

Sensitive Periods in Visual Development

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Abstract and Keywords

Patterned visual input during early infancy plays a key role in constructing and/or preserving the neural architecture that will be used later for both low-level basic vision and higher-level visual decoding. The high-contrast, low spatial frequencies that newborns can extract from their environment set up the system for later development of fine acuity, expert face processing, and specialization of the visual cortex for visual processing. Nevertheless, considerable plasticity remains in adulthood for rescuing the system from earlier damage.

Keywords: critical periods, plasticity, visual deprivation, blindness, acuity, face processing

Key Points

1. Evidence from children who missed all patterned visual input for a short time because of dense bilateral cataracts indicates that abnormal visual input during a critical period of development causes permanent visual deficits.
2. The period during which visual input is necessary for the normal development of vision differs for different aspects of vision. For example, the sensitive period for acuity is much longer than the sensitive period for some types of motion perception.
3. Even within one aspect of vision, such as acuity, there are at least three sensitive periods: (1) *the period of visually driven normal development*—the period when there are developmental changes in an organism raised with normal visual input that do not occur if the visual input is missing; (2) *the sensitive period for damage*—the time of vulnerability, including any time of vulnerability after normal development is complete; and (3) *the sensitive period for recovery*—the time during which the visual system has the potential to recover from the deleterious effects of an earlier period of abnormal input. For acuity, these three sensitive periods last 5 to 7 years, 10 years, and 5 to 9 years, respectively.
4. Scattered evidence of prolonged residual plasticity well beyond the traditional sensitive period for recovery has provided new hope for improving reduced visual

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acuity even in adulthood. Attempts at improving adults' acuity in an amblyopic eye have included extensive active near work, perceptual training, telescopic magnification, repetitive transcranial magnetic stimulation, and drug therapies.

5. Early patterned visual input during the first 6 months of life or even longer is not necessary for the later normal development of detecting that a stimulus is a face, nor for differentiating faces that differ only in the external contour or in the shape of the internal features. However, patterned visual experience during the first 2 to 6 months of life is essential for discriminating faces that differ only in the spacing of features and for the normal holistic processing of faces.

(p. 203) 6. Permanent deficits in visual acuity, in discriminating spacing changes in faces, and in holistic processing of faces are examples of sleeper effects: deprivation during the first few months of life—an age at which babies with normal eyes are very poor at these abilities—prevents the later normal development of these abilities.

7. Studies of face-deprived monkeys suggest that early patterned visual input, but not face input *per se*, is necessary to set up or preserve the neural architecture that underlies face processing. When the architecture is used, it becomes specialized for the type of face input it first receives.

8. Humans, like monkeys, show perceptual narrowing—generalized skills that are narrowed as a consequence of biased experience. For example, newborns look equally long at faces from their own racial/ethnic group and from other groups, but by 3 months they have a looking preference for faces from the racial/ethnic group(s) they encounter most often.

9. Face-processing skills, like visual acuity, can be altered beyond the traditional sensitive period. For example, the other-race effect can be largely overcome by training, even in adulthood.

10. Additional evidence of plasticity of the adult brain comes from studies of reorganization of the visual cortex after blindness or even after the temporary blindfolding of sighted adults.

Newborns can see, but there are serious limitations on their vision: they see only large, high-contrast stimuli in the central visual field, scan only limited regions of stimuli, and, under most conditions, fail to integrate local details into a percept of a whole object or face (reviewed in Maurer, Lewis, & Mondloch, 2008). Yet, as we will show in this chapter, the degraded visual input perceived by the newborn baby is instrumental in sculpting the visual nervous system for later visual development. When it is absent, normal visual capabilities fail to emerge at later points. For example, children who missed normal early visual input because of dense central cataracts in both eyes, or degraded binocular input because of unilateral cataract, misaligned eyes, or unequal refractive error, develop amblyopia, a permanent reduction in vision caused by abnormal early visual input. The eye problem can be corrected with surgery or optical correction, but permanent visual deficits remain, presumably because the abnormal input prevented normal development of the visual cortical pathway. Normal visual input during infancy appears to be necessary to set up the neural substrate that underlies the later development of these abilities and/

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or to prevent that substrate from being taken over by another sensory modality, as has been shown to occur in cases of congenital blindness.

When normal visual input is missing later in life, the damage is milder, and when it begins after middle childhood, there is no damage whatsoever. This profile suggests that there is a critical period during which visual input is necessary for normal development. Estimates of the end of the visual critical period in humans are typically given as 5 to 7 years of age, although the exact timing varies across visual capabilities from as little as the first few months of life for direction of global motion to as long as adolescence for peripheral light sensitivity (Bowering, Maurer, Lewis, & Brent, 1993; Ellemberg, Lewis, Maurer, Brar, & Brent, 2002). Animal models confirm that there are such critical periods during which misaligned or reduced visual input can cause behavioral visual deficits and permanent cortical damage (reviewed in Barrett, Bradley, & McGraw, 2004; in Hensch, 2005; in Mitchell, & MacKinnon, 2002; and in Morishita, & Hensch, 2008). Similarly, the visual cortex of the congenitally blind adult responds robustly to tactile, auditory, and language stimuli, but the cross-modal effects are much smaller when the blindness began after middle childhood (e.g., Burton, Sinclair, & McLaren, 2004; Burton et al., 2002; Sadato, Okada, Honda, & Yonekura, 2002). Combined, the evidence suggests that there is a critical period early in life when the human visual cortex is modified by visual input; after that critical period, it appears no longer to be plastic.

Yet there is scattered evidence that the visual system, and the nervous system more generally, remains plastic after middle childhood and even into adulthood. For example, when the cause of amblyopia is binocular imbalance between a normal eye and a misaligned eye or an eye with a refractive error, after the peripheral problem is fixed (by aligning the eyes or by giving the child corrective glasses), use of the amblyopic eye is encouraged by patching the “good” fellow eye. Usually the vision of the affected eye improves and the improvement is as large if the patching begins after age 7 as at earlier ages (Birnbaum, Koslowe, & Sanet, 1977; see also Oliver, Neumann, Chairmovitch, Gotesman, & Shimshoni, 1986). Even with adults, training has been successful in inducing improvements in the vision of amblyopic eyes (e.g., Kupfer, 1957; Levi & Polat, 1996; Levi, Polat, & Hu, 1997; Li & Levi, 2004; Polat, Ma-Naim, Belkin, & Sagi, (p. 204) 2004; Simmers & Gray, 1999; reviewed in Levi, 2005). There are even improvements in the vision of adults with normal eyes after training with feedback (reviewed in Fine & Jacobs, 2002) or the playing of action videogames (e.g., Green & Bavelier, 2007). Similar residual plasticity is evident in studies of blindness. In congenitally blind adults, the visual cortex responds to auditory and tactile input, and perhaps even language, and some of these effects are evident, to a lesser extent, in adults who became blind after 18 years of age or who were simply blindfolded for 5 days in the laboratory (Burton et al., 2002, 2004; Pascual-Leone & Hamilton, 2001).

In this chapter, we will reexamine the evidence for visual critical periods by focusing on the effects of visual input at different ages on the development of visual acuity, face processing, and the specialization of the visual cortex for visual processing. We will concentrate on findings from children who missed all patterned visual input either because of

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dense bilateral cataracts or blindness. We will contrast the findings on deficits in such children with evidence of plasticity of the adult brain, drawing on studies that have been successful in improving acuity or face processing in adults and in establishing auditory, tactile, or language responses from the visual cortex of the normal seeing adult. We will end by considering the general principles that emerge across these domains.

Multiple Sensitive Periods

In a classic study in the early 1960s, and in subsequent anatomical, electrophysiological, and behavioral studies of visually deprived animals, Hubel and Wiesel defined the “critical period”—the period during which normal visual input is necessary for normal visual development (Boothe, Dobson, & Teller, 1985; Hubel & Wiesel, 1963, 1970; Mitchell, 1991; Wiesel & Hubel, 1965; reviewed in Blakemore, 1988). They probed the duration of the critical period by sewing the eyelids of cats or monkeys shut to remove visual input beginning at different ages and then reopening the eyes to assess the effect of the visual deprivation on visual behavior, electrophysiological responses of neurons in the visual cortex, and anatomical measures of neuronal growth and connections in the visual cortex. From all three measures, they concluded that there is a critical period early in life and that visual deprivation beginning after that time causes no permanent damage. Later behavioral and physiological studies of animals established that there is not one critical period, but different critical periods during which visual input is necessary for the normal development of different aspects of vision (Blakemore, 1988; Daw, Fox, Sato, & Czepita, 1992; Harwerth, Smith, Duncan, Crawford, & von Noorden, 1986; Jones, Spear, & Tong, 1984; Singer, 1988). For example, Harwerth and colleagues (1986) found that, in the monkey, binocular deprivation has to begin before 3 months of age to affect scotopic sensitivity (sensitivity to the low levels of light that stimulate rods), before 6 months to affect photopic spectral sensitivity (sensitivity to light of different wavelengths at levels sufficient to stimulate cones), and before 18 to 24 months to affect spatial contrast sensitivity (sensitivity to different spatial frequencies at low contrast), but it affects binocularity even when it begins after 2 years of age.

The critical period does not end abruptly but rather tapers off such that deprivation has milder and milder effects. For that reason, it is often called the “sensitive period.” We have found evidence for more than one sensitive period for different aspects of human visual development, such as acuity versus the perception of motion (Elleberg et al., 2002; Maurer & Lewis, 1993, 2001a). The classic definition of the sensitive period is the time during normal development when input is necessary for a normal outcome. Thus, it corresponds to the period when there are developmental changes in an organism raised with normal visual input that do not occur if the visual input is missing. We call this the period of visually driven normal development. However, for some aspects of vision, abnormal visual input can have a permanent deleterious effect even when it starts after that aspect of vision is functionally adultlike. Thus, a second sensitive period is the time of vulnerability, including any time of vulnerability after normal development is complete—an example of what Worth called “amblyopia of extinction” (see Levi, 2005) because abnormal input

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eliminates or extinguishes what had already developed. We call this the sensitive period for damage. A third sensitive period is the time during which the visual system has the potential to recover from the deleterious effects of an earlier period of abnormal input. We call this period the sensitive period for recovery (for a fuller discussion of these sensitive periods, see Lewis & Maurer, 2005). Daw has made similar distinctions among different types of sensitive period (e.g., Daw, 1998, 2003).

We will begin by comparing the periods for the three indices of plasticity (visually driven normal development, the sensitive period for damage, and the sensitive period for recovery) for visual acuity. (p. 205) We do so by first considering the development of acuity in visually normal children and then comparing their vision to that of children who were deprived of visual experience at some point during development because they were born with, or developed, cataracts in one or both eyes. If a cataract is sufficiently large and sufficiently dense, as was the case for all the patients included in our studies, it blocks all patterned visual input to the back of the eye. Thus large, dense cataracts allow only diffuse light to reach the retina. The cataracts are treated by surgically removing the natural lens of the eye and replacing it with a suitable optical correction that restores patterned visual input. Subsequent comparisons of the results of visual assessment to those from children born with normal eyes indicate whether the period of visual deprivation adversely affected visual development.

Children treated for bilateral congenital cataracts afford an opportunity to examine the effects of visual deprivation from birth and hence the role of visual input in inducing the rapid developmental changes normally seen during infancy. Children treated for unilateral cataract afford the opportunity to examine the added effects of uneven competition between a weaker deprived eye and a stronger fellow nondeprived eye. Children treated for developmental cataracts originating at different ages afford an opportunity to examine the effects of comparable periods of visual deprivation after varying periods of normal visual input. Differences in the pattern of results across cases with different ages of onset allow inferences about sensitive periods for damage—that is, the role of patterned visual input during different developmental periods.

Visual Acuity

Normal Development

To understand the effects of visual deprivation from birth, it is useful to consider the vision of the infant with normal eyes—that is, to consider what type of functional input the visually deprived child misses before the cataracts are removed (see Atkinson & Bradick, this volume 1). Visual acuity typically is measured during infancy by determining grating acuity—the finest stripes that the infant can resolve. The most common measure of infants' grating acuity is preferential looking, a method that takes advantage of infants' preference to look at something patterned over something plain (reviewed in Maurer & Lewis, 2001a, b). The infant is shown black-and-white stripes paired with a gray stimulus

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of the same mean luminance, and the size of the stripes is varied across trials. The measure of grating acuity is the smallest size of stripe for which the baby shows a looking preference. For older children and adults, the procedure is similar except that subjects indicate where they see the stripes and/or whether any stripes are visible on the screen.

