Terri L. Lewis

Department of Psychology
McMaster University
Hamilton, Ontario
L8S 4K1, Canada

Department of Ophthalmology
The Hospital for Sick Children
Toronto M5G 1X8, Canada

Department of Ophthalmology
University of Toronto
Toronto M5T 2S8, Canada
E-mail: LewisTL@mcmaster.ca

Daphne Maurer

Department of Psychology
McMaster University
Hamilton, Ontario
L8S 4K1, Canada

Department of Ophthalmology
The Hospital for Sick Children
Toronto MSG 1X8, Canada

Multiple Sensitive Periods in Human Visual Development: Evidence from Visually Deprived Children

ABSTRACT: *Psychophysical studies of children deprived of early visual experience by dense cataracts indicate that there are multiple sensitive periods during which experience can influence visual development. We note three sensitive periods within acuity, each with different developmental time courses: the period of visually-driven normal development, the sensitive period for damage, and the sensitive period for recovery. Moreover, there are different sensitive periods for different aspects of vision. Relative to the period of visually driven normal development, the sensitive period for damage is surprisingly long for acuity, peripheral vision, and asymmetry of optokinetic nystagmus, but surprisingly short for global motion. A comparison of results from unilaterally versus bilaterally deprived children provides insights into the complex nature of interactions between the eyes during normal visual development.* © 2005 Wiley Periodicals, Inc. Dev Psychobiol 46: 163–183, 2005.

In the early 1960s, Wiesel and Hubel (1963) reported that unilateral deprivation brought about by a period of lid suture early in life causes permanent abnormalities in the distribution of ocular dominance columns in the cat's primary visual cortex. In that classic study and in subsequent anatomical, electrophysiological, and behavioral studies of lid-sutured animals, Hubel and Wiesel attempted to define 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 concluded that there is a critical period early in life and that visual deprivation beginning after that time causes no

permanent damage. It soon became evident that the critical period does not end abruptly but tails off, such that longer and longer deprivation is necessary to cause permanent deficits. As a result, it is now often called the sensitive period (reviewed in Elman et al., 1996).

Later behavioral and physiological studies of animals established that there is not one sensitive period, but different sensitive 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 et al. (1986) found that in the monkey, deprivation has to begin before 3 months of age to affect scotopic sensitivity, before 6 months to affect photopic spectral sensitivity, and before 18 to 24 months to affect spatial contrast sensitivity, but affects binocularity even when it begins after 2 years of age. In addition to different sensitive periods for different aspects of vision, there are different sensitive periods for electrophysiological and anatomical alterations to different visual cortical areas, different layers within the visual cortex, and

different properties of visual cortical cells (Blakemore, 1988; Daw et al., 1992; Jones et al., 1984; Singer, 1988).

Even within one aspect of vision, such as acuity, we have found evidence for more than one sensitive period. 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 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 the abnormal input 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, this issue). 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 deprivation. We call this period *the sensitive period for recovery*. Daw (e.g., 1998, 2003) made similar distinctions among different types of critical periods.

In the present review, we examine evidence for different sensitive periods for different aspects of vision. Wherever possible, we compare the periods for the three indices of plasticity (visually driven normal development, the sensitive period for damage, and the sensitive period for recovery) for aspects of vision mediated at different cortical levels. We do so by comparing the visual development of visually normal children 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 diffused 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.

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 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. To compare sensitive periods for different aspects of vision mediated at different cortical levels, in this article we compare the effects of early visual deprivation on four aspects of vision: visual acuity, peripheral vision, global motion, and the asymmetry of optokinetic nystagmus. Finally, in the last part of the article, we compare vision in children deprived from birth in one versus both eyes to gain insights on how uneven competition for cortical connections between a weaker deprived eye and a stronger fellow nondeprived eye alters the three indices of plasticity.

VISUAL ACUITY

Normal Development

Infants' acuity is measured with stripes of varying size, and the goal is to determine the finest stripes that the infant can resolve—a measure known as grating acuity. The most common measure of grating acuity during infancy is preferential looking (reviewed in Maurer & Lewis, 2001a, 2001b). This method takes advantage of infants' preference to look at something patterned over something plain (Fantz, Ordy, & Udelf, 1962). The infant is shown black-and-white stripes paired with a gray stimulus of the same mean luminance, and the size of the stripes is varied across trials. A tester watches the baby's eye movements, and the measure of grating acuity is the smallest size of stripe for which the tester can judge correctly from the baby's eye movements where the stripes are located. 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): Newborns preferentially look at stripes only if they are 30 to 60 min wide whereas adults can resolve stripes less than 1 min wide (One minute is $\frac{1}{60}$ of a degree of visual angle.) Grating acuity improves rapidly in the first 6 months after birth. Figure 1 shows measurements based on preferential looking. By 6 months of age, grating acuity has improved from being about 40 times worse than that of normal adults to being only 8 times worse. Thereafter, grating acuity improves more gradually and reaches adult values at 4 to 6 years of age (Courage & Adams, 1990; Ellemberg, Lewis, Liu, & Maurer, 1999; Mayer & Dobson, 1982; van Hof-van Duin & Mohn, 1986).

Poor acuity at birth is likely caused both by immaturities in the size and arrangement of retinal cones and by additional limitations beyond the retina (Banks &
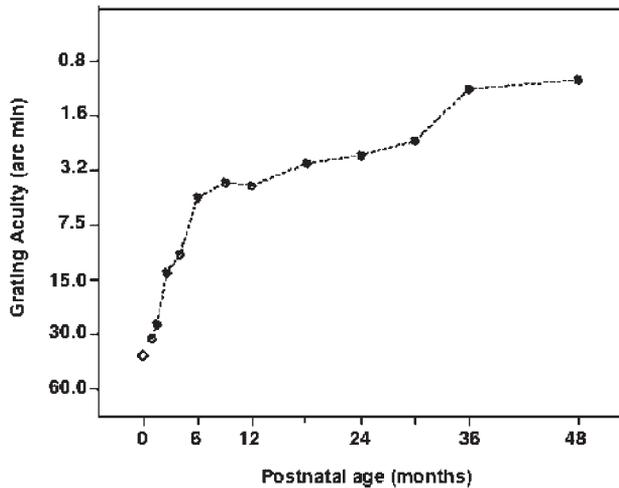
FIGURE 1 Changes in grating acuity between birth and 48 months when measured by preferential looking. The *y* axis shows the size of the smallest stripes to which subjects respond, plotted in minutes of arc where 1 min is $\frac{1}{60}$ of a degree of visual angle. Thus, the smaller the number, the better the grating acuity. Filled circles represent the mean acuity of 1- to 48-month-olds tested monocularly by Mayer et al. (1995). The open symbol represents the log mean grating acuity of newborns tested binocularly (reviewed in Maurer & Lewis, 2001a). From "Visual acuity and spatial contrast sensitivity: Normal development and underlying mechanisms," by D. Maurer and T. L. Lewis, 2001; in C. Nelson and M. Luciana (Eds.), Handbook of Developmental Cognitive Neuroscience, Cambridge, MA: MIT Press, Figure 1. Adapted with permission of the authors.

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., 1999).

Outcome after Early Bilateral Deprivation

Patterned visual input is necessary for the postnatal development of acuity. The evidence for that conclusion comes from comparisons of infants with normal eyes to infants who were deprived of early visual input because of dense central cataracts in the lenses of both eyes. The cataractous lenses were removed surgically; 1 to 3 weeks later, after recovery from the surgery, the eyes were given compensatory contact lenses to provide the first focused patterned visual input. We used preferential looking to

measure the grating acuity of 12 patients treated for bilateral congenital cataract within 10 min 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, with 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. These data suggest that the first 9 months of life are part of the period of visually driven normal development. Subsequent testing after 1 hr of visual input, 1 month later, and at 1 year of age revealed the effects of the delayed visual input.

After 1 hr 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 tested and reduced the gap compared to age-matched controls from about 2 to 1.4 octaves. (An octave is a halving or a doubling of a value.) There was additional improvement over the next month that reduced the deficit to about 1 octave (see Panels A and B of Figure 2). The improvements over the first hour and the next month were not related to the age at treatment. 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 6 bilateral cases between the first test and the retest after 1 hr of waking time, acuity in the unpatched eyes improved but acuity in the patched eyes did not.

By 1 year of age, the acuity of eyes treated for bilateral congenital cataract improved further and the acuity of most eyes fell within normal limits (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 et al., 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.

