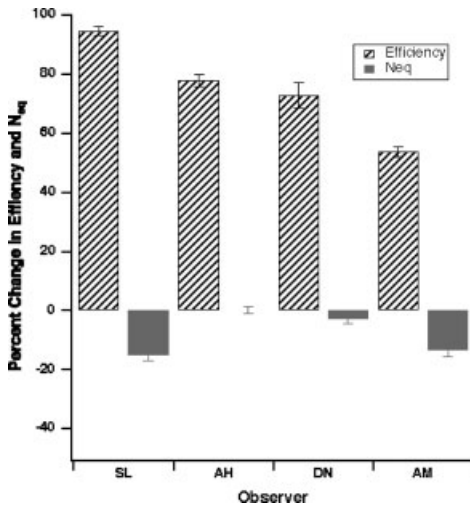


FIGURE 5 The change (in percent) in efficiency (black bars with diagonal stripes) and equivalent input noise (N_{eq} gray bars) following practice (about 5,000 trials over 14 sessions). Efficiency and equivalent input noise were estimated from the curves fit to the TvN data of Figure 4. Specifically, we averaged the estimates of efficiency and equivalent input noise from the first two sessions, taking those averaged values as a reasonable estimate of the initial efficiency and equivalent input noise, and compared them to the average of the last three sessions.

position discrimination transferred to two different tasks: Snellen acuity and counting. Specifically, Li and Levi (2004) found that all 7 adult amblyopes showed improvements in Snellen acuity. On average, acuity improved by approximately 33% for several mild amblyopes resulting in single letter acuity of 20/20 following practice. The close link between positional and visual acuities has been shown previously (Levi & Klein, 1982a, 1982b; McKee et al., 2003). Additionally, strabismic amblyopes are known to undercount features, i.e., they undercount the number of briefly flashed patches (Sharma, Levi, & Klein, 2000). After practicing the position task, several amblyopes showed an improvement in their ability to count briefly flashed features.

Why Does Practice Improve Performance in Adults with Amblyopia?

The foregoing discussion makes it clear that adults with amblyopia can improve the performance of their amblyopic eye through repeated practice. Practicing Vernier acuity (Levi & Polat, 1996; Levi et al., 1997), positional acuity (Li & Levi, 2004), letter identification (see Figures 4 and 5), and contrast sensitivity (Polat, Ma-Naim, Belkin, & Sagi, 2004) all result in improved performance on the

practiced task. As noted earlier, however, perceptual learning can be quite specific (to the trained task, orientation, eye, etc.). Specificity of perceptual learning poses some interesting difficulties. If the improvement following practice was solely limited to the trained stimulus, condition, and task, then the type of plasticity obtained through perceptual learning would have very limited (if any) therapeutic value for amblyopia since amblyopia is defined primarily on the basis of reduced visual acuity. On the other hand, the Vernier acuity of amblyopes is very highly correlated with their visual acuity (e.g., McKee et al., 2003), suggesting that the same mechanisms might limit both tasks, and as noted earlier, improvements in Vernier and position acuity may transfer to improvements in Snellen acuity. It also is interesting to note that practicing contrast detection also transfers to improved Snellen acuity (Polat et al., 2004). This leads to some speculations about why perceptual learning might be so effective. First, during perceptual learning experiments, the preferred eyes of amblyopic observers are patched while they perform the task. Brief periods of occlusion have been shown to result in improvements in young children with amblyopia (Ciuffreda et al., 1991). Second, during perceptual learning experiments, observers are engaged in making fine visual discriminations using their amblyopic eyes under conditions where their visual system is “challenged,” therefore the learning is “active.” Third, observers receive repeated exposure to the same stimuli and are given feedback. Thus, it is tempting to speculate that perceptual learning in amblyopia reflects the amblyopic brain learning to attend to and use the most salient or reliable information for the task when viewing with the amblyopic eye. This may be akin to strengthening connections that were there in the first place rather than the development of new connections, perhaps by learning to attend to the information from the (normally suppressed) amblyopic eye. This speculation is consistent with the improvement in efficiency. It also might explain why learning transfers to some tasks (such as Snellen acuity and counting), but not others.