When tested with preferential looking, newborns' grating acuity is typically about 40 times worse than that of visually normal adults tested under the same conditions (Brown & Yamamoto, 1986; Courage & Adams, 1990; Dobson, Schwartz, Sandstrom, & Michel, 1987; Mayer & Dobson, 1982; Miranda, 1970; Van Hof-van Duin & Mohn, 1986). Grating acuity improves rapidly during the next few months so that by 6 months of age, it is only about eight times worse than that of adults. Thereafter, grating acuity improves more gradually and does not reach adult values until about 4 to 6 years of age (Courage & Adams, 1990; Ellemberg, Lewis, Liu, & Maurer, 1999a; Mayer & Dobson, 1982; Van Hof-van Duin & Mohn, 1986).

Poor acuity at birth is likely caused by both immaturities in the size and arrangement of retinal cones and by additional limitations beyond the retina (Banks & Bennett, 1988; Candy & Banks, 1999). The rapid improvement in the first 6 months reflects, in part, the development of foveal cones so that they filter out less information and allow finer and finer detail through to tune cells in the visual cortex (Banks & Bennett, 1988; Wilson, 1988, 1993). The more gradual changes through age 4 to 6 years likely reflect further refinement of the retinal and cortical architecture (Garey & De Courten, 1983; Huttenlocher, 1984; Huttenlocher, De Courten, Garey, & Van Der Loos, 1982; Kiorpes & Movshon, 1998; Wilson, 1988, 1993; Youdelis & Hendrickson, 1986; reviewed in Ellemberg et al., 1999a).

Outcome After Early Deprivation

Patterned visual input is necessary for the postnatal development of acuity. The evidence for that conclusion comes from comparisons of infants with normal visual input to infants who were deprived of early patterned input because of dense central cataracts in the lenses of one or both eyes. The cataractous lenses were removed surgically and, 1 to 3 weeks later, after recovery from the surgery, the treated eyes were given compensatory contact lenses to provide the first focused patterned visual input. We used preferential looking to measure the monocular grating acuity of 12 patients treated for bilateral congenital cataract and of 16 patients (p. 206) treated for unilateral congenital cataract within 10 minutes of that first patterned input (Maurer, Lewis, Brent, & Levin, 1999). Despite variation in the age at treatment from 1 week to 9 months, acuity was, on average, like that of normal newborns, whether deprivation had been unilateral or bilateral. There was no sign that improvement had occurred with increasing age in the absence of patterned visual input. As a consequence, acuity fell farther below the norm for the patient's age the later during the first year that treatment occurred and on average was more than 2 octaves worse than the norm, where an octave is a halving or a doubling of a value. These data suggest that, in the child with normal visual input, the first 9 months of life are part of the period of visually driven normal development. Subsequent testing after 1 hour of

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visual input, 1 month later, and at 1 year of age revealed rapid improvement from the delayed visual input.

After 1 hour of patterned visual input, the acuity of treated eyes improved—to the level of a visually normal 6-week-old (Maurer et al., 1999). The improvement occurred in 20 of the 24 eyes from bilateral cases and in 12 of the 16 treated eyes from unilateral cases. There was additional improvement over the next month such that the deficit compared to age-matched controls decreased from more than 2 octaves to about 1 octave. The improvements over the first hour and the next month were not related to the age at treatment nor, in unilateral cases, to the amount of time that the good eye had been patched. A control experiment showed that the improvement after the first hour of patterned visual input was in fact a consequence of visual experience: when we patched one eye of six bilateral cases between the first test and the retest after 1 hour of waking time, acuity in the unpatched eyes improved but acuity in the patched eyes did not.

Our subsequent studies, like others in the literature, indicated that by 1 year of age, the acuity of treated eyes improved further so that the acuity of most eyes fell within normal limits, whether deprivation had been bilateral or unilateral (Birch & Stager, 1988; Birch, Stager, & Wright, 1986; Birch, Swanson, Stager, Woody, & Everett, 1993; Catalano, Simon, Jenkins, & Kadel, 1987; Jacobson, Mohindra, & Held, 1983; Lewis, Maurer, & Brent, 1995; Lloyd, Dowler, Kriss, Speedwell, Thompson, Russell-Eggitt, & Taylor, 1995; Mayer, Moore, & Robb, 1989). The implication is that acuity improved faster than normal as it changed from the newborn level immediately after treatment (well below normal if the patient was older than 2 months) to within normal limits at 1 year of age. Like the results during the first hour and month after treatment, these findings indicate a readiness of cortical neurons to respond to visually driven activity after deprivation ends. Another finding is that although the acuity of most treated eyes was within normal limits when tested at 12 months of age, in unilateral cases, the more the good eye had been patched since treatment, the better the acuity at 1 year (Lewis et al., 1995). Thus, the deleterious effects of uneven competition between the eyes are beginning to take effect by 1 year of age.

The rapid improvement in our patients upon the first visual input is consistent with studies of unilaterally deprived and dark-reared cats, which, upon the first exposure to light, show rapid changes in measured acuity and in markers of plasticity in the visual cortex (Beaver, Mitchell, & Robertson, 1993; Mitchell, Beaver, & Ritchie, 1995; Mitchell & Gingras, 1998; Mower, 1994). Thus, the system appears to be experience-expectant: ready to respond rapidly to visual input but able to do so only once the patterned visual input is received. When the input is delayed, the system increases its readiness for rapid response. One possible explanation is that spontaneous retinal activity, which has been shown to play an important role in sculpting cortical connections in the cat before eye opening (reviewed in Katz & Shatz, 1996), is sufficient to alter the visual cortical connections during the period of visual deprivation from congenital cataracts.

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Although the grating acuity of children treated for bilateral or unilateral congenital cataract is within normal limits by 1 year of age and continues to improve during early childhood, it fails to keep pace with normal development. Grating acuity begins to fall below normal limits by 2 years of age (Lewis et al., 1995) and after bilateral deprivation is, on average, 3.5 times worse than normal by 5 to 18 years of age (Ellemborg et al., 2002). Overall, in our sample, acuity was no different after unilateral than after bilateral deprivation, likely because most unilateral cases had reduced the deleterious effects of uneven competition between the eyes by patching the good eye more than 3 hours per day throughout early childhood. In fact, the three unilateral cases with the most exposure to uneven competition between the eyes because they had the longest deprivation (>8 months) and the least occlusion therapy (<3 hours per day throughout early childhood) had very poor grating acuity—acuity that was, on average, nearly 15 times worse than that of the rest of the unilateral cases.

(p. 207) Evidence for permanent deficits in asymptotic grating acuity after unilateral or bilateral deprivation also has been reported in other human cohorts and in visually deprived monkeys (reviewed in Maurer & Lewis, 2001b). There are similar deficits in asymptotic letter acuity, with the deficits greater after unilateral than after bilateral deprivation, unless the good eye was patched aggressively after unilateral deprivation (Birch et al., 1993, Birch, Stager, Leffler, & Weakley, 1998; Lundvall & Kugelberg, 2002; Magnusson, Abrahamsson, & Sjöstrand, 2002; Maurer & Lewis, 1993; Mayer et al., 1989; reviewed in Maurer & Lewis, 2001a, b). However, if the deprivation is extremely short—ending before 10 days of age—the outcome seems to be better and some children even achieve normal linear letter acuity of 20/20 (Kugelberg, 1992; Lundvall & Kugelberg, 2002; see also Magnusson et al., 2002). Thus, the visual system appears to be less sensitive to visual input (or its absence) before 10 days of age, and the period of visually driven normal development for grating acuity may begin not at birth, but shortly thereafter.

Why are there deficits in acuity after early visual deprivation? Studies of monkeys deprived of visual input to one or both eyes indicate that early visual deprivation damages the visual cortex. The retina by every measure is normal and cells in the lateral geniculate nucleus (LGN), although smaller than normal, have normal electrophysiological properties (Crawford, Blake, Cool, & von Noorden, 1975; Hendrickson & Boothe, 1976; Blakemore & Vital-Durand 1986; reviewed in Boothe et al., 1985). It is at the level of the primary visual cortex that damage from early visual deprivation becomes apparent, with the damage greater after unilateral than after bilateral deprivation. Specifically, after bilateral deprivation, most cells respond more sluggishly than normal, have abnormally large receptive fields, are poorly tuned to orientation and spatial frequency, and have reduced acuity (Blakemore, 1990; Blakemore & Vital-Durand, 1983; Crawford et al., 1975; Crawford, Pesch, von Noorden, Harwerth, & Smith, 1991). After unilateral deprivation, some cells are completely unresponsive, and the few cells drivable by the previously deprived eye have a much greater reduction in acuity than those in the primary visual cortex of bilaterally deprived monkeys (Blakemore, 1988; Crawford, 1988; Crawford et al., 1991; Hubel, Wiesel, & LeVay, 1977; LeVay, Wiesel, & Hubel, 1980). Reverse-suturing (sewing shut the good eye after the reopening of the originally deprived eye) increases the pro-

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portion of cells that can be driven by the originally deprived eye (Blakemore, 1988, 1990; Blakemore, Garey, & Vital-Durand, 1978; Crawford, de Faber, Harwerth, Smith, & von Noorden, 1989; Swindale, Vital-Durand, & Blakemore, 1981). Thus, both early deprivation and uneven competition appear to have their impact at the level of the cortex. The pattern of damage in the visual cortex is consistent with findings of worse acuity after unilateral than after bilateral deprivation, unless after unilateral deprivation the good eye is patched aggressively.

Sensitive Period for Damage

To delineate the sensitive period for damage to the normal development of grating acuity and to determine the end of the period of visually driven normal development, we tested the grating acuity of 15 patients who had an early history of normal visual input until they developed dense central cataracts in one or both eyes between the ages of 4 months and 15 years (Ellemberg et al., 2002). Thirteen of the patients had onset of deprivation before 5 years of age, and every deprived eye of these patients had abnormal grating acuity. In contrast, the two patients with later onset (>11 years) had normal grating acuity. Our distribution of patients did not allow us to ascertain the effects of deprivation beginning between 5 and 11 years of age. Thus, visual deprivation anytime up to at least 5 years of age (except possibly the first 10 days of life) leads to a permanent deficit.

Studies of letter acuity demonstrate that the sensitive period for damage lasts even longer, beyond the period of normal development. We tested linear letter acuity in each eye of 40 children who had a normal visual history until they developed a cataract in both eyes between 7 months and 10 years of age (Maurer & Lewis, 2001a, b). Asymptotic letter acuity was generally better, the later the onset of deprivation, but was abnormal in all but 3 of the 80 deprived eyes even with deprivation beginning as late as 10 years of age. Tests of the deprived eye of 29 children who had a normal visual history until they developed a cataract in one eye after 3 months of age revealed abnormal letter acuity if the deprivation began before 8 years of age, but not if it began after 10 years of age (Maurer & Lewis, 2001a, b). Similarly, Vaegan and Taylor (1979) concluded from their cohort of patients unilaterally deprived of pattern vision beginning at various ages that the sensitive period for damage lasts until about 10 years of age.

(p. 208) In summary, cataracts that become dense and central before about 10 years of age cause permanent deficits in linear letter acuity, whether the deprivation had been unilateral or bilateral. Yet, in visually normal children, letter acuity reaches adult values by about 6 years of age (Simons, 1983). These findings suggest that visual input is necessary for the refinements of visual acuity throughout the 6 years of normal development of letter acuity (that is, the period of visually driven normal development lasts from 10 days to 6 years of age) and that acuity is susceptible to damage for approximately 3 to 5 years thereafter, so that the sensitive period for damage lasts from 10 days to 10 years of age. Presumably, visual input is necessary to crystallize functional connections and/or to prevent them from being pruned or inhibited by competition between a stronger good eye and the previously deprived eye and/or between inputs to the visual cortex from two pre-

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viously deprived eyes versus from other normally functioning sensory modalities (e.g., Bavelier & Neville, 2002; Rauschecker, 1995).

Sensitive Period for Recovery from Deprivation

The studies of grating acuity indicate that during the early postnatal period, the visual system is experience-expectant: able to respond rapidly to visual input so that grating acuity improves quickly and preparing to do so even during a period of monocular or binocular deprivation. However, the studies of later grating and letter acuity indicate that missing visual input during this early postnatal period, when visually normal infants have poor acuity that limits them to seeing only wide stripes, leads to later deficits. This is an example of a “sleeper effect” in which the adverse effects of early visual deprivation are apparent only later when a visual capability fails to emerge or be perfected at the normal time.

To learn more about the origins of this sleeper effect and about the sensitive period for the recovery of vision after early visual deprivation, we conducted a longitudinal study of contrast sensitivity (Elleberg, Lewis, Maurer, & Brent, 2001; Lewis, Elleberg, Maurer, & Brent, 2000; Maurer, Elleberg, & Lewis, 2006, unpublished data). Contrast sensitivity is a measure of the minimum contrast necessary to see sine waves of different frequency. Between 5 and 7 years of age, the contrast sensitivity of visually normal children improves to adult levels for all spatial frequencies (Elleberg et al., 1999a). When first tested at 5 to 7 years of age, patients treated for bilateral or unilateral congenital cataract were most sensitive to low spatial frequencies (wide stripes), with the unilateral group showing normal sensitivity and the bilateral group needing more contrast than age-matched normals to see the sine waves, except for a few bilateral patients who had normal sensitivity. When retested 1 and/or 2 years later (i.e., when 6 to 9 years old), both unilaterally and bilaterally deprived patients had improved at low spatial frequencies, sometimes more than controls, so that the unilateral group remained normal and the bilateral group reduced the size of the average deficit.