Perhaps 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 maintain and even further the cortical connections underlying human grating acuity in infants with bilateral congenital cataracts. 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
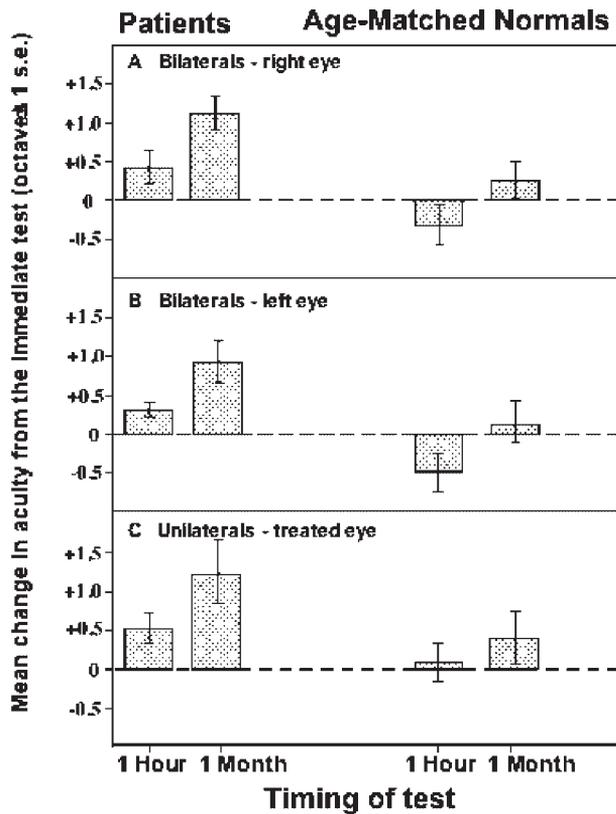
FIGURE 2   Mean change in acuity (±1 *SE*) after first exposure to focused patterned visual input in children treated for congenital cataract. Shown are the changes in acuity between the immediate test and the test after the first hour of visual input and between the immediate test and the test 1 month later. The *y* axis plots the amount of change in octaves, where one octave is a doubling or a halving of a value. Values above zero represent an improvement from the immediate test; values below zero represent a decline. The left half of each panel shows the results for infants treated for congenital cataract; the right half of each panel shows the results for age-matched control groups. Panels A and B show the results for bilateral cases and their comparison groups. Panel C shows the results for the treated eye of unilateral cases and their comparison groups. In every comparison, patient groups improved more than the age-matched controls. From "Rapid improvement in the acuity of infants after visual input," by D. Maurer, T. L. Lewis, H. P. Brent, and A. V. Levin, 1999, Science, 286, 108–110, Figure 3. Copyright 1999, American Association for the Advancement of Science. Adapted with permission from the authors.

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).

Although the grating acuity of bilaterally deprived children is within normal limits by 1 year of age and continues to improve during early childhood, it fails to keep pace with normal development and falls below normal limits by 2 years of age (Lewis et al., 1995).
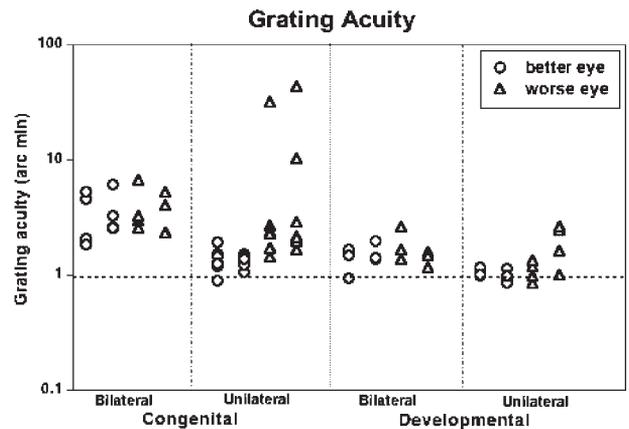
FIGURE 3   Grating acuity of patients treated for bilateral congenital cataract (first panel, n = 8), unilateral congenital cataract (second panel, *n* = 14), bilateral developmental cataract (third panel, *n* = 6), or unilateral developmental cataract (fourth panel, *n* = 9). Circles represent the data from the better eyes of bilateral cases (determined from clinical history of alignment and Snellen acuity) and the nondeprived eyes of unilateral cases. Triangles represent the data from the worse eyes of bilateral cases and the deprived eyes of unilateral cases. Bilateral cases with equal alignment and acuity histories for the two eyes had one eye assigned randomly to each category. The dashed line represents the mean of 14 comparably aged participants with normal vision. From "Better perception of global motion after monocular than after binocular deprivation," by D. Ellemberg, T. L. Lewis, D. Maurer, S. Brar, and H. P. Brent, *Vision Research*, 42, p. 175. Copyright 2002 by Elsevier Press. Reprinted with permission from the authors.

Continued assessment of the patients revealed the extent of the deficits in grating acuity after 5 years of age, an age at which acuity of visually normal children is near adult functional levels. The left panel of Figure 3 shows grating acuity of 8 patients treated for bilateral congenital cataract who had been deprived for the first 3 to 8 months of life and, at the time of the test, ranged in age from 5 to 18 years. Relative to comparably aged controls, all 16 eyes of these patients had reduced grating acuity, averaging $3\frac{1}{2}$ times (1.8 octaves) worse than normal (Ellemberg, Lewis, Maurer, Brar, & Brent, 2002). The deficits were not related to the age of treatment, at least when treatment occurred between 3 and 8 months of age. Evidence for permanent deficits in asymptotic grating acuity also have been reported in other human cohorts (Birch, Stager, Leffler, & Weakley, 1998; Mioche & Perenin, 1986) and in bilaterally deprived monkeys (Harwerth, Smith, Paul, Crawford, & von Noorden, 1991). There are similar deficits in asymptotic letter acuity (Birch et al., 1998; Lundvall & Kugelberg, 2002; Magnusson, Abrahamsson, & Sjöstrand, 2002; Maurer & Lewis, 1993); however, if the bilateral deprivation is extremely short—ending before 10 days of age—the outcome seems to be better

and some children even achieve a normal linear letter acuity of 20/20 (Kugelberg, 1992; Lundvall & Kugelberg, 2002; also see 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 start shortly after birth. In the next section, we consider how long the period of visually driven normal development for grating acuity might last by examining how long the visual system is susceptible to damage from abnormal visual input.

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. Although their grating acuity was significantly worse than the comparably aged control group, it was better overall than that of patients treated for bilateral congenital cataract (see Figure 3). 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 2 patients with later onset (>11 years) had normal grating acuity. Thus, visual deprivation anytime up to 5 years of age (except possibly the first 10 days of life) leads to a permanent deficit. These results suggest that the period of visually driven normal development continues throughout the 5 years of normal functional development. Nevertheless, the accelerated improvements during the first year after treatment for congenital cataract (see previous Outcome after Early Deprivation section) indicate that some increasing readiness to respond can occur even in the absence of visual input.

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, 2001b). 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 resulted in abnormal letter acuity if the deprivation began before 8 years of age, but not if it began after 10 years of (Maurer & Lewis, 2001a, 2001b). 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.

In summary, cataracts that become dense and central before about age 10 cause permanent deficits in linear letter acuity, whether the deprivation was 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 (i.e., 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 the functional connections and/or to prevent them from being pruned or inhibited by a process of Hebbian competition if visual input from a deprived eye is weaker than input from the fellow eye or if it is reduced relative to that from other modalities (e.g., Bavelier & Neville, 2002; Rauschecker, 1995).