CLINICAL STUDIES

Although it is often stated that humans with amblyopia cannot be treated beyond a certain age, a review of the literature suggests otherwise. For example, Carl Kupfer (1957) showed marked improvement in acuity in 7 adult strabismic amblyopes, aged 18 to 22 years. All 7 showed improvements ranging from 71% (20/70 to 20/20) to a very dramatic improvement from hand movements only to 20/25 after 4 weeks. All of these patients had relatively late onset (2 years or later), were highly motivated, and Kupfer’s treatment was aggressive. The patients

were hospitalized for 4 weeks, during which time they were continuously patched and given fixation training. However, the very fact that adults with amblyopia can improve suggests that there is no clear upper age limit for recovery of acuity, at least in strabismic amblyopia with an onset later than 2 years or so. Since Kupfer’s study, there have been many reports of improvement in acuity of older people with amblyopia (e.g., Birnbaum, Koslowe, & Sanet, 1977; Wick, Wingard, Cotter, & Scheiman, 1992). In a case report, Simmers and Gray (1999) showed that occlusion therapy appeared to improve not only visual acuity but also position acuity in an adult strabismic amblyope.

Plasticity in adults with amblyopia also is dramatically evident in the report of El Mallah, Chakravarthy, and Hart (2000) of amblyopic patients whose visual acuity spontaneously improved in the wake of visual loss due to macular degeneration in the fellow eye. Other reports have suggested that some adult amblyopes recover vision in their amblyopic eye following loss of vision in their fellow (nonamblyopic) eye (Rahi et al., 2002; Vereecken & Brabant, 1984). These studies are consistent with the notion that the connections from the amblyopic eye may be suppressed rather than destroyed. Loss of the fellow eye would allow these existing connections to be unmasked, as occurs in adult cats with retinal lesions (Chino et al., 1992).

Recent work (Fine, Smallman, Doyle, & MacLeod, 2002) also has suggested that there is some, albeit limited, postoperative adaptation to the removal of congenital bilateral cataracts in adults. Presumably, the mechanism of this adaptation is quite different than that occurring in monocular amblyopia when one eye is lost. One might speculate that the adaptation reflects the subject learning to attend to and make use of the information that became available once the cataracts were removed.

PERCEPTUAL LEARNING AND THE CLINICAL TREATMENT OF AMBLYOPIA

As noted earlier, treatment for amblyopia is generally only undertaken in children; however, as discussed earlier, there is now considerable evidence that treatment of amblyopia can be effective in adults. Our hypothesis is that perceptual learning accounts for at least some of the improvement that occurs in the clinical treatment of amblyopia. Indeed, perceptual learning may be thought of as a form of “active” treatment. Observers are engaged in making fine judgments near the limit of their performance using their amblyopic eyes (with their preferred eye occluded), and they receive feedback. The results reviewed previously show that perceptual learning is effective in improving visual performance and that the

effects may transfer to visual acuity. These findings, along with a number of new clinical trials, suggest that it might be time to reconsider our notions about neural plasticity in amblyopia, in much the same manner as we had to change our concepts about stroke in the last century.

CONCLUSIONS

Experience-dependent plasticity has been closely linked with the development of sensory function (see Figure 1); however, the evidence reviewed previously suggests that in the face of injury or deprivation, there may be residual plasticity in the adult visual system. In particular, there may be previously unsuspected plasticity in the visual system of adults with amblyopia. Two separate mechanisms may account for improvements in adults with amblyopia: (a) unmasking of connections that have been suppressed and (b) learning to attend to and make efficient use of the salient information for accomplishing a visual task. Perhaps the same mechanisms are at work in the clinical treatment of amblyopia.

NOTES

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