The results were quite different at middle and high spatial frequencies (medium and narrow stripes), for which both groups initially needed more contrast than age-matched control groups. Over the next 1 and/or 2 years (i.e., until 6 to 9 years of age), the sensitivity of bilateral patients improved for middle spatial frequencies, sometimes more than the amount of change in visually normal children over the same period. The result was a constant or decreased deficit. In contrast, unilateral patients lost sensitivity over the same period so that their absolute performance was worse on the retest and their deficit grew compared to normal. Thus, the results for middle and low spatial frequencies indicate some potential for recovery, especially in bilateral patients, until roughly 9 years of age.

In contrast, over the 1 and/or 2 years, for high spatial frequencies, the sensitivity of bilateral patients was static while that of unilateral patients decreased, unlike age-matched controls, who improved at all spatial frequencies until age 7 (Elleberg et al., 1999b). The consequence is that patients’ deficits in both groups increased at high spatial fre-

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quencies after age 5. The cutoff for improvements at high spatial frequencies is probably around age 5 and not earlier: the letter acuity of patients treated for bilateral congenital cataract improves between a test at age 4 and a test at age 7 (Magnusson et al., 2002), but their sensitivity to high spatial frequencies does not improve after a test at age 5 (our study). The implication is that visual input during the first few months after birth is necessary to set up the cortical neural architecture that will become fine-tuned to resolve narrow stripes after age 5. In contrast, recovery of sensitivity to low and middle spatial frequencies continues after age 5 until roughly age 9, often allowing full or nearly full recovery.

The differences between unilateral and bilateral patients at low spatial frequencies (unilateral better) versus middle and high spatial frequencies (bilateral (p. 209) better) suggest that interocular competition between a nondeprived eye, which is nearing adult levels of contrast sensitivity, and a deprived eye can have very different effects at low and higher spatial frequencies. Interocular competition may contribute to recovery at low spatial frequencies but may erase part of the earlier recovery at higher spatial frequencies. The results also suggest that the deficits after unilateral deprivation may be underestimated if assessments are made too early in childhood, as has been true in many previous studies. The better outcome for the unilateral group at low spatial frequencies is surprising, given behavioral and electrophysiological evidence of a worse outcome after monocular than after binocular deprivation. However, there have been few direct comparisons of contrast sensitivity after unilateral versus binocular visual deprivation (Birch et al., 1998; Ellemberg et al, 1999b, 2000; Tytla, Maurer, Lewis, & Brent, 1988), and no other study has limited the comparison to patients old enough to measure the final outcome.

These results, along with those of Magnusson and colleagues (2002), provide the only measurements of the sensitive period for recovery after early pattern deprivation in humans. They illustrate that there is some potential of the visual system to recover once the deprivation is ended and normal visual input is restored—without any explicit rehabilitative training.

Together, the results for acuity and contrast sensitivity illustrate three sensitive periods with different time courses: (1) the period of visually driven normal development that is over by 5 to 7 years of age, (2) the sensitive period for damage lasting until about age 10, and (3) the sensitive period for recovery that lasts until about age 9 for low spatial frequencies but only until about age 5 for higher spatial frequencies and letter acuity.

Rehabilitation of Visual Acuity

We have described a sensitive period for recovery, a period during which the visual system has the potential to partially or fully recover from the deleterious effects of deprivation when exposed to a normal visual environment. As discussed in the previous section, the sensitive period for the (partial) recovery of acuity lasts until about 5 to 7 years of age. It has been assumed commonly that improvements in acuity after that age are unlikely, if not impossible, whether the original problem was bilateral (e.g., bilateral

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cataracts) or unilateral (e.g., misaligned eyes, unequal refractive error, or unilateral cataract). Studies evaluating the premise have studied the efficacy of later intervention in improving vision in unilateral cases in which the patient had developed one amblyopic eye secondary to the earlier abnormal input to that eye. To date, there are no such studies of interventions in bilateral cases.

The standard treatment for unilateral amblyopia is to fix the peripheral problem (by aligning the eyes surgically, giving corrective glasses, or removing the cataract) and then to patch the good eye to force usage of the amblyopic eye. The common premise is that the patching will be effective only during the period of normal acuity development—that is, until 5 to 7 years. To test the validity of that common belief, Birnbaum and colleagues (1977) conducted a meta-analysis of 23 studies of acuity in amblyopes of unspecified origin and found, surprisingly, equal beneficial effects of patching the good eye for those treated before versus after 7 years of age. In the 17 studies providing sufficient information to permit a finer analysis of age categories, results indicated that patching therapy was equally successful in children under 7 as for children aged 7 to 10 years and even those aged 11 to 15 years. Specifically, 55% to 59% of children 15 years of age or younger showed at least a four-line improvement in acuity (i.e., were able to read four lines farther on a letter acuity chart), whereas significantly fewer (42%) of those with patching therapy beginning after age 15 showed such good improvement.

Other researchers have evaluated the efficacy of combining patching with other specific interventions.

Active Near Work

The prognosis for improvement in visual acuity is even better and can be extended well into adulthood if patching is supplemented by active near work such as eye–hand coordination exercises and/or stimulating the amblyopic eye with moving gratings for 30 hours over an 8-week period (Ciuffreda, Goldner, & Connelly, 1980; Hokoda & Ciuffreda, 1986; Kupfer, 1957; Terrell, 1981; Wick, Wingard, Cotter, & Scheiman, 1992). In a pioneering study, Kupfer (1957) hospitalized seven adult amblyopes, six of whom had misaligned eyes and vision of 20/200 or worse in the amblyopic eye (the seventh had acuity of 20/70). During their 4 weeks of hospitalization, patients had the good eye patched full time and were given extensive fixation exercises for the amblyopic eye. Snellen acuity improved in all seven cases and improved to at least 20/40 in five of them, improvements that were still present on 6-month follow-up.

(p. 210) Using a less intensive approach, Wick and colleagues (1992) attempted to improve the vision of 19 previously untreated anisometropic amblyopes (amblyopia secondary to unequal refractive errors between the eyes that were uncorrected during early childhood) aged 6 to 49 years. Each was given suitable refractive corrections, prisms to correct any misalignment of the eyes, 2 to 5 hours per day of patching, and 30 minutes per day of active eye exercises such as tracking, eye–hand coordination, and fusion. After 15 weeks of treatment, improvements in visual acuity ranged from 75% improvement in a 49-year-old to 100% improvement in 8 of the 18 remaining patients. Retests in four pa-

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tients 1 year after treatment was discontinued showed that all had maintained their improvements in acuity. Thus, near activities combined with patching of the good eye can extend the potential for recovery well into adulthood. Such therapy is not nearly as successful, or not successful at all, if patching does not accompany the training or if the training is short (cf. Ciuffreda et al., 1980; Terrell, 1981). It is unclear why active near work improves visual acuity. One possibility is that the extra visual stimulation operates via mechanisms analogous to exposing rats to enriched environments (see Section on Mechanisms Underlying Improvements in Visual Acuity).

Perceptual Training

More recent studies have used various forms of perceptual training as the near activity, combined with patching and many trials of training (Chung, Li, & Levi, 2006; Huang, Zhou, & Lu, 2008; Levi & Polat, 1996; Levi et al., 1997; Li & Levi, 2004; Li, Provost, & Levi, 2007; Li, Young, Hoening, & Levi, 2005; Polat et al., 2004; Zhou et al., 2006; reviewed in Levi, 2005). The usual approach is to measure vision before and after extensive training in a task such as contrast thresholds for detecting a grating (Huang et al., 2008; Polat et al., 2004; Zhou et al., 2006), contrast thresholds for letter identification (Chung et al., 2006), vernier acuity (sensitivity to slight misalignments between two stimuli) (Levi & Polat, 1996; Levi et al., 1997), or similar tasks involving positional discriminations (Li & Levi, 2004; Li et al., 2005, 2007). Training in these studies involved thousands of trials over many days, with feedback about the accuracy of response.

Overall, the perceptual training studies show excellent improvement in the amblyopic eye on the trained task, typically ranging from 32% to 65% (Levi & Polat, 1996; Levi et al., 1997; Li et al., 2005, 2007). Such improvements were evident not only in children older than age 7 (Li et al., 2005, 2007) but even in adults (Chung et al., 2006; Huang et al., 2008; Levi & Polat, 1996; Levi et al., 1997; Li & Levi, 2004; Polat et al., 2004; Zhou et al., 2006).

There is considerable transfer of training for the trained task to the good eye, typically ranging from 24% to 60% (e.g., Levi & Polat, 1996; Levi et al., 1997). This transfer of training indicates that the learning has occurred beyond the site of binocular convergence. However, there is little transfer of training to different stimuli, even when the trained task, such as vernier acuity or positional discrimination, is tested with the same stimuli but at a novel orientation (Levi & Polat, 1996; Levi et al., 1997; Li & Levi, 2004). There is also little transfer of learning from contrast-defined letters to luminance-defined letters (Chung et al., 2006). Such limited transfer suggests that the training affects specific populations of visual neurons and not just generalized learning.

When the training is titrated to be near the amblyopic eyes' threshold, improvements can be much larger (averaging over 200% at the trained spatial frequency) (Zhou et al., 2006) and transfer more widely (Huang et al., 2008). Huang and colleagues (2008) trained teenagers and adults with anisometropic amblyopia on a contrast-detection task at one spatial frequency near their individual contrast threshold. Improvements in contrast sen-

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sitivity after training spread over a wide range of spatial frequencies, a much wider range than in a comparably aged visually normal group that had received the same training.

Moreover, at least in amblyopes, training in tasks such as contrast detection or positional discriminations transfers to improvements in Snellen acuity (Huang et al., 2008; Levi & Polat, 1996; Levi et al., 1997; Li et al., 2005, 2007; Polat et al., 2004; Zhou et al., 2006). For example, Zhou and colleagues (2006) trained 23 anisometric amblyopes, aged 14 to 27 years, on a contrast-detection task. A group that was trained with gratings of varying spatial frequency showed an improvement in the Snellen acuity of the amblyopic eye of 46%. A second group trained on a contrast-detection task only at one spatial frequency near their individual contrast threshold showed an improvement in the Snellen acuity of the amblyopic eye of 70%, an improvement that was retained in five of the six participants when retested 18 months later. No such improvements occurred in a control group that was given the same pretests and posttests but no intervening training.

Such learning does not come easily—it takes many trials to reach asymptote (Levi et al., 1997; (p. 211) Li et al., 2007; Zhou et al., 2006). In fact, so many trials are required to reach asymptote that the number is now sometimes expressed in kilo-trials. For example, in one study, amblyopes who were experienced in perceptual training tasks reached half the pretraining value after 5,000 to 6,000 trials, whereas those who were new to perceptual training tasks reached only 40% of pretraining values after 10,000 trials (Levi et al., 1997). Nevertheless, these studies indicate that the adult visual system is sufficiently plastic to allow substantial recovery from amblyopia when patching is combined with training on specific types of visual discrimination and that the training generalizes to improved letter acuity. Training is also effective in inducing modest improvements in control adults with normal eyes, but the potential for substantial and generalized improvement appears to be larger in amblyopes.

Telescopic Magnification

A recent approach to vision therapy has involved telescopic magnification in order to provide a clearer image to the amblyopic eye while patching the fellow eye (Nazemi, Markowitz, & Kraft, 2008). The participants consisted of 18 anisometric amblyopes, aged 7 to 16 years, who were no longer attempting patching therapy. The patients were instructed to watch their favorite television show for 30 minutes every day while patching the dominant eye and wearing a telescopic device over newly prescribed glasses. At the 6-month follow-up, acuity had improved, on average, from 20/63 to 20/35, with 15 of the 18 participants achieving an acuity of 20/40 or better. Unfortunately, there were no control groups, and so it is unclear the extent to which the observed improvement was a result of occlusion, magnification, and/or watching television. Moreover, it would be interesting to determine whether even greater improvements could be achieved if the telescopic magnification was combined with active near work or perceptual training rather than with passive television viewing.