Sensitive Period for Recovery from Bilateral Deprivation

The studies of grating acuity indicate that bilateral deprivation during the early postnatal period, when visually normal infants have poor acuity that limits them to seeing only wide stripes, allows accelerated improvements during infancy but prevents the later development of sensitivity to fine detail. To learn more about the origins of this sleeper effect and about the sensitive period for the recovery of spatial vision after early visual deprivation, we conducted a longitudinal study of contrast sensitivity (Ellemberg, Lewis, Maurer, & Brent, 2001; Lewis, Ellemberg, Maurer, & Brent, 2000). Contrast sensitivity is a measure of the minimum contrast necessary to see sine waves of different frequency. When first tested at 5 to 7 years of age, patients treated for bilateral congenital cataract needed more contrast than age-matched normals to see sine waves of all spatial frequencies—except for a few patients who were normal at the lowest spatial frequencies (the widest stripes). When retested 1 and/or 2 years later, patients had improved, often more than controls, at low and medium spatial frequencies (wide and medium stripes) but not at high spatial frequencies (narrow stripes). Together, the results indicate that patients treated for bilateral congenital cataract had hit an asymptote in sensitivity to high spatial frequencies by age 5. Evidence that letter acuity improves in patients treated for bilateral congenital cataract between a test at age 4 and a test at age 7 (Magnusson et al., 2002) and our results for changes in sensitivity to high spatial frequencies after a test at age 5 suggest that the cutoff is around

age 5. Age-matched controls improved at all spatial frequencies until age 7 (Ellemberg et al., 1999). The consequence is that patients' deficits remained constant or decreased at low spatial frequencies but increased at high spatial frequencies after age 5. In other words, recovery was still possible around age 7 for wide stripes, but not for fine stripes. 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. The sleeper effects may be related to the absence of the normal pruning of cortical synapses, pruning that is typically evident in the visual cortex after 1 year of age and in higher visual cortical areas after 2 years of age (Huttenlocher, 1979; Huttenlocher & Dabholkar, 1997; Huttenlocher, & De Courten, 1987).

These results, along with those of Magnussen et al. (2002), provide the only measurements of the sensitive period for recovery after early pattern deprivation in humans. In fact, even in animals, little is known about the sensitive period for the recovery of functional vision after early pattern deprivation other than a few studies on the development of grating acuity after early deprivation in cats (Mitchell, 1988, 1991).

Together, the results for acuity and contrast sensitivity illustrate three sensitive periods with different time courses: the period of visually driven normal development that is over by 5 to 7 years of age, the sensitive period for damage lasting until about age 10, and the sensitive period for recovery that lasts until about age 7 for low spatial frequencies but only until about age 5 for higher spatial frequencies; however, note that even in adulthood, it is possible to recover at least some spatial vision after visual training (see Levi, this issue).

PERIPHERAL VISION

Normal Development

Although the results across studies vary with the testing method and characteristics of the stimulus such as its size, luminance, contrast, the meridian on which it falls, and whether it is static or flickering, the overall pattern remains the same: Even newborns will orient toward peripheral targets if they are large, luminant, and of high contrast. With increasing age, babies orient towards targets increasingly far in the periphery (reviewed in Maurer & Lewis, 1998). For example, we charted the development of orienting towards targets presented at 15-degree intervals along the horizontal meridian. In every case, a baby's fixation was first attracted to the center of the field before a target was presented at a predetermined location in the periphery or a blank control trial was presented. Each group of babies was credited with detecting and orienting towards a target when the proportion of
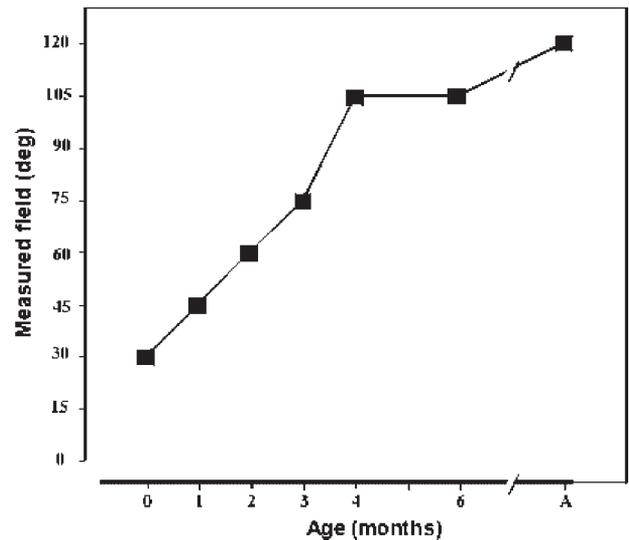
FIGURE 4   Extent of the temporal field for infants of various ages and adults (A) tested with the 6-degree light. From ''The development of the temporal and nasal visual fields during infancy,'' by T. L. Lewis and D. Maurer, *Vision Research*, 32, p. 908. Copyright 1992 by Elsevier Press. Adapted with permission from the authors.

first eye movements towards that target was higher than the proportion in the same direction on blank control trials. All testing was monocular so that we could compare orienting towards targets in the temporal visual field (e.g., the right visual field when looking with the right eye) and in the nasal visual field (e.g., the left visual field when looking with the right eye). Figure 4 shows the extent of the temporal visual field for infants, 0 to 6 months of age, tested with a 6-degree light flashing at 3 Hz, which at its peak luminance of 167 cd/m^2 had a contrast of 99% (Lewis & Maurer, 1992). Newborns orient towards these lights out to 30 degrees in the temporal field. With increasing age, there is a steady increase in the farthest location with significant orienting until, at 4 months of age, babies orient toward lights almost as far in the periphery as do adults (see Figure 4).

Not surprisingly, the age at which the visual field approaches adult limits depends on the testing method and the size and luminance of the target. For example, the extent of the horizontal visual field is nearly adultlike at 4 to 6 months of age for a large luminous target, but is still not fully adultlike even at 7 years for dim pinpoints of light, at which point there is no remaining difference in sensitivity in the midperiphery but still a significant difference in the far temporal and inferior visual fields (Bowering, 1992; Bowering, Maurer, Lewis, Brent, & Riedel, 1996; Tschopp et al., 1998; reviewed in Maurer & Lewis, 1998) and perhaps in the far superior visual field (cf. Bowering et al., 1996; Tschopp et al., 1998). The age at which the entire visual field is fully adultlike is

unclear, but the far temporal field is the last to reach an adult extent.

Interestingly, development of sensitivity in the nasal visual field lags behind that in the temporal visual field. When tested with a 3-degree light flashing at 3 Hz with a peak luminance of 167 cd/m^2, 2-month-olds orient towards the light out to 30 degrees in the temporal field, but fail to orient towards it even at 15 degrees in the nasal field (Lewis & Maurer, 1992; see Figure 5). By 3 months, they do orient towards it at 15 degrees in the nasal field, but by then the measured temporal field has grown to at least 60 degrees. Although less dramatic, differences also are apparent with the 6-degree light (see Figure 5): From birth to 3 months of age, the measured nasal field does not extend beyond 30 degrees while the temporal field grows to 75 degrees (Lewis & Maurer, 1992). Similarly, when we tested 1-month-olds with a 26-degree line (10 cd/m^2; 77% contrast) of varying width, we found that a line just 1.5 degrees wide (the narrowest tested) was adequate to attract orienting when it was located at 30 degrees in the temporal field, but that a ''line'' even 12.8 degrees wide was inadequate when its nearest edge was at 20 degrees in the nasal field (Lewis, Maurer, & Blackburn, 1985). These results are in sharp contrast to those of adults and children at least 7 years old (the youngest age tested), who show higher sensitivity at 20 degrees in the nasal field than at 30 degrees in the temporal field (Bowering, 1992; Fahle & Schmid, 1988). The development of peripheral vision likely reflects changes in many parts of the visual system beginning in the retina as well as improved control of eye movements (reviewed in Maurer & Lewis, 1998).

Outcome after Early Bilateral Deprivation

We have used three methods to examine peripheral vision following an earlier period of visual deprivation: kinetic perimetry to plot the edges of the visual field; contrast sensitivity along the horizontal meridian; and static perimetry to measure sensitivity at 20 degrees in the nasal field and 30 degrees in the temporal field—the locations that revealed poorer sensitivity nasally than temporally during early infancy. In each case, patients were required to maintain central fixation and signal as soon as they detected a target in the periphery. The results indicate that visual deprivation causes large deficits in peripheral vision, even when the deprivation began after infancy. (Patients unable to maintain central fixation could not be tested, and hence the results may underestimate the deficits.)

One effect of visual deprivation is a constriction of the visual field. This was evident when we measured the visual fields of 13 eyes from 10 children who had been born with dense and central cataracts in both eyes, with visual deprivation lasting 6 weeks to 18 months
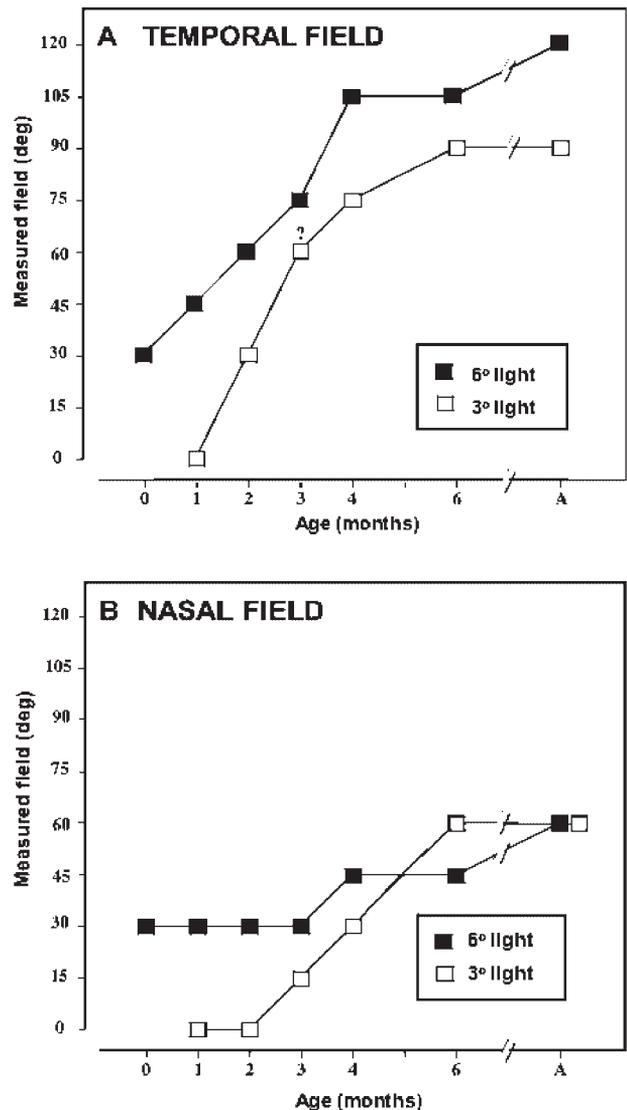
FIGURE 5 Extent of the temporal field (Panel A) and nasal field (Panel B) for infants of various ages and adults (A). Filled symbols are for tests with the 6-deree light; open symbols are for tests with the 3-degree light. A question mark indicates that we did not find the limit of the field because infants oriented significantly toward the plotted location, which was the most peripheral position tested. From ''The development of the temporal and nasal visual fields during infancy,'' by T. L. Lewis and D. Maurer, *Vision Research*, 32, pp. 906 and 908. Copyright 1992 by Elsevier Press. Adapted with permission from the authors.

(Bowering, 1992; Bowering, Maurer, Lewis, & Brent, 1997). Compared to age-matched controls, the bilaterally deprived children had restrictions that averaged about 20 degrees across the visual field but which reached about 40 degrees in the temporal visual field, the part of the field that is slowest to reach an adult extent for a pinpoint of light. The losses also were larger in eyes that were

deprived for more than 6 months than in eyes that were deprived for a shorter time. Thus, bilateral deprivation interferes with the normal development of the edges of the field, with the largest effect on the part of the field that is slowest to develop during childhood.

Studies of sensitivity along the horizontal meridian indicate that visual deprivation also interferes with sensitivity to targets throughout the periphery. Thus, when we measured the contrast sensitivity of 5 children treated for bilateral congenital cataracts after 5 months of age, we found that sensitivity was depressed both when the sine waves were located in the center of the field and when the edge closest to center was located at 10, 20, or 30 degrees in the periphery along the horizontal meridian (Maurer & Lewis, 1993; Tytla, Lewis, Maurer, & Brent, 1991). In every case, the contrast had to be higher for the patient to detect the grating than for an age-matched visually normal control, with a larger difference at higher spatial frequencies. The loss of sensitivity was constant across the visual field: At each eccentricity, every patient required 1 to 1.5 log units more contrast than normal to see the highest spatial frequency the eye could resolve. Similarly, there is an equivalent loss of sensitivity to a pinpoint of light located at 20 degrees nasally or 30 degrees temporally (Bowering, Maurer, Lewis, & Brent, 1993) and to pinpoints of light located throughout the periphery (Bowering, 1992). Thus, deprivation also interferes with the development of sensitivity to peripheral targets along the horizontal meridian and throughout the visual field. Because there have been no studies of the sensitive period for the recovery of peripheral vision, we cannot determine whether losses were greater immediately after deprivation and then recovered, remained stable over time, or were initially smaller and then got worse.

Thus, bilateral deprivation from birth causes deficits in all aspects of peripheral vision that have been measured: the extent of the visual field, sensitivity along the horizontal meridian, and sensitivity to a pinpoint of light located anywhere in the visual field. This pattern of results is consistent with that reported for cats (e.g., Sherman, 1973) and for a few case studies of humans bilaterally deprived from birth (Mioche & Perenin, 1986). Our studies show that unlike acuity, the duration of the initial deprivation affects the size of the deficit in the extent of the visual field, although not sensitivity within the visual field (Bowering, 1992; Bowering et al., 1997). The effect of the duration of deprivation indicates that visual input may play different roles in driving normal development at different times during infancy.

Sensitive Period for Damage

To delineate the sensitive period for damage to the normal development of peripheral vision, and hence the end of the period of visually driven normal development, we tested children with a normal early visual history who then developed cataracts in one or both eyes sometime after birth. Measurements of 18 eyes of bilateral cases and 11 deprived eyes of unilateral cases, all of whom developed cataracts sometime after birth, revealed large restrictions in the extent of the field even when the deprivation had begun as late as 6 years of age (the latest onset tested) (Bowering et al., 1997). Three unilateral cases with onset of deprivation between 6 and 9 years of age all showed subtle losses in contrast sensitivity at high spatial frequencies at all locations tested along the horizontal meridian (Tytla et al., 1991). Those data indicate that the sensitive period lasts until at least 9 years of age. However, the most informative data come from tests of 27 deprived eyes with onset of deprivation between 6 months and 13 years, all of whom showed large losses in sensitivity at both 20 degrees in the nasal field and at 30 degrees in the temporal field (Bowering et al., 1993). In contrast, 2 adults with onset of deprivation at 41 and 46 years of age showed no such loss in either field. Thus, the sensitive period for damage to peripheral vision seems to continue beyond the early teenage years, well after the end of the sensitive period for acuity and contrast sensitivity. The common pattern across all three aspects of vision is that visual input is necessary for some time after normal development is complete.

In summary, our studies of peripheral vision indicate that visual input is necessary through at least early adolescence, and hence the period of visually driven normal development lasts from birth (or near birth—there is no case in our sample of deprivation shorter than 1 month) until at least the end of normal development (which is by age 7 for sensitivity in the midperiphery); however, note that the datasets are incomplete, and it is possible that the sensitive periods differ for different aspects of peripheral vision (e.g., the extent of the field, sensitivity close to center vs. in the far periphery, sensitivity in the temporal vs. nasal visual field, and sensitivity in the upper vs. lower visual fields), especially given their different rates of development and different neural bases (reviewed in Bowering, 1992, and Maurer & Lewis, 1998). The fact that we found that the duration of bilateral deprivation from birth affects the degree of loss in the extent of the visual field (Bowering et al., 1997), but not sensitivity within the visual field (Bowering, 1992; Bowering et al., 1993), adds weight to that possibility.

GLOBAL MOTION

Normal Development

The perception of global motion requires the integration of local cues into a global percept specifying the overall

direction of motion. It is typically tested with random dot kinematograms in which an array of dots moves in some overall direction, but individual dots are replaced every few milliseconds (''limited lifetime dots'') so that the predominant direction of motion cannot be determined by looking at any one dot. A typical measure of sensitivity, called the coherence threshold, is the minimum percentage of the dots that have to move in the same direction, among randomly moving dots, for the participant to accurately perceive that predominant direction of motion.

Babies as young as 6 weeks old (the youngest age tested) detect global motion provided that at least 36% of the dots in the random dot kinematogram are moving coherently (Banton & Berenthal, 1996); however, the range of displacements (i.e., distance traveled) and speeds to which infants respond changes with age. For example, the maximum displacement for which infants show detection of coherent motion in a random dot kinematogram increases from 0.8 visual degrees at 8 to 9 weeks of age to 1.25 visual degrees at 12 to 13 weeks of age (Wattam-Bell, 1992), and the slowest effective speed decreases from 3.5 degrees s^{-1} for 13-week-olds to 1.2 degrees s^{-1} for 20-week-olds (Berenthal & Bradbury, 1992). Even within the range of detectable speeds and displacements, there is substantial improvement in the perception of global motion between infancy and adulthood. For example, coherence thresholds improve threefold between 11 and 15 weeks of age and sevenfold between 15 weeks of age and adulthood (Wattam-Bell, 1994).