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Repetitive Transcranial Magnetic Stimulation

Another approach to visual rehabilitation, repetitive transcranial magnetic stimulation, is a technique borrowed from the literature on stroke recovery. Transcranial magnetic stimulation (TMS) is a noninvasive method to excite neurons in the brain: weak electric currents are induced in the tissue by rapidly changing magnetic fields (electromagnetic induction). Repetitive TMS (rTMS) produces effects that last longer than the period of stimulation. rTMS can increase or decrease the excitability of neural pathways depending on the intensity of stimulation, coil orientation, and frequency of stimulation. The mechanism of these effects is not clear, although it is widely believed to reflect changes in synaptic efficacy akin to long-term potentiation and long-term depression (see Fitzgerald, Fountain, & Daskalakis, 2006, for a review).

First-time stroke patients suffering severe hand and motor impairment on the side contralateral to the affected motor cortex benefit from rTMS over the motor cortex on both the affected and unaffected side (Delvaux, Alagona, Gérard, De Pasqua, Pennisi, & de Noordhout, 2003). Clues to the mechanisms underlying this recovery come from a recent study of visually normal participants showing that rTMS can either facilitate or suppress perceptual functions depending on the baseline level of activity of the targeted brain region (Silvanto, Cattaneo, Battelli, & Pascual-Leone, 2008). Not surprisingly, rTMS over area MT/V5 in visually normal humans caused impaired performance on a motion-detection task. Paradoxically, if MT/V5 activity had first been suppressed by stimulating it with a 1-Hz TMS for 10 minutes, subsequent rTMS had a facilitatory effect on motion detection. Thus, the baseline activation level of the targeted brain area is critically important in determining the behavioral impact of rTMS— rTMS has an inhibitory effect on behavior when the targeted neural population is in an excitatory state but can have an unexpected facilitatory effect on behavior when the targeted neural population is in a suppressed state. Thus, TMS likely promotes recovery in stroke patients not only by decreasing neural activity in the unaffected hemisphere, thereby reducing intracortical inhibition of a healthy cortex on a weakened one (Liepert, Hamzei, & Weiller, 2000; Manganotti, Patuzzo, Cortese, Palermo, Smania, & Fiaschi, 2002; Sale, Maya Vetencourt, Medini, Cenni, Baroncelli, De Pasquale, & Maffei, 2007) but also by facilitating activity in the affected hemisphere, thus restoring intracortical balance.

Mansouri and colleagues (Mansouri, Thompson, Koski, & Hess, submitted; Thompson, Mansouri, Koski, & Hess, 2008) tested the possibility that rTMS could have a beneficial effect in amblyopia just as it has in stroke recovery. Like patients suffering from a unilateral motor stroke, the amblyopic patient suffers from cortical imbalance whereby neurons receiving input from the unaffected eye suppress the weaker neurons that receive input from the amblyopic eye. Based on the findings of Silvanto (p. 212) and colleagues (2008), rTMS in amblyopes might facilitate responses from neurons receiving input from the amblyopic eye and suppress responses from neurons receiving input from the fellow normal eye, thus reducing cortical imbalance and improving visual function in the amblyopic eye. That is exactly what happened in all six strabismic and/or anisometropic amblyopes given 900 pulses of rTMS of 10 Hz over the primary visual cortex: contrast sensitivity for a spa-

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tial frequency close to the individual's acuity cutoff improved significantly from baseline to retests immediately after stimulation and 30 minutes later. No such improvements in contrast sensitivity occurred after rTMS over the motor cortex, a result indicating that improvements were a consequence of rTMS over visual cortex and not an artifact nor merely a consequence of practice. Contrast sensitivity also did not improve under other conditions tested, namely for a spatial frequency close to the individual acuity cutoff with rTMS of 1 Hz and for a low spatial frequency of 1 cpd after rTMS of 1 or 10 Hz. Nonetheless, although the beneficial effects were no longer evident on 1-week follow-up tests, the technique holds promise and, like the results for near work and perceptual training, the results indicate that there is residual plasticity in the adult visual system.

Drug Therapies

The drug levodopa, when taken by mouth, crosses through the blood-brain barrier, where it is converted to dopamine. Levodopa has been used successfully to treat Parkinson's disease (Rinne et al., 1997), a disease known to involve reduced levels of dopamine in the retina (Nguyen-Legros, 1988). Monocularly deprived monkeys also have reduced levels of dopamine in the retina of the deprived eye (Iuvone, Tigges, Fernandes, & Tigges, 1989). Moreover, the catecholamines, of which dopamine is an example, are known to play a major role in cortical plasticity. For example, Kasamatsu (1982; Kasamatsu & Heggelund, 1982) restored cortical plasticity by perfusing the visual cortex with the catecholamine norepinephrine in adult cats in which norepinephrine had been depleted by a drug that stops cortical plasticity or by prior monocular deprivation. Thus, drug therapies involving the catecholamines are an obvious candidate for improving the vision of amblyopes, and several investigators have studied the effectiveness of levodopa (Algaze, Leguire, Roberts, Ibinson, Lewis, & Rogers, 2005; Gottlob, Charlier, & Reinecke, 1992; Gottlob & Stangler-Zuschrott, 1990; Leguire, Rogers, Bremer, Walson, & Neff, 1992; Leguire, Rogers, Bremer, Walson, & McGregor, 1993; Leguire, Rogers, Walson, Bremer, & McGregor 1998; Procianoy, Fuchs, Procianoy, & Procianoy, 1999).

In a pioneering study, Gottlob and Stangler-Zuschrott (1990) gave nine adult patients with severe strabismic or anisometric amblyopia a single dose of 200 mg levodopa with 50 mg benzerazide to reduce peripheral side effects. From just before drug administration to 90 minutes thereafter, contrast sensitivity improved in all nine patients at one or more spatial frequencies and visual acuity improved modestly in two of them. There was no change in acuity or contrast sensitivity after placebo administration or in visually normal controls. The success rate was higher in adult amblyopes given 1 week of daily drug administration (Gottlob et al., 1992) and in younger amblyopes, 4 to 17 years of age, given one high dose of levodopa or lower doses of levodopa (to avoid negative side effects of the drug) combined with patching (Leguire et al., 1992, 1993, 1998; Procianoy et al, 1999). Moreover, improvements in vision were still evident at a follow-up test 4 weeks after treatment was discontinued (Leguire et al., 1998). However, it is still unclear whether improvements in acuity are dose-related (cf. Leguire et al., 1993; Procianoy et al, 1999) and whether the improvements last beyond 4 weeks. Nevertheless, like the short-term im-

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provements demonstrated with rTMS, the results from adult amblyopes provide additional evidence for residual plasticity in the adult visual system.

Mechanisms Underlying Improvements in Visual Acuity

The mechanisms responsible for improvements in visual acuity after the traditional sensitive period for recovery has ended likely differ for different rehabilitative therapies. One likely candidate is the reduction in cortical inhibition that prevents normal functioning of neurons that receive input from the amblyopic eye. In fact, the reduction of intracortical inhibition is thought to be one of the key factors underlying the restoration of plasticity in the adult visual system. This is evident in studies of ocular dominance in rats—studies of the number of neurons that can be driven by either eye. After early unbalanced binocular input, ocular dominance shifts so that most neurons can be driven only by the normal eye. Restoration of binocular input after the sensitive period for damage is not sufficient to shift ocular dominance back toward normal, but a number of interventions in adulthood (p. 213) have been successful in restoring the plasticity of ocular dominance so that it can be at least partially altered to match the current balance of binocular input, rather than that which occurred early in development. Specifically, ocular dominance plasticity can be restored by exposing adult rats to an enriched environment, by infusing drugs such as mycophenolic acid (MPA) that inhibit the synthesis of GABA (the chief inhibitory neurotransmitter in the central nervous system), or by long-term administration of fluoxetine (Prozac), a selective serotonin reuptake inhibitor widely prescribed for the treatment of depression (Maya Vetencourt, Sale, Viegi, Baroncelli, De Pasquale, O’Leary, Castrén, & Maffei, 2008; Sale et al., 2007; reviewed in Spolidoro, Sale, Berardi, & Maffei, 2009). All of these manipulations are thought to reduce intracortical inhibition. In fact, adult amblyopic rats given fluoxetine show not only a reinstatement of ocular dominance plasticity but also corresponding improvements in visual acuity, as measured electrophysiologically and behaviorally (Maya Vetencourt et al., 2008). Conversely, increasing intracortical inhibition by the cortical infusion of a benzodiazepine after environmental enrichment or cortical infusion of diazepam after the administration of fluoxetine causes a corresponding decrease in plasticity (Maya Vetencourt et al., 2008; Sale et al., 2007).

The manipulation of adult plasticity in animal models by drugs that increase or decrease intracortical inhibition indicates that the apparent reduction in intracortical inhibition induced by rTMS makes it a promising approach for restoring plasticity in adult amblyopes. It is possible that active near work, telescopic magnification, and perceptual training might, at least in part, be analogous to the environmental enrichment that caused reductions in intracortical inhibition in adult rats (Sale et al., 2007).

Other mechanisms underlying the observed improvements in visual acuity after perceptual training have been proposed (reviewed in Levi, 2005). First, improvements in acuity might be attributable to reductions in internal noise (a type of uncertainty, perhaps arising from insufficient sampling of the visual stimulus) and/or an increase in the efficiency with which the stimulus information is used. The contribution of each of these two factors can be evaluated by using Pelli’s (1990) external noise paradigm. The approach is to mea-

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sure thresholds with varying amounts of external noise added to the stimulus while the subject performs a task such as identifying a letter. Adding external noise will have no effect on thresholds so long as the level of external noise is less than the level of internal noise. Thresholds will rise as soon as the level of external noise exceeds that of the internal noise, thereby providing an indirect measure of the level of internal noise (Pelli, 1990). Thus, if training causes only a reduction in internal noise in amblyopes, the shape of the function relating threshold to level of external noise should change before versus after training: less and less external noise should cause an increase in threshold, indicating that the level of internal noise has decreased. However, if training causes only an increase in efficiency, thresholds should improve with training, but equally for all levels of external noise. Pelli, Levi, and Chung (2004) tested these possibilities by measuring letter identification thresholds in amblyopes as a function of the amount of external noise in the stimulus before and after 5,000 training trials. For all four patients, thresholds improved after training nearly equally for all levels of external noise, indicating that the improvement with training was primarily a consequence of increased efficiency with little or no reduction in internal noise. Others have reached similar conclusions after training involving many days and thousands of trials (Li & Levi, 2004; Li et al., 2005, 2007; reviewed in Levi, 2005).

As suggested by the evidence for increased efficiency, improvements in acuity with extensive training might be attributable, at least in part, to the challenge of making fine discriminations and/or to learning through practice and feedback to attend to the most salient or relevant information when looking with the amblyopic eye (reviewed in Levi, 2005). The notion of learning to use the most relevant information is consistent with the findings of increased efficiency with training in the amblyopic visual system (Pelli et al., 2004) and evidence that the training alters existing networks rather than establishing new ones (Levi, 2005). An additional contribution may come from the fact that the dominant eye is patched during the extensive training and the patching alone may have a beneficial effect by reducing intracortical inhibition.

These alternatives are not mutually exclusive and may, in fact, be different levels of explanation of the same or interrelated mechanisms. To date there have been no studies of rehabilitation after the traditional sensitive period in patients treated for bilateral deprivation. We can predict that interventions will be even more effective than they are in unilateral cases in inducing improvements for low-level aspects of vision because there is no, or less, abnormal intracortical inhibition to offset. On (p. 214) the other hand, higher-level vision may be harder to rehabilitate in bilateral cases because there was no signal from a nondeprived eye during the period of deprivation to tune the neurons in higher cortical areas that receive converging input from both eyes.

Face Processing

Adults are experts at face processing: they can rapidly recognize individual faces, their facial expressions, and direction of gaze even when other cues are varied and, under

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many conditions, do so more accurately than they make comparable judgments about objects (see Lee et al., this volume 1). In this section, we consider the role of visual input in the development of those face-processing skills by contrasting the capabilities of children who missed early visual input because of dense, bilateral cataracts to those of age-matched controls. The results indicate that some, but not all, aspects of face processing are damaged. Because only congenital cases have been studied, we cannot draw conclusions about the sensitive period for damage or visually driven normal development. However, we will present some indirect evidence from studies of the effect of biased input (e.g., from one race) at different points in development and studies of rehabilitation of adults with cortical damage.

Normal Development of Face Processing

Children born with dense, central cataracts in both eyes that are removed within the first few months of life do not miss much detailed input from faces. In babies with normal eyes, poor visual acuity and contrast sensitivity limit the information they can pick up to the largest, most “contrasty” features of faces: an outline of the head and dark blobs where the prominent internal features are located. Nevertheless, they are sensitive to the shape of that contour and the arrangement of those dark blobs: they orient preferentially toward visual stimuli comprising a black egg-shaped oval contour containing large dark elements located toward the top of the figure, whether tested with schematic black-and-white drawings or facial photographs in which the features have been rearranged (e.g., Cassia, Turati & Simion, 2004; Simion, Valenza, Cassia, Turati & Umiltà, 2002; Turati, Simion, Milani & Umiltà, 2002; Turati, 2004). Critical to this preference appears to be top-heaviness (more energy at the top) and congruency (fit between the shape of the external contour and the distribution of internal elements) (Cassia, Valenza, Simion & Leo, 2008). It is only later, at 2 to 4 months of age, that infants begin to prefer faces with the internal features in their correct location over arrangements of facial features with more visible energy or more high-contrast elements in the top half (Turati, Valenza, Leo & Simion, 2005; see also Mondloch et al., 1999).