Two studies have measured sensitivity to global motion in older children and have come to very different conclusions about when the perception of global motion reaches adult values. A study from our lab using random dot kinematograms (Ellemberg et al., 2002) reported that coherence thresholds are adultlike by 6 years of age whereas Gunn et al. (2002), using motion-defined-form (i.e., the coherent motion moved in opposite directions so as to define stripes), reported that coherence thresholds were not adultlike until 10 to 11 years of age. One explanation for the different outcomes is differences in the speed of dots: Dots moved at 18 degrees s^{-1} in the study by Ellemberg et al. (2002) whereas they moved only at 6 degrees s^{-1} in the study by Gunn et al. In a study using more complicated stimuli, we found that sensitivity to global motion is more immature in 5-year-olds for slower speeds (1.5 degrees s^{-1}) than for faster speeds (6 or 9 degrees s^{-1}) (Ellemberg et al., 2004). Similarly, sensitivity to global motion might reach adult functional levels more slowly for dots moving at 6 degrees s^{-1} than for dots moving at 18 degrees s^{-1}. Alternatively, sensitivity to the global direction of moving dots might develop more rapidly than sensitivity to form defined by global

motion because the latter involves additional processing in higher visual areas (Oram & Perrett, 1996). Thus, the perception of global motion is very immature during infancy, and sensitivity reaches adult values sometime between 6 and 11 years of age.

Outcome after Early Bilateral Deprivation

We measured sensitivity to the direction of global motion in the same 8 patients treated for bilateral congenital cataract who were described in the section on grating acuity. On each trial, patients were shown limited lifetime random dot kinematograms composed of large dots (30 arc min diameter) designed to compensate for reduced acuity in the patients. The dots moved at 18 degrees s^{-1}, and the percent coherence was varied systematically over trials to determine the minimum percentage dots necessary for the discrimination of upward versus downward motion. The left panel of Figure 6 shows the coherence thresholds for each eye of each patient. All 16 eyes of these patients had abnormal coherence thresholds, averaging five times worse than normal (Ellemberg et al., 2002). The deficits were not related to the age of treatment, at least when treatment occurred between 3 and 8 months of age. Thus, as with grating acuity, deprivation during even just the first 3 months of life is sufficient to permanently alter sensitivity to global motion. To our knowledge, this is the only published study of sensitivity to global motion after early pattern deprivation in any species.
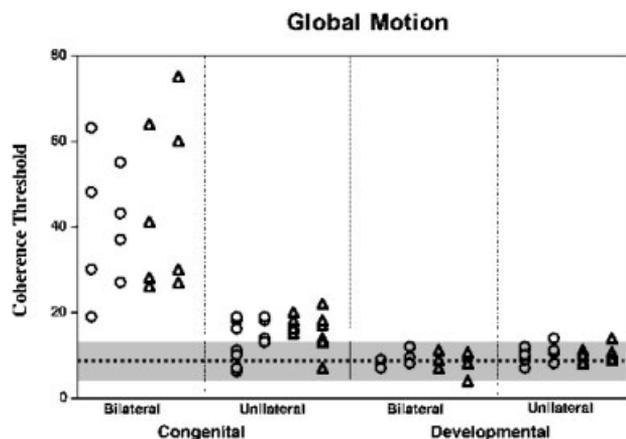
FIGURE 6 Global motion coherence thresholds for each patient described in Figure 3. The dashed line and surrounding shaded area represent the mean (± 2 *SD*) of 24 controls with normal vision. Other details as in Figure 3. From ''Better perception of global motion after monocular than after binocular deprivation,'' by D. Ellemberg, T. L. Lewis, D. Maurer, S. Brar, and H. P. Brent, *Vision Research*, 42, p. 174. Copyright 2002 by Elsevier Press. Reprinted with permission from the authors.

Sensitive Period for Damage

To delineate the sensitive period for damage to the normal development of global motion, and hence the end of the period of visually driven normal development, we tested coherence thresholds in the same 15 patients described in the section on grating acuity who had been treated for developmental cataracts in one or both eyes between the ages of 4 months and 15 years. As shown in the two right panels of Figure 6, every single deprived eye had normal coherence thresholds. This was true even in the six eyes with onset of deprivation between 4 and 9 months of age. Yet, every one of these six eyes had abnormal grating acuity. Thus, the sensitive period for the disruption of global motion, and thus the period of visually driven normal development, appears to be very short, starting at or near birth. (There is no case in our sample of deprivation from birth less than 3 months long.) and ending sometime during the first year of life. This period is much shorter than that for grating acuity (which lasts at least until 5 years of age), Snellen acuity (which lasts until about 10 years of age), and peripheral vision (which lasts at least until the early teenage years). A similar conclusion arises from a case study of an individual with deprivation lasting almost 40 years beginning in the third year of his life: His acuity and contrast sensitivity are worse than that of a visually normal 3-year-old, but he performs normally on a variety of motion tasks and shows normal levels of activation in the MT-complex to moving patterns (Fine et al., 2003). Moreover, for global motion, the sensitive period for damage is over long before the age of functional maturity (between 6 and 11 years). This pattern of an unusually short sensitive period for damage relative to the period of normal development is very different than that observed for acuity or peripheral vision (see Visual Acuity and Peripheral Vision sections) and very different from the typical pattern described by Daw (2003).

ASYMMETRY OF OPTOKINETIC NYSTAGMUS

Normal Development

Optokinetic nystagmus (OKN) is a series of reflexive eye movements elicited by a repetitive pattern moving through the visual field. In visually normal adult humans, monkeys, and cats, horizontal OKN is symmetrical—the alternating pursuit and saccadic eye movements are similar whether the stimulus moves leftward or rightward and whether subjects look with one eye or both (e.g., Braun & Gault, 1969; Lewis, Maurer, Smith, & Haslip, 1992; Pasik & Pasik, 1964). When tested binocularly, even newborn babies, like young monkeys and kittens, show symmetrical OKN in response to horizontally moving patterns (Atkinson, 1979; Krementizer, Vaughan, Kurtzberg, & Dowling, 1979; van Hof-van Duin, 1978). In contrast, when tested monocularly, all three species show asymmetrical OKN during early infancy: OKN is elicited easily when a pattern moves temporally to nasally, but not when it moves nasally to temporally (e.g., Atkinson, 1979; Lewis, Maurer, Smith, & Haslip, 1992; van Hof-van Duin, 1978). Developmental reductions in the size of the OKN asymmetry likely reflect maturation of structures such as the medial superior temporal visual area within the cortical motion stream (reviewed in Braddick, 1996b) and/or in the cortical projections to subcortical areas known to be involved in the mediation of OKN, namely the dorsal terminal nucleus of the accessory optic tract and the nucleus of the optic tract in the pretectum (Hoffmann, 1986, 1989; reviewed in Maurer & Lewis, 1993).

Several authors have attempted to determine when OKN becomes symmetrical in visually normal human infants and have concluded that it does so sometime between 3 and 6 months of age (Atkinson, 1979; Atkinson & Braddick, 1981; Lewis, Maurer, Smith, & Haslip, 1992; Naegele & Held, 1982, 1983; Roy, Lachapelle, & Lepore, 1989; van Hof-van Duin & Mohn, 1984, 1985, 1986). All these studies used wide stripes or large random dots of high contrast to elicit OKN; however, the age at which OKN becomes symmetrical likely varies with the visibility of the stimulus (i.e., the size and contrast of the elements). With lower contrast (Teller, Succop, & Mar, 1993) or narrower stripes (Lewis, Maurer, Chung, Holmes-Shannon, & Van Schaik, 2000), the asymmetry is large in 2-month-olds and decreases systematically between 3 months and 2 years of age, such that only at 2 years of age has the OKN asymmetry decreased to a trivially small size.

Outcome after Early Bilateral Deprivation

To examine the effects of early bilateral deprivation on the symmetry of OKN, we measured the symmetry of OKN in 10 eyes of children treated for bilateral congenital cataract (Lewis, Maurer, & Brent, 1985, 1989). As shown in Figure 7, 8 of 10 eyes treated for bilateral congenital cataract showed a significant OKN asymmetry: In those 8 cases, OKN was observed on a median of about 85% of the trials when wide, high-contrast stripes moved temporally to nasally, but only on about 12% of the trials when they moved in the opposite direction. Moreover, not shown in Figure 7 is the fact that the size of the asymmetry was unrelated to the duration of deprivation: The size of the asymmetry was as large after 6 months of deprivation as after more than 18 months of deprivation. Thus, in humans, as in cats (Harris, Lepore, Guillemot, & Cynader, 1980; van Hof-van Duin, 1978), early bilateral deprivation
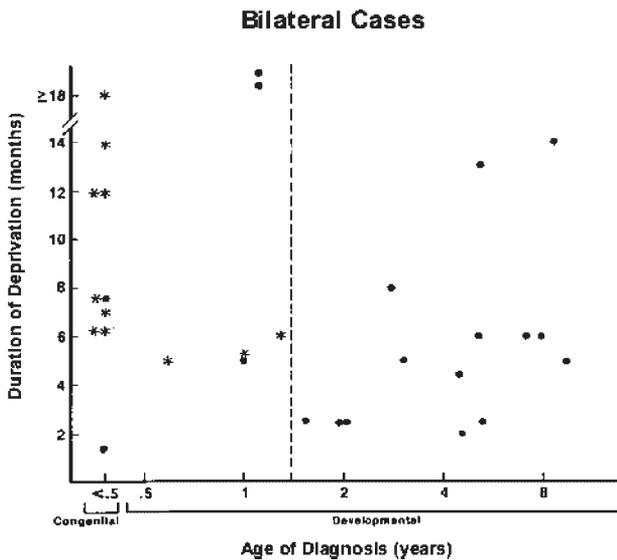
FIGURE 7 Asymmetry of OKN in children treated for bilateral congenital or developmental cataracts as a function of (a) the age of diagnosis of a dense cataract and (b) the duration of deprivation. Each point represents the results for one eye. Asterisks indicate that the asymmetry was significant, and the dots indicate that it was not. The vertical dashed line separates eyes that had cataracts diagnosed before and after 18 months of age. From ''Optokinetic nystagmus in normal and visually deprived children: Implications for cortical development,'' by T. L. Lewis, D. Maurer, and H. P. Brent, *Canadian Journal of Psychology*, 43, 121–140, Figure 6. Copyright 1989 by Canadian Psychological Association. Adapted with permission from the authors.

prevents the development of symmetrical OKN even to wide stripes and thus seems to cause permanent damage to the cortical pathways mediating nasal-to-temporal OKN.

Sensitive Period for Damage

To delineate the sensitive period for damage to the normal development of symmetrical OKN elicited by wide, high-contrast stripes and hence the end of the period of visually driven normal development, we measured the symmetry of OKN in 20 eyes of children treated for bilateral developmental cataract with onset beginning between $7\frac{1}{2}$ months and 10 years of age (Lewis, Maurer, & Brent, 1985, 1989). None of the 14 eyes that developed cataracts after 18 months of age had asymmetrical OKN even though 3 of the eyes that developed cataracts after $2\frac{1}{2}$ years of age had deprivation lasting more than 7 months. In contrast, 3 of the 6 eyes that had a normal early history and then developed cataracts before 18 months of age had asymmetrical OKN, even with deprivation lasting less than 6 months (see Figure 7).

Taken together, the results indicate that the sensitive period for the development of symmetrical OKN to wide

stripes lasts from birth (or near birth—there were no cases of deprivation of less than 6 weeks) until 18 months of age. This period is much longer than that for global motion, but much shorter than that for spatial vision. Moreover, the sensitive period for damage lasts well beyond the period of normal development, which for wide, high-contrast stripes is over by at least 6 months of age.

In summary, studies of children treated for bilateral deprivation indicate that the sensitive period for damage is far longer for acuity, peripheral vision, and asymmetrical OKN than for global motion. In each of these three cases, the absence of visual input causes a permanent deficit whether it occurs near or after birth and even when it starts sometime after the age when the performance of visually normal children reaches adult levels. That pattern indicates that visual input is necessary to drive development during the entire period of functional changes and to crystallize connections for some time after normal development is complete. Nevertheless, our longitudinal studies of acuity indicate that some changes occur during the period of deprivation that allow substantial, but incomplete, recovery once visual input is received, recovery that appears to asymptote before the age at which normal development is complete. The findings for global motion indicate a surprising sparing of function when visual deprivation begins after early infancy and belie the notion that the degree of plasticity (and hence of damage from abnormal input) is greater for aspects of vision mediated higher in the visual pathway (e.g., global motion) than for those mediated lower in the system (e.g., visual acuity and peripheral vision).

UNILATERAL DEPRIVATION

Competitive Interactions between the Eyes

Anatomical and physiological studies in animal models indicate that early bilateral deprivation has adverse effects on the primary visual cortex: Cells in the monkey's primary visual cortex have sluggish responses, abnormally large receptive fields, and reduced spatial resolution (Blakemore, 1990; Blakemore & Vital-Durand, 1983; reviewed in Movshon & Kiorpes, 1993). However, the consequences of early unilateral deprivation are much more severe: In the primary visual cortex of the monocularly deprived monkey, most cells are driven only by the nondeprived eye, and the few cells drivable by the previously deprived eye have a much greater reduction in acuity than is the case after binocular deprivation (Blakemore, 1988; Crawford, 1988; Crawford, de Faber, Harwerth, Smith, & von Noorden, 1991; Hubel, Wiesel, & LeVay, 1977; LeVay, Wiesel, & Hubel, 1980). Moreover, ocular dominance columns are nearly normal after early

bilateral deprivation, but are shrunken and fragmented for the deprived eye after early unilateral deprivation (Crawford et al., 1991; LeVay et al., 1980). The deleterious effects of early unilateral deprivation on the primary visual cortex are reduced if the fellow eye was occluded after the initial unilateral deprivation, at least if the period of deprivation was short (Blakemore, 1988; Blakemore, Garey, & Vital-Duran, 1978; Crawford, de Faber, Harwerth, Smith, & von Noorden, 1989; LeVay et al., 1980; Swindale, Vital-Durand, & Blakemore, 1981). Behavioral tests of spatial vision after unilateral versus bilateral deprivation in monkeys have led to similar conclusions (Harwerth, Smith, Boltz, Crawford, & von Noorden, 1983a, 1983b; Harwerth et al., 1991).

Findings of a worse outcome after early unilateral than after early bilateral deprivation in animals have been attributed to the consequences of (a) uneven competition for cortical connections between a deprived eye and a stronger fellow eye and (b) after the deprivation ends, between a deprived eye sending weaker signals and a non-deprived fellow eye sending stronger signals. Synapses involving input from the deprived eye are pruned through Hebbian competition and/or are silenced through an inhibitory process (reviewed in Maurer & Lewis, 2001a; also see Maurer & Mondloch, 2004). This can result in sparse representation of input from the deprived eye and in abnormal connections between the remaining cells driven by the deprived eye (Jeffrey, Wang, & Birch, 2004). The benefits from occlusion are explained similarly: The uneven competition is reduced by aggressive occlusion of the ''good'' eye throughout early development because there is less pruning or silencing of synapses involving the weak signals from the previously deprived eye and/or because occlusion induces a reversal of the original competitive effects. Even so, sometimes the recovery in the deprived eye that is induced by occlusion of the ''good'' eye is not permanent (e.g., evidence of bilateral amblyopia following reverse occlusion in kittens; Murphy & Mitchell, 1987) and/or is accompanied by permanent deficits in the good eye (discussed later).

To evaluate the role of competitive interactions between the eyes in human visual development, we tested the deprived eyes of children treated for unilateral cataract. These children suffer not only from the initial deprivation of input to one eye, just like the deprivation to both eyes in children treated for bilateral cataract, but also from the additional adverse effect of uneven competition between the deprived and nondeprived eyes for cortical connections. The adverse effect of the uneven competition should be reduced with increasing occlusion of the nondeprived eye. As in our studies of bilateral congenital cataract, we included only children with cataracts that were sufficiently large and dense to block all patterned visual input and with no other abnormalities likely to

interfere with visual development. Treatment involved surgical removal of the cataractous lens and fitting the eye with a contact lens to focus patterned visual input. After treatment, parents were instructed to patch the nonde-prived eye 50 to 90% of the waking time until at least 5 years of age. The recommended amount of patching varied among ophthalmologists and decades, but was independent of the severity of the deficit. There was even more variability in the actual amount of patching because compliance with the recommended amount varied among parents. This variability in a sufficiently large sample allows statistical assessment of the independent influences of age of treatment and amount of patching.