Nevertheless, the early attentional bias guarantees that human newborns will be drawn to human faces—which do have egg-shaped contours with more visible energy in the upper half—and hence acquire face experience. The information they extract comes mainly from the external contour. When looking at real faces, young infants (<2 months old) are biased to process the external features rather than their internal details, perhaps because of the high contrast between the skin and hair: they typically scan only a limited part of the external contour (Haith, Bergman, & Moore, 1977; Hainline, 1978; Maurer & Salapatek, 1976) and, after repeated exposure to an individual face, they respond to changes in the external features but not to changes in the internal features, unless the external features were occluded during learning (Turati, Macchi Cassia, Simion, & Leo, 2006). Such discriminations are based on information only from very low spatial frequencies (<0.5 cycles/degree)—that is, very large features (de Heering et al., 2008). Newborns do pick up gross information from the internal features: they look longer at faces with direct gaze than with averted gaze if the faces are enface and upright (Farroni, Menon & Johnson,

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2006) and, by 2 to 3 days of age, they look longer at a face with an intense happy expression than a face with an intense fearful expression (but fail to discriminate fearful from neutral expressions, perhaps because the differences are more subtle) (Farroni, 2007). Thus, newborns' first experience with faces conveys only limited information about the details of the internal structure of the face or how it varies between individuals or with changes in facial expression.

There are dramatic changes in sensitivity to internal details around the third month of life. Scanning shifts from an external bias to an internal bias favoring the eyes (Haith et al., 1977; Hainline, 1978; Hunnius & Geuze, 2004; Maurer & Salapatek, 1976), and face preferences depend on the correct arrangement of the internal facial features rather than top-heaviness and congruency (Turati et al., 2005; see also Mondloch et al., 1999). At the same time, babies show evidence of forming a prototype representing the average location and shape of the features in the faces they have seen recently (de Haan, Johnson, Maurer, & Perrett, 2001). New faces are compared to this prototype, allowing for the (p. 215) cumulative effect of experience. By 4 months, they show the first evidence of integrating the internal and external features of faces into a Gestalt so that alterations in either one make the face look novel (Cashon & Cohen, 2004). These changes launch a long developmental period during which children become increasingly sensitive to the details of internal features, with improvements in some face-processing skills continuing past 10 years of age (Mondloch, Geldart, Maurer, & Le Grand, 2003; Mondloch, Le, & Maurer, 2002; Mondloch, Le Grand, & Maurer, 2003). These refinements lead to face expertise: the tuning of face processing to the characteristics of faces encountered in everyday life—namely, upright human faces, often only of one's own race or ethnic group and close to one's own age. Discrimination and recognition for the expert category is better than for other types of faces (inverted, monkey, other race, other age) or nonface objects.

Outcome After Early Binocular Deprivation

Implications of Acuity Deficits for Face Processing

Our work with children treated for bilateral congenital cataract has allowed us to assess the influence on the development of face expertise of the input from faces during the first few months of life, a period during which effective face input is limited by poor acuity, poor sensitivity to contrast, and limited scanning. As in the studies described for acuity, the cataracts were removed surgically during infancy and the eyes given compensatory contact lenses to focus visual input. After treatment, the children had years of visual input from faces and objects with which to tune the system. However, because of the emergent deficit in visual acuity (see the section "Outcome After Early Deprivation" above), the effective input never included the high spatial frequencies that define the sharp edges of features (Elleberg et al., 1999b; Elleberg, Lewis, Maurer, & Brent, 2000; Maurer et al., 2006). Patients treated for bilateral congenital cataracts also require more contrast than normal to see midspatial frequencies (3 to 10 cycles per degree) (Elleberg et al., 1999b; Maurer et al., 2006), the frequency range most critical when adults with normal eyes recognize facial identity or facial expressions (reviewed in Ruiz-Soler & Beltran,

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2006). Thus, the patient's deficits in acuity and contrast sensitivity limit the effective information he or she receives from faces even after treatment—and it is possible that any residual deficits reflect the reduced input the patient receives throughout childhood from the midspatial frequencies on which normal adults come to rely. Nevertheless, adults with normal eyes can perform many face tasks well based only on low spatial frequencies (reviewed in Ruiz-Soler & Beltran, 2006), for which the patient's sensitivity is normal or nearly normal (Elleberg et al., 1999b; Maurer et al., 2006).

Face Detection

Adults with normal eyes can rapidly detect that a stimulus is a face when it contains two eyes above a nose above a mouth—even when the features are not physically present but the facial configuration can be inferred. For example, they can see a face in paintings by Archimbaldo in which the features are replaced by pieces of fruit or vegetables, in two-tone Mooney stimuli in which shadows have been altered to eliminate feature edges, and in some random patterns of rocks, clouds, or white noise, at least when the images are upright (reviewed in Maurer, Grand, & Mondloch, 2002). To measure the effect of early visual deprivation on the development of such skilled face detection, we tested patients treated for bilateral congenital cataract and normal controls with Mooney images forming a face or scrambled image (Mondloch et al., 2003). The 11 patients had missed patterned visual input to both eyes for the first 2 to 6 months of life ($M = 4$ months), the period during which more complex face preferences emerge. Nevertheless, their accuracy ($M = 92\%$) and reaction times ($M = 824$ msec) were as good as those of the control group (89% and 799 msec, respectively). Thus, early visual input from faces or other patterned visual stimuli is not necessary for the later development of normal face detection. Studies of infants immediately after treatment suggest that this normal performance likely reflects recovery from an earlier deficit (Mondloch, Lewis, Maurer, & Levin, 1998).

Processing Identity and Changing Aspects of Faces

Human adults are experts at processing the identity of faces despite changes in their appearance that occur as the individual talks, changes facial expression, or looks off to the side. At the same time, they are good at deciphering the changeable cues: they can lip-read, decode facial expression, and detect precisely where the person is looking off to the side. To assess the effect of early visual deprivation on the development of these skills, we developed a matching-to-sample task in which participants saw a face, and then saw three faces, one of which matched the first face on one dimension while varying on (p. 216) another (Geldart, Mondloch, Maurer, de Schonen, & Brent, 2002; Mondloch et al., 2003). The matching face could have the same identity despite a change in point of view (e.g., from looking up to looking down) or change in facial expression (e.g., from smiling to sad). For these sets, the task was to ignore the point of view and facial expression and to report which of the faces matched the identity of the target. It could instead be a different person but with the same facial expression, the lips forming the same sound, or the eyes gazing in the same direction. For these sets, the task was to ignore identity and to report which of the three faces matched the facial expression, sound being mouthed, or

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direction of gaze of the target. For all sets, the models wore shower caps to eliminate superficial hair cues and to encourage processing of the physiognomy of the face.

We tested 17 patients who had missed patterned visual input for the first 1.5 to 16 months of life (Geldart et al., 2002). Patients performed normally in picking up the changeable aspects of the faces (sound being mouthed, direction of gaze, facial expression), with accuracy as high and reaction times as low when deprivation lasted throughout the first year of life as when it ended during the first few months. These results indicate that sensitivity to the changeable aspects of faces that are important for social interactions can develop normally when the nervous system does not receive patterned visual input during the first year of life or functional input from high spatial frequencies at any point, at least for the gross types of discrimination tested in this experiment that likely can be performed well based only on featural processing. Unlike these normal results, the patients made more errors than controls in matching facial identity despite changes in point of view, with a trend in the same direction for matching identity despite changes in facial expressions, with deficits as large when deprivation ended by 2 to 3 months of age as when it lasted longer. These results indicate that input during the first few months is necessary for the later development of normal sensitivity to the cues to identity that can be used across viewpoints and facial expressions. These cues arise from the bone structure of the face and the systematic way its visibility is altered as the head is rotated or the face adopts a nonneutral expression. Those cues include the spacing among internal facial features, a configural cue called second-order relations.

Cues to Facial Identity

Adults use a variety of cues to discriminate between faces and to recognize their identity: eye and hair color, head shape, shape of individual features (chin, eyebrows, eyes, nose, mouth), skin texture, and the location of individual features—that is, metric differences among faces in the location of features relative to one another (see Lee et al., this volume 1). To assess the influence of early visual experience on the development of sensitivity to these various cues—and to understand the origin of the deficit in matching identity through changes in viewpoint and facial expression—we devised what has come to be known as the Jane task (Mondloch et al., 2002). Jane and her sisters are face images that were manipulated to create sets differing only in the shape of the external contour, only in the shape of the eyes and mouth, or only in the spacing between the two eyes and between the eyes and mouth. The task is a same/different sequential matching task in which the sets are blocked to emphasize the processing of contour, features, and spacing (second-order relations), respectively. For the spacing set, adults are much more sensitive to such small metric differences in upright human faces than in inverted faces, monkey faces, or houses (e.g., Mondloch et al., 2002; Mondloch, Dobson, Parsons, & Maurer, 2004; Mondloch, Maurer, & Ahola, 2006; Rhodes, Hayward, & Winkler, 2006; Robbins, Nishimura, Mondloch, Lewis, & Maurer, 2010). (Depending on the stimuli in the set, there can also be an inversion effect for featural sets.)

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We tested 14 patients who had been deprived of patterned visual input for the first 2 to 6 months of life and compared their accuracy to that of age-matched normative control groups. Patients performed normally on the contour and feature sets but made significantly more errors than controls for the spacing set (Le Grand, Mondloch, Maurer, & Brent, 2001; Le Grand, Mondloch, Maurer, & Brent, 2003; Mondloch et al., 2003). Like the results for visual acuity (see the section above “Outcome After Early Deprivation”), this deficit is an example of a sleeper effect: visual input during the first 2 months of life, a period when the baby with normal eyes is not sensitive to even gross distortions of the spacing of facial features (Bhatt, Bertin, Hayden, & Reed, 2005), prevents the later normal development of sensitivity to feature spacing. To verify that featural processing is indeed normal after early deprivation, in a subsequent study we tested 60 pairings spanning a range of difficulty for normal adults. Even with this larger set of featural differences, the eight patients treated for bilateral congenital cataract performed normally, with a mean accuracy of 0.90 (Mondloch, Robbins, & p. 217 Maurer, 2010). Thus, patterned visual input during early infancy and functional high-spatial-frequency input later in life are not necessary for the development of normal featural face processing.

Holistic Processing

Adults with normal eyes process faces holistically—they glue the features together into a Gestalt, making it more difficult to parse the face so as to attend to the details of an individual feature. One demonstration of holistic processing is the composite face effect (e.g., Hole, 1994; Young, Hellawell, & Hay, 1987): when the top half of one face is combined with the bottom half of another face, adults make errors in identifying the top half, presumably because holistic processing integrates it with the novel bottom half, creating the impression of a novel identity. The difficulty is manifested if they are asked to identify a famous face based just on the top (or bottom) half and if they are asked to make same/different judgments about sequential faces. If holistic processing is broken by misaligning the top and bottom halves, or by inverting the face, accuracy improves and reaction times decrease (Hole, 1994; Young et al., 1987). Children show a composite face effect for upright faces—better accuracy on misaligned than on aligned trials—that is as large as that seen in adults by 4 to 6 years of age (Cassia, Picozzi, Kuefner, Bricolo, & Turati, 2009; de Heering, Houthuys, & Rossion, 2007; Mondloch, Pathman, Maurer, Le Grand, & de Schonen, 2007), and like adults, they show no such effect for cars (Cassia et al., 2009). Studies using a different measure (the part/whole effect) also indicate that adults process upright faces, but not objects, holistically (Tanaka & Farah, 1993).

Patients with a history of early visual deprivation from cataract, however, fail to develop any composite face effect whatsoever during childhood: their accuracy on aligned trials is just as high as their accuracy on misaligned trials and in fact is significantly higher than that of normal controls (Le Grand, Mondloch, Maurer, & Brent, 2004). This was the pattern we found when we tested 12 patients treated for congenital bilateral cataracts who missed early patterned visual input for the first 3 to 6 months of life and who were, on average, 15 years old at the time of testing. The absence of a composite face effect suggests that cataract-reversal patients fail to process faces holistically and hence can easily use

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their intact featural processing to make same/different judgments about the top (or bottom) half of the aligned composite face. Thus, early visual experience is necessary for the later development of holistic face processing. This is another example of a sleeper effect: young infants process faces in a piecemeal fashion and show the first manifestation of integrating information across the face (viz, the inner features and outer contour) at 4 months of age (Cashon & Cohen, 2004), yet missing visual input during the period of piecemeal processing (the first 3 months) prevents the later development of holistic processing during childhood.

Specificity of Deficits

An important question is whether the deficits we observed are specific to faces or reflect more general difficulties in object processing. In some sense, the answer is obvious: the patients have deficits in capabilities that adults with a normal visual history can apply well to upright faces but that they use much more poorly, if at all, with inverted faces, monkey faces, or objects (e.g., Cassia et al., 2009; Mondloch et al., 2006; Tanaka & Farah, 1993). From this perspective, these deficits have to be face-specific, although the patients may have additional deficits in object processing, as suggested by elevated thresholds to integrate dot patterns into a global form (Lewis et al., 2002). Empirical evidence supports the face specificity of the deficits in sensitivity to metric differences in feature spacing. We tested 10 patients treated for bilateral congenital cataracts whose deprivation had lasted as little as 9 days to as long as 10 months on sensitivity to spacing in human faces (the original Jane task), in monkey faces (with exactly the same variation in the location of the eyes and mouth as in the Jane task), and in houses varying in the spacing between windows and between the windows and doors (a task on which the spacing differences were made large enough so that the accuracy of normal adults matched that on the Jane task) (Robbins et al., 2010). Patients were as accurate as normal controls in detecting spacing changes in the houses and monkey faces but, as in the original study (Le Grand et al., 2001), worse than controls for human faces. Thus, early visual experience appears to be necessary specifically for the later development of the exquisite sensitivity to spacing that adults are able to apply to upright human faces.

Summary of the Effects of Early Binocular Deprivation

In sum, patients are able to develop normal face detection; normal sensitivity to changeable aspects of faces (direction of eye gaze, lip-reading, facial (p. 218) expression), at least for the gross differences we tested; and normal sensitivity to differences between individual identities in the shape of the external contour and of the internal features. These capabilities are normal later in life even when deprivation lasted throughout the first 6 months of life or even longer. Because we did not study these capabilities longitudinally, we do not know whether the ultimately normal performance reflects a normal developmental trajectory or complete recovery from an earlier deficit, although our preliminary longitudinal studies of face detection point to the latter.

Our results also indicate that early patterned visual input is essential for the later normal development of holistic processing, normal sensitivity to metric differences between indi-

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vidual identities in the spacing of internal features (second-order relations), and normal ability to recognize the identity of individuals despite a change in point of view. Visual deprivation for as little as the first 1 to 3 months of life, a period during which poor acuity and limited scanning restrict the information babies with normal eyes can pick up from faces, is sufficient to prevent later normal development. These sleeper effects may be interrelated: the spacing of features arises from the bone structure of the face, which does not change with rotation of the head, and which can often be inferred even when specific features are occluded (see McKone, 2008, for empirical evidence). Moreover, it is possible that holistic processing—which develops long before the fine-tuning of feature spacing in the child with normal eyes (by age 4 to 6 years)—facilitates the development of acute sensitivity to spacing differences by allowing the proportionate relations among features to be processed despite changes in viewing distance.

Sensitive Period for Damage

It is tempting to conclude that the development of the spared capabilities is not subject to a critical period during which visual input from faces is necessary for normal development. However, that conclusion would be premature. Our results show only that visual input during early infancy is not necessary for the normal development of face detection, featural processing, and discrimination of facial expressions, direction of gaze, and sound being mouthed, at least as tested here. There may well be a period later in development during which such input is critical. To test that possibility, it is necessary to study children who began life with normal eyes and who then developed cataracts that blocked visual input for a period later in life, as we have done in the studies on acuity reported in the earlier section “Sensitive Period for Damage.” We are currently conducting such studies of face processing.

Our studies indicate that deprivation near birth is sufficient to prevent the development of other face-processing abilities. We do not know if later deprivation would have the same or a lesser effect. Nor do we know whether the deficits arose from deprivation of face input or more general deprivation of patterned visual input. It is possible that patterned visual input during early infancy is necessary to set up or preserve the neural architecture that is required for face expertise to develop later in life, at some point tuned by the diet of faces to which it is exposed (e.g., same race, own age). When the input is missing, that architecture may fail to develop or may be recruited for the processing of stimuli from another modality (as happens in individuals who miss visual input permanently because of congenital blindness—see the section below, “Reorganization of the Visual Cortex After Blindness”).

A recent study of monkeys suggests that later face expertise does indeed depend on early patterned visual input rather than face input *per se*. These monkeys were raised in a complex visual environment but with no exposure to human or monkey faces for 0.5, 1, or 2 years (Sugita, 2008). At the end of the period of deprivation, the monkeys demonstrated a preference to look at monkey or human faces over objects and discriminated easily among monkey faces and among human faces, based on either featural or spacing differ-

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ences. However, after 1 month of exposure to exclusively human or exclusively monkey faces, there was evidence for perceptual narrowing: after that month monkeys showed a preference for only the exposed category of faces over objects and discriminated only among faces from that category. Subsequent exposure to the other category did not alter the narrowing: even after months of living in a monkey colony, the monkeys who saw human faces for the first month could discriminate among human but not monkey faces (Sugita, 2008) and it was only those faces that elicited neural responses in the superior temporal sulcus (Manaka, Tsukiura, & Sugita, 2008). The ability of monkeys to discriminate among faces based on featural or spacing differences even after 2 years of face deprivation (equivalent to roughly 8 years in humans) suggests that there is no critical period during which face input is necessary. Without any face experience at all for the first 2 years, the monkeys were able initially to discriminate among both (p. 219) human and monkey faces. Rather, it was the first face input received that drove the specialization of face processing, regardless of when that occurred. Combined with our data from patients treated for congenital cataract, the results suggest that early patterned visual input, but not face input *per se*, is necessary to set up or preserve the neural architecture that underlies face processing. When the architecture is used, it becomes specialized for the type of face input it first receives.

Sensitive Period for Specialization

There is evidence in humans of a similar process of perceptual narrowing. Six-month-old infants discriminate among individual monkey faces as readily as among individual human faces, but 9-month-old infants fail the test for monkey faces while continuing to readily discriminate among human faces (Pascalis, de Haan, & Nelson, 2002). As in the face-deprived monkeys, the narrowing depends on biased exposure: infants typically see many human faces and few, if any, monkey faces. However, if the diet of faces is made more balanced between species, by exposing infants to named pictures of six monkeys between 6 and 9 months, infants continue to readily discriminate both human and monkey faces at 9 months of age (Pascalis et al., 2005). Anecdotal evidence suggests that once the system has narrowed, it is difficult to gain expertise in distinguishing among monkey faces, as evidenced by difficulties reported by animal handlers (Pascalis, personal communication). The attunement continues as children slowly acquire expertise in perceiving the small differences in feature spacing that distinguish individual faces: by 8 years of age, children, like adults, are more sensitive to such differences in upright human faces, with lower (and nearly equal) accuracy for inverted human faces and monkey faces (Mondloch et al., 2006).

There is similar perceptual narrowing based on the race or ethnicity of the faces the infant sees over the first months of life. Newborns look equally long at faces from their own racial/ethnic group and from other groups (Kelly et al., 2005). By 3 months, they have a looking preference for faces from the racial/ethnic group(s) they encounter most often. Specifically, when tested with Middle Eastern, Chinese, African, and Caucasian faces at 3 months of age, white babies growing up in a predominantly white area of a British city look preferentially toward white faces (Kelly et al., 2005) and Han Chinese babies grow-

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ing up in China without exposure to foreigners look preferentially toward Chinese faces (Kelly et al., 2007a; see also Bar-Haim, Ziv, Lamy, & Hodes, 2006). Thus, by 3 months of age the ethnicity of the faces babies encounter has tuned their looking preferences.

There is conflicting evidence on the extent to which biased exposure to faces of one racial/ethnic group affects infants' ability to discriminate among and recognize faces. In one study, 3-month-old white French babies showed evidence of discriminating among Caucasian but not Asian faces (Sangrigoli & De Schonen, 2004). In contrast, in another study, white British babies discriminated among faces in all four ethnic categories tested (Caucasian, Chinese, Middle Eastern, and African), and it was only later that babies began to fail the discrimination/recognition test for other-race faces (Kelly et al., 2007b), a precursor to adults' other-race effect—that is, better accuracy in recognizing the identity of own-race than other-race faces. However, there is converging evidence that the system is plastic during infancy and able to learn to discriminate/recognize faces from a category to which there was originally little exposure. Thus, in the study of 3-month-old white French babies, familiarization with as few as three Asian faces was sufficient to induce discrimination among novel Asian faces (Sangrigoli & De Schonen, 2004). In fact, the direction of the other-race effect can be completely reversed if the bias in the diet of faces is reversed: Korean children adopted into French families between the ages of 3 and 9 later show an other-race effect as if they had grown up in a white community in France (Sangrigoli, Pallier, Argenti, Ventureyra, & de Schonen, 2005). Like white French adults and unlike Koreans who moved to France as adults, they are better at recognizing an unfamiliar face if it is Caucasian rather than Asian.

The results for attunement to species versus racial/ethnic group are puzzling. On the one hand, in both domains there is perceptual narrowing or attunement to the types of faces the baby encounters. But the system shows signs of narrowing for race/ethnicity at 3 months of age, the period when babies can still readily discriminate among monkey faces. Moreover, the narrowing for species may be less modifiable by later input than that for race/ethnicity, as suggested by the contrasting irreversibility of the narrowing to exposed species in face-deprived monkeys described in the earlier section “Sensitive Period for Damage” compared to the reversal of the other-race effect in the Korean adoptees. One possibility is that the narrowing for species serves to define what is a face—and hence what is processed differently from objects. Although primate (p. 220) faces do elicit the neural markers of face processing—the N170 in the event-related potential and activation in the fusiform face area (FFA) measured by functional magnetic resonance imaging (fMRI), the amplitude of the N170 and the amount of FFA activation are both smaller (de Haan, Pascalis, & Johnson, 2002; Kanwisher, Stanley, & Harris, 1999). Thus, it is possible that when an adult looks at a monkey face, there is activation of networks involved in processing nonface objects but no or minimal activation of the networks beyond the FFA involved in processing facial identity (e.g., Maurer et al., 2007; Rotshtein, Geng, Driver, & Dolan, 2007). For that reason, exposure to monkey faces later in life may not be effective in inducing modifications in face-processing networks.

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Something similar may happen with inverted human faces. By 4 to 5 months of age, infants scan inverted faces differently from upright faces (Gallay, Baudouin, Durand, Lemoine, & Lécuyer, 2006), generalize habituation across point of view only for upright faces (Turati, Sangrigoli, Ruel, & de Schonen, 2004), and discriminate between faces with differences in feature spacing only if the faces are upright (Bhatt et al., 2005; Hayden, Bhatt, Reed, Corbly, & Joseph, 2007). Thereafter, all of the specific face-processing skills become tuned to upright faces: adults have faster face detection for upright faces, show evidence of holistic processing for upright but not inverted faces, are better at perceiving differences in feature spacing and, at least under some testing conditions, differences in feature shape in upright faces (reviewed in Maurer et al., 2002; Rhodes et al., 2006). Inverted faces elicit a delayed N170 and, at least in some designs, less fMRI activation of the FFA (Rossion et al., 2000; Kanwisher, Tong, & Nakayama, 1998; Yovel & Kanwisher, 2005). As would be expected if inverted faces do not engage face-processing networks beyond the FFA, it appears to be difficult, if not impossible, to train adults to distinguish accurately among inverted faces. In one study, even after 1,100 trials of training to distinguish a variety of inverted photos of twins, adults' accuracy was poor, based on detection of tiny local featural differences, and did not lead to any signs of holistic processing (Robbins & McKone, 2003). Together with the results for monkey faces, these findings indicate that once the face-processing system becomes attuned to upright faces of one's own species, it is difficult to retrain. Attunement to faces of one's own race or age group appears more malleable, as we will discuss in the next section, perhaps because faces from these unfamiliar categories are nevertheless processed as faces, not objects, and hence leave open the possibility that later exposure can modify their processing. (The results of studies assessing whether it is possible to attain facelike expertise in adulthood for another object category are inconsistent [cf. Gauthier, Skudlarski, Gore & Anderson, 2000 vs. Robbins & McKone, 2007] and do not allow firm conclusions about whether there is a sensitive period for gaining such expertise.)

Alterations of Face Processing in Adulthood

The other-race effect can be largely overcome by training, even in adulthood. White university students who were at chance in recognizing Japanese faces improved after training not only on the trained faces but also novel examples: there was some improvement after short-term training with 30 faces (Elliott, Wills, & Goldstein, 1973) and considerable improvement after 2 to 3 weeks of training with 67 to 94 faces, with no loss over 5 months (the longest period tested; Goldstein & Chance, 1985). Such successful training indicates that face processing can be tuned to an unfamiliar category of faces even in adulthood. It is consistent with evidence that the prototype(s) to which individual faces are compared are constantly updated by the diet of faces to which an individual is exposed (e.g., Rhodes & Jeffery, 2006; Rhodes, Jeffery, Watson, Clifford, & Nakayama, 2003; Webster, Kaping, Mizokami, & Duhamel, 2004).