As would be expected, we found that children treated for unilateral congenital cataract show deficits in grating acuity during infancy, asymptotic acuity, and contrast sensitivity, and those deficits are worse when there was little patching of the nondeprived eye (Ellemberg, Lewis, Maurer, & Brent, 2000; Lewis et al., 1995; Tytla, Maurer, Lewis, & Brent, 1988). These findings are similar to those reported from other labs (e.g., Lundvall & Kugelberg, 2002; Mayer et al., 1989). Among good patchers (good compliance with the prescribed 6–8 hr/day), those treated earlier (before 6–8 weeks of age) achieve a better final letter acuity and better spatial contrast sensitivity than those treated later (up to 8 months of age). After such early treatment and aggressive patching, the overall outcome is like that after bilateral deprivation of comparable or longer duration, and a few individual eyes have achieved normal or nearly normal sensitivity (Birch et al., 1998; Birch et al., 1993; Birch & Stager, 1996; Tytla et al., 1988). Without early treatment and aggressive patching, the outcome is much worse than in children treated for bilateral cataracts of comparable duration (Birch et al., 1998; Ellemberg et al., 2000; Lundvall & Kugelberg, 2002; Tytla et al., 1988).

Together, the data on acuity and contrast sensitivity suggest that uneven competition for cortical connections affects human visual development after the first 2 months postnatally, such that its effects cannot be reversed even by aggressive patching. However, the conclusions are complicated by evidence that a comparably good acuity can be achieved by extensive patching beginning immediately after early treatment or by progressively increasing the amount of patching from 1 hr per day at the time of treatment to 50% of waking time at 8 months of age (Jeffrey, Birch, Stager, & Weakley, 2001).

Our longitudinal study of spatial contrast sensitivity beginning when patients were 4 to 7 years of age revealed that despite a history of early treatment and extensive patching, some of the children treated for unilateral congenital cataract actually lost sensitivity to higher spatial frequencies when retested 1 and/or 2 years later (Ellemberg et al., 2001). Thus, a history of uneven

competition between the eyes can cause a later loss of acuity, presumably reflecting the loss of functional cortical connections that had been formed in the initial recovery from deprivation. The loss in this age range may reflect interocular competition between strong signals from the good eye and slightly weaker signals from the previously deprived eye that can be offset by continued aggressive patching. That hypothesis is supported by the finding that 2 children in another study lost letter acuity when they stopped patching at ages 4 and 6 (Jeffrey et al., 2001). Such losses of cortical connections after unilateral deprivation also are implicated in monkeys in which the visual resolution of cells in primary visual cortex driven by the deprived eye is sometimes less than that of normal newborn monkeys (Blakemore, 1988).

Interestingly, uneven competition between a formerly deprived eye and a nondeprived eye leads to subtle deficits in the spatial resolution of the nondeprived eye (Ellemberg et al., 2000; Lewis, Maurer, Tytla, Bowering, & Brent, 1992; McCulloch, & Skarf, 1994; Thompson, Møller, Russell-Eggitt, & Kriss, 1996). Group analyses of vision in the nondeprived eyes reveal small, but statistically significant, losses in grating acuity, in contrast sensitivity for high spatial frequencies (narrow stripes), and in letter acuity, losses which are not an aftermath of patching the good eye—the losses are not related to the amount of time that the nondeprived eye had been patched during early childhood. The implication is that optimal development of acuity for both eyes requires balanced visual activity. When there is an initial period of advantage for one eye—until the acuity of the deprived eye approaches that of the nondeprived eye at about 1 year of age—the ultimate acuity of both eyes will be compromised, with major deficits in the deprived eye and subtle deficits in the nondeprived eye. The only exceptions reported in the literature are when the nondeprived eye is paired with a nonfunctioning eye that remains untreated (Thompson et al., 1996) or when the imbalance is minimized because of very early treatment for unilateral congenital cataract (before 6 weeks of age) followed by very aggressive patching (at least 75% of waking time) (Birch et al., 1993).

We also found evidence for competitive interactions between the eyes in our tests of peripheral vision. As described earlier, children treated for bilateral congenital cataract later had severely constricted visual fields, with the greatest constriction in the temporal field; however, at least for a dim light, the constrictions were even greater after unilateral than after bilateral deprivation, and the extent of the constriction in the temporal visual field was reduced when there had been aggressive patching of the nondeprived eye (Bowering, 1992; Bowering et al., 1997). The large restrictions after bilateral deprivation indicate that visual deprivation interferes with the normal devel-opment of peripheral vision. The fact that the restrictions are even greater after unilateral deprivation indicates that uneven competition between the eyes can have an additional adverse effect.

Children treated for bilateral congenital cataract also have reduced sensitivity along the horizontal meridian. Unlike bilaterally deprived children who showed constant losses in sensitivity across the visual field, unilaterally deprived children all showed larger losses when the gratings were in the nasal field than when they were in the temporal field (Maurer & Lewis, 1993; Tytla et al., 1991). Similarly, the light sensitivity of children treated for unilateral congenital cataract is reduced significantly more when the target is in the nasal field (at 20 degrees) than when it is in the temporal field (at 30 degrees) (Bowering et al., 1993). In contrast, children treated for bilateral congenital cataract and children who had a normal early history and then developed cataracts in one or both eyes later all showed equal reductions in light sensitivity at both locations. The pattern of findings after unilateral, but not after bilateral, deprivation parallels our findings that during infancy there is lower sensitivity for targets at 20 degrees in the nasal field than for targets at 30 degrees in the temporal field (Lewis, Maurer, & Blackburn, 1985; Lewis & Maurer, 1992). Thus, slowly developing parts of peripheral vision seem to be affected not only by visual deprivation but also by uneven competition between the eyes.

No Interactions between the Eyes

We argued in the previous section that two patterns of outcome signified competitive interactions between the eyes, namely a worse outcome after unilateral than after bilateral deprivation and a reduction in the difference between the two types of deprivation with increased occlusion of the nondeprived eye in unilateral cases. Thus, comparable results after unilateral and bilateral deprivation, regardless of the amount of patching of a nondeprived eye, would provide evidence for no interactions between the eyes. That is precisely the pattern of results for grating acuity tested immediately after deprivation ended (Maurer et al., 1999). Specifically, on the first test, which occurred within 10 min after the first focused patterned visual input, the mean acuity of the deprived eyes of 16 children treated for unilateral congenital cataract was no different than that of children treated for bilateral cataract—both groups had acuity that was no better than that of newborns regardless of the duration of deprivation. In the unilaterally deprived group, there was significant improvement after the first hour of visual input and over the next month that was of similar magnitude to that after treatment for bilateral congenital cataract (see bottom panel of Figure 2). Moreover, the amount of

improvement over the first month was not related to the amount of patching of the nondeprived eye, which in this cohort varied from none to 9 waking hr/day. In other words, despite the large differences in the signals reaching the visual cortex from a normally developing eye versus an eye receiving no pattern before treatment or from an eye with much lower acuity than the fellow eye after treatment, there is no evidence that the uneven signals result in competitive suppression of the deprived eye. Visual activity induced by patterned input is sufficient to drive the initial recovery from deprivation. These results are consistent with the finding described earlier that letter acuity is as good in children treated for unilateral congenital cataract before 3 months of age, followed by progressively increasing occlusion over the first 8 months, as in those who patch 80% of the waking time from the start (Jeffrey et al., 2001). The initial lack of competitive interactions may be related to the lack of any functional binocular input to the cortex during the first 2 to 3 months postnatally in visually normal infants (e.g., Braddick, 1996a) and to the slow development of sensitivity in the nasal visual field and hence of overlapping input from the two eyes to each cerebral hemisphere (cf. Le Grand, Mondloch, Maurer, & Brent, 2003).