Studies of the other-age effect also suggest that some aspects of the specialization of face processing can be modified in adulthood. When given a sequential matching-to-sample task, adults show an "other-age" effect: they are better at recognizing adults' faces than

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the faces of children or newborns, at least when the faces are presented upright (Kuefner, Macchi Cassia, Picozzi, & Bricolo, 2008). In contrast, preschool teachers are equally good at recognizing adults' and children's faces (newborn faces were not tested: Kuefner et al., 2008), presumably because their job requires them to individuate children on a daily basis. Unlike other adults, they show evidence of holistic processing as strong for children's faces as for adult faces, and the size of the composite face effect for children's faces is correlated with the number of years they have taught preschool (de Heering & Rossion, 2008). These data suggest that face processing is modifiable at any age if it becomes important for the individual to individuate faces from an unfamiliar class.

Additional evidence for the plasticity of face processing in adulthood comes from studies that (p. 221) have been successful in training individuals with prosopagnosia, impaired face recognition of congenital origin or as a result of brain injury. An adult with congenital prosopagnosia was trained over 14 months to classify faces on the basis of spacing cues: the spacing between the eyes and eyebrows and between the mouth and nose (DeGutis, Bentin, Robertson, & D'Esposito, 2007). During training, her accuracy on the task improved to normal levels and reaction times dropped from their original 10-fold elevation to normal levels. After training, she scored within the normal range on standardized tests of face recognition, a face-selective N170 emerged, and face-selective regions identified by fMRI showed greater coherence among one another. In another study, an adult with acquired prosopagnosia resulting from brain damage profited, at least over the short term (the only test point), from training that called attention to the characteristics of facial features ("This is Tracy. She has a large forehead and small eyes"). After this training, his accuracy was nearly perfect in distinguishing unfamiliar faces from the previously presented faces even when both had a novel facial expression (Powell, Letson, Davidoff, Valentine, & Greenwood, 2008). Both of these studies suggest that face-processing networks may still be plastic during adulthood, although there are not sufficient data to speculate about the most effective training protocol or the mechanisms underlying the improvement.

In sum, at least some aspects of face processing for upright faces remain modifiable in adulthood by training or by a change in the diet of faces with which the individual interacts. Studies to date do not allow conclusions about the optimal training protocols, limits to their efficacy, or the extent to which the training alters neurons in normal networks for processing faces or makes use of neurons that normally process other classes of stimuli. Indirect evidence that the face-processing networks themselves remain plastic comes from a study of a patient who developed prosopagnosia and object agnosia (difficulty recognizing objects) after an accident (Behrmann, Marotta, Gauthier, Tarr, & McKeef, 2005). After extensive training in differentiating between members of an unfamiliar class of stimuli (greebles), his accuracy in discriminating among greebles improved, but his limited ability to discriminate among faces decreased and the initially face-selective voxels in his FFA lost their tuning for faces and became greeble-selective.

Reorganization of the Visual Cortex After Blindness

Another way to study human visual plasticity is to examine individuals in whom the visual cortex did not receive visual input because of blindness caused by a problem in the eye, the retina, or the optic nerve. In such cases the visual cortex comes to be involved in the processing of input from other sensory modalities and higher-order cognitive tasks such as language. By examining adults who became blind at various ages, it is possible to determine the sensitive period for such reorganization, a sensitive period analogous to the sensitive period for damage described above for cataract-reversal patients. When the visual cortex of the early blind is temporarily deactivated by TMS, their auditory and tactile sensitivity is reduced, a result indicating that the reorganized visual cortex is functionally involved in the processing of input from other sensory modalities. In this section, we summarize the evidence for such cortical reorganization, its timing, and the underlying mechanisms.

Outcome After Congenital Blindness: Responses to Other Sensory Modalities

In this section we consider the results for those blind from birth or an early age (typically defined as before 1 to 3 years).

Touch

In adults blind from birth or an early age, neuroimaging techniques have revealed that the visual pathway is active during the reading of Braille, the discrimination of embossed Roman letters, the tactile recognition of manmade objects, the detection of the displacement of a tactile dot to the right or left, and the discrimination among vibrotactile gratings (Burton, McLaren, & Sinclair, 2006; Burton et al., 2004; Gizewski, Gasser, de Greiff, Boehm, & Forsting, 2003; Pietrini et al., 2004; Sadato et al., 1996, 1998, 2002; Stilla et al., 2008; reviewed in Théoret, Merabet, & Pascual-Leone, 2004). The active areas include the primary visual cortex and both the dorsal and ventral streams of the extrastriate visual cortex. When the visual cortex is deactivated by TMS over the midoccipital region, adults blind from an early age report that Braille dots no longer make sense because of missing and phantom dots and their errors increase whether they are reading a familiar (Cohen et al., 1997) or foreign language (Kupers et al., 2007). In some blind adults, such stimulation over the visual cortex induces tactile sensations in the fingers (Ptito et al., 2008a). The (p. 222) functional importance of occipital activity was verified in a case study of a woman who was blind from birth, learned to read Braille from an early age, and used Braille proficiently in her daily work. When a stroke at age 50 caused extensive bilateral occipital damage, the woman lost the ability to read Braille, despite normal peripheral tactile sensitivity (Hamilton, Keenan, Catala, & Pascual-Leone, 2000). In sighted adults, in contrast, tactile tasks are associated with decreased visual cortical activity and TMS over

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the visual cortex has no effect (Sadato et al., 1998; Stilla et al., 2008; Wittenberg, Werhahn, Wassermann, Herscovitch, & Cohen, 2004).

Collectively, the results suggest that when the visual cortex fails to receive visual input from an early age, it develops functional neuronal responses to tactile stimuli. Interestingly, in the early blind, stimulation of the somatosensory cortex by TMS leads to increased activity in the occipital cortex bilaterally that is not seen in the sighted, as well as in some areas of the frontoparietal cortex but not in the thalamus (Wittenberg et al., 2004). Converging evidence comes from fMRI connectivity analysis showing connections from the somatosensory cortex to the visual cortex that are active during tactile spatial discrimination in the blind but not the sighted (Stilla et al., 2008). These results point to excitatory connections between the somatosensory cortex and visual cortex in the blind that lead to synergistic interactions in contrast to the inhibitory interactions in the typical adult.

Sound

After early blindness, auditory input also activates the visual cortex. For example, when adults blind from an early age discriminate changes in the location of sounds, there is activation in the primary visual cortex and both the dorsal and ventral extrastriate cortices (Voss, Gougoux, Zatorre, Lassonde, & Lepore, 2008; Weeks et al., 2000). This arises because of increased activity in these regions during auditory localization in the early blind in contrast to decreased activity in the sighted. The activation of the visual cortex, including the primary and extrastriate cortices, when the early blind attend to auditory stimuli has been observed with both MEG and fMRI (Kujala et al., 1995, 2005). There is some evidence that the particular visual structures recruited are those that play a similar functional role across modalities (e.g., dorsal extrastriate visual pathway for spatial localization of sound; ventral extrastriate visual pathway for features of objects recognized via a visual-to-auditory substitution device) (reviewed in Collignon, Voss, Lassonde, & Lepore, 2009). In the cat, after the removal of the eyes at birth, electrophysiological recordings have revealed that neurons in the primary visual cortex respond to auditory stimuli (Yaka, Yinon, & Wollberg, 1999).

In humans, the responses of the visual cortex of the blind to sound appear to occur quite early in auditory processing, but only if the task requires attention to the features of the auditory stimulus: such stimuli evoke a large N1 and P3 over the occipital pole and a large P3 over the parietal cortex that are not seen in sighted subjects (Leclerc, Saint-Amour, Lavoie, Lassonde, & Lepore, 2000). In oddball paradigms, unexpected auditory stimuli (e.g., a decrease in intensity) evoke a mismatch negativity in the early blind that, unlike the sighted, is observed over the visual cortex and posterior parietal sites (Liotti, Ryder, & Woldorff, 1998). The functional significance of the altered visual cortex has been revealed in a TMS study: repetitive TMS over the right dorsal extrastriate cortex (Brodmann's area 18) disrupted auditory localization in the early blind but not the sighted control group and increased the blind group's errors in using a prosthesis that translates

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visual object characteristics into auditory signals (Collignon, Lassonde, Lepore, Bastien, & Veraart, 2007).

Language

Surprisingly, the visual pathway of congenitally blind adults is also active during the processing of language. For example, when adults blind from an early age make judgments about the meaning of spoken words or the grammaticality of word order in spoken sentences, fMRI reveals activation throughout the visual pathway, including the primary visual cortex and dorsal and ventral extrastriate pathways, as well as a number of higher cognitive pathways (Burton, Diamond, & McDermott, 2003; Roder, Stock, Bien, Neville, & Rosler, 2002). There are similar effects when the early blind covertly generate verbs after hearing a noun or reading it with Braille (Burton et al., 2002; reviewed in Burton, 2003). The visual responses are often stronger in the left than the right hemisphere. Although some of these effects may be from auditory or tactile processing (see previous sections), the modulation of the responses by language features (e.g., semantics, unusual word order) suggest that the visual cortex of the blind can be recruited for linguistic as well as auditory and tactile processing. That interpretation is supported by evidence of activation in the visual pathway, particularly on the left and including the primary visual cortex (p. 223) when congenitally blind adults generate words from memory (Amedi, Raz, Pianka, Malach, & Zohary, 2003). Moreover, disrupting the activity in the left primary visual cortex by rTMS causes the early blind to make more semantic errors in generating verbs from heard nouns (Amedi, Floel, Knecht, Zohary, & Cohen, 2004). Finally, in the congenitally blind, the level of activation in the left primary visual cortex correlates with verbal memory for a list of abstract words learned 6 months earlier (Amedi et al., 2003). None of these effects are observed in the sighted. Collectively, the results suggest that when an individual is blind from an early age, the visual pathway, particularly the left primary visual cortex, is used for the processing of language.

Sensitive Period for Visual Cortical Plasticity

It is difficult to identify the sensitive period during which the visual cortex can become specialized for touch, hearing, and language from the existing literature because of the small number of blind subjects in each study, the uneven distribution of ages when the blindness began, and the reality that blindness often, but not always, progresses gradually. In several studies, the extent of visual cortex activation was smaller when the onset of blindness was after early childhood, with the late group defined variously as those with onset after age 6, 7, 10, 14, or 20 years. For example, when blind adults read Braille or discriminate between vibrotactile stimuli, there is increased activity in the primary visual cortex when blindness began near birth (before age 3) (Sadato et al., 2002) or age 5 years (Burton et al., 2004) but deactivation of the same areas in those who became blind after age 6 (Burton et al., 2004) or in adulthood (Sadato et al., 2002), as there is in sighted controls. Similarly, TMS over the visual cortex increases errors while reading Braille in those who became blind before age 13 but not those who became blind after age 14 (Cohen et al., 1999). As well, visual cortical activity is greater during spatial tactile discrimi-

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nations in those blind before age 3 compared to those totally blind after age 10, and age of blindness correlates with the strength of connectivity during the task between V1/V2 and object processing areas within the right visual cortex (Stilla et al., 2008).

However, regardless of age of onset, there is activation in extrastriate dorsal and ventral structures in the blind during tactile tasks that is not seen in the sighted, in whom deactivation is more likely. In two individuals who became blind as adults and who did not know Braille, moving Braille characters across their fingers activated areas in higher visual areas that are not activated in sighted adults (Sadato, Okada, Kubota, & Yonekura, 2004). Because these individuals had not learned Braille, it is unlikely that visual imagery can account for the visual activation. Similarly, for sound localization, event-related potentials suggest reorganization in both those blind from childhood (before age 14) and those who became blind as adults, but in different parts of the visual pathway, with changes in the right ventral extrastriate cortex and right parietal cortex in the early blind and in the medial and lateral occipitotemporal cortex in the late blind (Voss, Gougoux, Lassonde, Zatorre, & Lepore, 2008). Images from positron emission tomography (PET) confirm that areas of the visual cortex that are deactivated in the sighted during the localization of sounds are instead more active in those who became blind as adults (Voss, Gougoux, Lassonde, Zatorre, & Lepore, 2006).

The pattern for tactile and auditory processing suggests that the sensitive period for recruitment of the primary visual cortex is limited to preadolescence, while higher visual areas remain plastic throughout life. The pattern is the opposite for language tasks: there is evidence of activation in the primary visual cortex and cortical areas immediately surrounding it regardless of the age of onset of blindness, but activity in higher visual areas declines as the age of onset increases (Burton, 2003; Burton et al., 2002, 2003).

Residual Plasticity in Adulthood: Effects of Blindfolding on Sighted Adults

Even in visually sighted adults, changes occur in the visual cortex after short-term visual deprivation from blindfolding. In the most extensive study, adults were given 6 to 8 hours of intensive training of the right index finger with Braille and other tactile tasks while blindfolded continuously for 5 days (Merabet et al., 2008). fMRI activation in the visual cortex of the trained group increased bilaterally when the index finger was stroked with a wooden loofa brush. The activation included an area within the calcarine sulcus likely to be the primary visual cortex. No such increase occurred in the control group, which was not blindfolded except for the 6 to 8 hours of daily training and the fMRI scans. At the end of training, the blindfolded group was better than the control group at discriminating Braille characters but lost this advantage when the visual cortex was temporarily deactivated by rTMS. The cortical (p. 224) changes disappeared when normal visual input was restored on the sixth day. Combined, the results suggest that the adult visual cortex can be quickly and reversibly recruited to respond to another sensory modality when its normal visual input is removed, and that these rapid changes contribute to increased perceptual sensitivity. Visual imagery—which in sighted adults activates the visual pathway,

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sometimes including the primary visual cortex—is not likely to account for the cortical changes because it would have been equally likely in the two groups, both of which were blindfolded during tactile training. In an earlier study of sighted adults involving intensive training of both tactile and auditory spatial discrimination while blindfolded for 5 days, fMRI activation increased in the visual cortex during both tactile stimulation and auditory tone comparison, a task during which visual imagery is unlikely (Pascual-Leone & Hamilton, 2001). The rapidity of the changes suggests that they may result from the unmasking of latent connections rather than rewiring of the visual pathway.

Further evidence of visual plasticity in normal adults comes from studies of short-term visual deprivation. After just 45 to 60 minutes of blindfolding, the visual cortex appears to be more excitable: the intensity of TMS needed to induce the perception of visual phosphemes decreases, with further decreases over the next 1 to 2 hours of visual deprivation (Boroojerdi et al., 2000; Pitskel, Merabet, Ramos-Estebanez, Kauffman, & Pascual-Leone, 2007). After short-term blindfolding, the fMRI activation elicited by a flashing grid of red LEDs also increases both in overall magnitude and in number of activated voxels (Boroojerdi et al., 2000). Such short-term removal of visual input also induces changes in tactile and auditory perception of the type seen after early blindness, although to a smaller extent: the accuracy of head orientation toward peripheral sounds improves (Lewald, 2007), as does sensitivity to the orientation of tactile gratings (Facchini & Aglioti, 2003). A similar increase in tactile sensitivity of the left hand occurs when the right hand is temporarily deafferented by anesthesia: its thresholds to discriminate tactile orientation decrease and there are increases in the potentials over the somatosensory cortex evoked by stimulating the left hand electrically (Werhahn, Mortensen, Van Boven, Zeuner, & Cohen, 2002). Such rapid plasticity suggests that latent connections can be revealed when the normal dominant input is removed, perhaps by releasing inhibition between modalities or between hemispheres. When the deprivation continues, those connections may be consolidated.

Related evidence comes from adult rats with a normal visual history given a short period (3 days) of monocular deprivation that normally has no effect in the adult rat; when the monocular deprivation occurs immediately after 3 or 10 days in complete darkness, however, ocular dominance begins to shift in favor of the nondeprived eye, at least as measured by the amplitude of the visually evoked potential (He, Hodos, & Quinlan, 2006; He, Ray, Dennis, & Quinlan, 2007). The period of darkness leads to decreases in the cortical levels of GABA receptors involved in cortical inhibition. Indeed, after very-long-term monocular deprivation early in the rat's life, the deprivation-induced shift in ocular dominance and reduced acuity can be partially offset, even in adulthood, by 10 days in the dark followed by binocular experience; if the nondeprived eye is occluded after the period of darkness, the recovery in the previously deprived eye is even greater.

Together, these studies suggest considerable residual visual plasticity in the adult visual cortex that can be revealed if the normal, dominant visual input is removed.

Mechanisms of Plasticity After Blindness

When visual input is missing from an early age, much of the visual pathway degenerates: there is a significant reduction in the volume of the optic radiation, the lateral geniculate nucleus, the pulvinar, the primary visual cortex, extrastriate visual structures, and the splenium of the corpus callosum that links the two hemispheres, as well as some nonvisual structures such as the hippocampus (Ptito, Schneider, Paulson, & Kupers, 2008; see also Pan et al., 2007; Park et al., 2007). On average, the volume of the primary visual cortex is reduced by 25% and its resting connectivity to other sensory cortical areas and temporal multisensory areas is decreased, especially if the blind individual did not learn Braille from an early age (Liu et al., 2007). Yet the functional neuroimaging results summarized above indicate that the remaining visual neurons are active during the processing of auditory, tactile, and language stimuli, with some suggestion of specialization among them for different novel functions. Moreover, there is some evidence for increased connectivity in the early blind between the visual cortex and the frontal cortex (Liu et al., 2007; Ptito et al., 2008b) and between the visual cortex and the thalamus (Liu et al., 2007).

(p. 225) The anatomical losses are the expected consequence of experience-dependent pruning of connections to and within the visual cortex. There is ample evidence that during development there is an initial proliferation of projections, which are then shaped by Hebbian mechanisms: when visual input causes neuronal firing, the synapse is strengthened and becomes more likely to fire to subsequent visual input. When an exuberant connection is not used, it is eliminated through pruning (reviewed in Collignon et al., 2009). Visual neurons also fire spontaneously and, initially, can be activated by cross-modal input from other sensory modalities (reviewed in Collignon et al., 2009; Spector & Maurer, 2009). The visual input is probably advantaged over that from other modalities because it is stronger, faster, and more coherent.

In the child with normal vision, through Hebbian competition, the visual inputs to neurons in the visual cortex are strengthened and the cross-modal inputs are weakened and to a large extent pruned away. However, when visual input is missing because of early blindness, the remaining connections—the cross-modal ones—are used, reinforced, and retained. The studies of the early blind summarized above indicate that those retained cross-modal connections are functional. Animal studies have confirmed the early presence of such cross-modal connections (e.g., Dehay, Kennedy, & Bullier, 1988), and studies of sighted human infants have supplied indirect evidence that they are functional (reviewed in Spector & Maurer, 2009). For example, sound initially elicits an evoked potential not only over the auditory cortex but over the visual cortex as well (Neville, 1995). Over the first 3 years, the response over the visual cortex diminishes as the response over the auditory cortex is refined. Similarly, in the newborn, the somatosensory evoked response elicited by stimulation of the wrist is enhanced if it is accompanied by white noise (Wolff, Matsumiya, Abrams, van Velzer, & Lombroso, 1974).

Experience-dependent pruning of exuberant connections in the visual cortex is a gradual process, with a different time course documented for different layers of the visual cortex

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and likely for different cross-modal connections. Using early anatomical techniques, Huttenlocher observed a peak in synaptic density in the visual cortex toward the end of the first year of life, and then a decline until about 10 years of age, although the sparsity of cases creates uncertainty about the age at which synaptic density reaches the level of the young adult (Huttenlocher, 1984, 1990; Huttenlocher et al., 1982; Huttenlocher & de Courten, 1987; Huttenlocher & Dabholkar, 1997). Nevertheless, the decline clearly occurs before age 20, and thus cortical changes in the late blind or blindfolded sighted adults likely arise from a different mechanism. One possibility is that only some of the cross-modal inputs to the visual cortex are pruned and that others remain but are normally inhibited, in part by reentrant feedback from higher visual cortical areas (reviewed in Spector & Maurer, 2009; see also Merabet et al., 2007). When the normal visual input is removed, those connections may be released from inhibition and contribute to perception. This interpretation is consistent with evidence for direct projections from the auditory and somatosensory cortices to the primary visual cortex in the adult monkey (Cappe & Barone, 2005; Falchier, Clavagnier, Barone, & Kennedy, 2002; see also Rockland & Ojima, 2003) and evidence that the firing rate of neurons in the monkey's primary visual cortex increases when a peripheral visual stimulus is accompanied by sound (Wang, Celebrini, Trotter, & Barone, 2008). It also fits with the evidence summarized above for deactivation of the visual cortex during tactile tasks in the normally sighted and late blind, unlike the activation seen in the early blind. Indeed, when the auditory cortex of the normally sighted is deactivated by TMS, visual phosphemes are easier to elicit; conversely, when the visual cortex is deactivated, auditory stimuli are easier to detect (Romei, Murray, Merabet, & Thut, 2007; but see Collignon et al., 2008, for a negative effect on auditory localization). Both results suggest increases in sensitivity when inhibitory influences are removed. Collectively, these data suggest that some cross-modal inputs to visual cortical neurons remain after the period of experience-dependent pruning but are normally inhibited. When visual input is removed—because of late-onset blindness or blindfolding—the inhibition is reduced, allowing the cross-modal inputs to drive the visual cortex and contribute to functional perception.

In addition to the reinforcement of exuberant cross-modal connections and atrophy of visual connections, blindness may lead to subcortical changes and changes in long-distance connections. As noted above, in the early blind, there is increased connectivity between the thalamus and the visual cortex (Liu et al., 2007) and between the visual cortex and frontal areas, including ones involved in language (Liu et al., 2007; Ptito et al., 2008b). Thus, some of the visual cortical changes may arise from altered thalamocortical inputs, rather than corticocortical connections, and from unusual connections with the frontal cortex.

Summary and Conclusions

We have summarized the effects of altered visual input on the development of visual acuity, face processing, and the specialization of the visual cortex for visual processing. Although the details vary across areas, some common themes emerge:

1. Some capabilities are spared despite early abnormal input. They are able to develop normally based on innate wiring and/or recovery based on delayed visual input, recovery that can take longer than the period of normal development. We saw this for sensitivity to low spatial frequencies; lip-reading, decoding of facial expression, and sensitivity to direction of eye gaze (at least as measured by our tasks); and the identification of faces based on contour shape or eye and mouth shape.
2. For some visual capabilities, visual input is necessary to set up the neural architecture used for later specialization; when it is missing, the later abilities fail to emerge. We saw examples of such sleeper effects for visual acuity, contrast sensitivity, holistic face processing, and identification of faces based on feature spacing. In each case, an ability not present during early infancy failed to develop when visual input had been missing for the first few months after birth.
3. All parts of the visual pathway can be changed by altered visual input, including the primary visual cortex and both the dorsal and ventral extrastriate cortices. Some of the changes appear to result from altered balance between the eyes or between sensory modalities when one eye or a nonvisual modality is favored instead of the normal balanced binocular input.
4. The sensitive period for damage cannot be inferred from congenital cases alone nor from the period of normal development. It can be shorter than the period of normal development (e.g., global motion) or much longer (e.g., linear letter acuity).
5. Despite evidence that the sensitive periods for damage end during childhood, there is residual potential for recovery in adulthood. This was evident in the success of a number of interventions in improving the acuity of adult amblyopes, the effectiveness of training to eliminate the other-race effect in normal adults and to improve face processing in adult prosopagnosics, and the use of the visual cortex for tactile and auditory processing after blindfolding in sighted adults. The results indicate that the sensitive period for recovery/plasticity lasts into adulthood and is different from the sensitive period for damage. It is not yet clear whether the plasticity only reflects the unmasking of established connections or also involves the formation of new ones.

In conclusion, the studies reviewed here indicate that patterned visual input during early infancy plays a key role in constructing and/or preserving the neural architecture that will be used later for both low-level basic vision and higher-level visual decoding. The high-contrast, low spatial frequencies that newborns can extract from their environment set up the system for later development of fine acuity, expert face processing, and specialization of the visual cortex for visual processing. Nevertheless, considerable plasticity remains in adulthood for rescuing the system from earlier damage.

Questions for Future Research

1. What is the optimal treatment for amblyopia and how does it vary with the patient's age?
2. Does effective treatment of amblyopia require the reduction of inhibition and restoration of interocular balance?
3. What is the contribution of intermodal competition to the sensitive periods for damage and for recovery?
4. When visual deficits diminish after training or other manipulations in adulthood, is the restored visual capability mediated by the normal visual pathway or by an alternative pathway not normally used for this purpose? If it is based on the normal visual pathway, does it represent the formation of new connections or the better use of existing connections? Is the process similar when the visual cortex of the sighted adult changes after blindfolding to respond to nonvisual input? What is the role of changes in the excitatory/inhibitory balance?
5. How can the insights from stroke recovery be applied to effect long-term improvement in amblyopia? Is the plasticity observed after brain damage in adulthood (e.g., recovery from stroke) governed by principles and mechanisms that are useful for understanding the plasticity of adult vision?
6. Is the plasticity observed for audition (e.g., learning to speak after a cochlear implant or learning the phonology of a second language) governed by principles and mechanisms similar to those for vision?

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