However, evidence of adverse effects from uneven competition emerges by the first birthday. Although the acuity of the majority of the eyes from unilateral cases has improved to be within normal limits, more than 20% are outside normal limits and acuity is worse in patients who did less patching of the nondeprived eye (Lewis et al., 1995; Mayer et al., 1989). In fact, as shown in Figure 8, children who had patched the nondeprived eye for less than 3 hr per day have acuity in the deprived eye that is
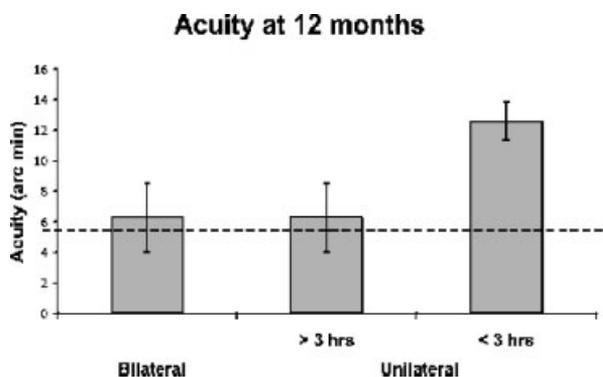
FIGURE 8 Grating acuity at 12 months of age in children treated for bilateral congenital cataract, unilateral congenital cataract who had patched the nondeprived eye more than 3 hr per day, and unilateral congenital cataract who had patched the nondeprived eye less than 3 hr per day. Mean amount of patching per day was calculated from the time of the first optical correction until 5 years of age. The dashed line represents the mean grating acuity of visually normal 12-month-olds.

significantly worse than the acuity of children treated at the same age for bilateral congenital cataract (Lewis et al., 1995).

These results imply that by 1 year of age, competitive interactions have begun to limit recovery from deprivation; however, note that although more patching of the nondeprived eye was correlated with better acuity in the treated eye, the direction of causality is uncertain: It is possible that those with better acuity in the treated eye were more likely to be compliant with the prescribed patching regimen. Support for a causal influence from occlusion comes from studies of cats in which compliance is not an issue. Mitchell and Gingras (1998) obtained results similar to ours from unilaterally deprived kittens. They found that the initial recovery of acuity from deprivation was similar in kittens with or without reverse suture (permanent closure of the initially nondeprived eye to eliminate the competitive disadvantage of the initially deprived eye). Only later did the kittens with reverse suture show greater recovery. Mitchell and Gingras concluded that the initial recovery after unilateral deprivation is driven solely by visually driven cortical activity, and only later, after a scaffold of connections from the deprived eye has been established in the primary visual cortex, does uneven competition between the eyes limit the amount of recovery. Similarly, in humans the initial recovery appears to be driven exclusively by visual activity, perhaps taking advantage of the normal postnatal exuberant proliferation of synapses in the visual cortex (Huttenlocher & De Courten, 1987; Huttenlocher et al., 1982). Once the visual activity has induced functional changes, presumably by strengthening responses in the primary visual cortex driven by the previously deprived eye, competitive interactions emerge and quickly become the strongest determinant of the recovery of acuity.

Implications for understanding normal visual development can be derived from three findings from our studies of acuity. First, there are no signs of interocular competition immediately after the end of deprivation or in the subsequent weeks when the signals from the previously deprived eye are much weaker than those from the good eye. Second, the ultimate acuity is poorer than in bilateral cases if the initial deprivation lasted more than about 2 months, even when there was aggressive patching. Finally, case reports indicate adverse effects of discontinued patching even at 6 years of age. Together these results imply that the two eyes compete for cortical connections beginning around 2 months of age, when acuity has increased twofold since birth, and continue to do so past 6 years of age. Unbalanced competition may result in elimination of connections so that the deprived eye can drive fewer neurons in the primary visual cortex, silencing of synapses by an inhibitory process, and/or scrambled connections among the remaining neurons in the primary

visual cortex that degrade input to higher visual areas (Maurer & Lewis, 2001a; see also Maurer & Mondloch, 2004).

Unlike acuity, for asymmetry of OKN, there is no evidence of competitive interactions on the final outcome following a history of early visual deprivation. The degree of OKN asymmetry is as large after bilateral as after unilateral deprivation, regardless of the duration of deprivation and of how much the good eye had been patched after unilateral deprivation (Lewis, Maurer, & Brent, 1985, 1989). Thus, at least for the asymmetry of OKN, there appears to be no evidence of interaction between the eyes even in the measure of final outcome after a history of early visual deprivation.

Another way in which the outcome after visual deprivation is not affected by competitive interactions between the eyes is in the duration of the sensitive period for damage. As discussed earlier, whether the deprivation is unilateral or bilateral, there are permanent deficits in peripheral vision if the onset occurs even in early adolescence, in acuity if the onset is before about 10 years of age, in asymmetry of OKN if it is before 18 months, and in global motion only if the deprivation begins near birth. The similarity of results after unilateral and bilateral deprivation suggests that the end of the sensitive period for damage is governed by visual input, per se, without additional influences of uneven competition between the eyes. Depending on the aspect of vision, that end can come during early infancy (global motion) or long after normal development is complete (acuity, peripheral vision, asymmetry of OKN).

Collaborative Interactions between the Eyes

Our discussion in this article thus far about the consequences of uneven competition between a nondeprived eye and a deprived eye involved data from animal models about the effects on lower visual cortical areas and tests in unilaterally deprived humans of visual capabilities such as visual acuity, contrast sensitivity, and peripheral sensitivity, which are mediated mainly by those lower cortical areas. Because there are virtually no anatomical or physiological data from animals on the effects of early bilateral versus unilateral deprivation on higher cortical areas, we expected to find the same deleterious effects of uneven competition between the eyes for the perception of global motion (involving primarily the middle temporal visual complex in the extrastriate dorsal stream) as has been reported for spatial and temporal vision (Birch et al., 1998; Bowering et al., 1993; Ellemberg et al., 1999; Ellemberg et al., 2002; Ellemberg et al., 2000; Lewis et al., 1995; Mioche & Perenin, 1986; Tytla et al., 1991; Tytla et al., 1988; also see Outcome after Early Bilateral Deprivation in the Visual Acuity section and Outcome

after Early Bilateral Deprivation in the Peripheral Vision section).

Much to our surprise, that was not the case at all. In fact, impairments in global motion were significantly *smaller* after early unilateral deprivation than after early bilateral deprivation. As described in Outcome after Early Bilateral Deprivation in the Global Motion section, patients treated for bilateral congenital cataract had marked deficits in global motion averaging five times worse than normal (Ellemberg et al., 2002). In contrast, the deficits after unilateral deprivation from birth were only 1.6 times worse than normal and three times smaller than the deficits after bilateral deprivation from birth (Ellemberg et al., 2002; also see Figure 6). These are the same patients who had worse grating acuity after unilateral than after bilateral deprivation unless they had patched the good eye aggressively (see Figure 3). Moreover, as shown in Figure 6, sensitivity was impaired slightly, but similarly, for the nondeprived and deprived eyes of unilateral cases.

The findings for global motion were the first to document greater losses in any aspect of vision after bilateral deprivation than after unilateral deprivation (Ellemberg et al., 2002). They indicate that the absence of patterned and motion information to both eyes from birth prevents the normal development of sensitivity to global motion in either eye; however, normal visual input to one eye from birth is enough to allow the development of nearly normal sensitivity in both eyes. Recently, we have discovered a similar pattern of results for the perception of global form, an aspect of vision involving mainly the extrastriate ventral stream, particularly area V4 (Lewis et al., 2002). Specifically, sensitivity to global form in deprived eyes was significantly better after early unilateral deprivation than after early bilateral deprivation, although the difference between unilateral and bilateral cases was not as marked as for global motion; however, note that better outcomes after unilateral than after bilateral deprivation may not be generalizable to aspects of vision mediated by other parts of the ventral stream (Le Grand, Mondloch, Maurer, & Brent, 2001, 2003). Thus, competitive interactions between a deprived and a nondeprived eye evident in primary visual cortex co-occur with complementary interactions in at least some extrastriate areas. These complementary interactions enable a relative sparing of some visual functions after early unilateral deprivation.

In summary, the results from unilateral cases indicate that the nature of interactions between the eyes varies depending on the time during development and the cortical level involved. Thus, aspects of vision mediated primarily by the striate cortex, such as visual acuity, spatial contrast sensitivity, and peripheral vision, are usually affected adversely by competitive interactions

between a deprived and a nondeprived eye—except, at least for acuity, prior to treatment and immediately after treatment when there is no evidence for these competitive interactions. The implication is that visually dependent normal development is not influenced by competitive interactions in the initial postnatal months, at least for the neural networks underlying visual acuity. In contrast, some aspects of vision mediated primarily by the extrastriate streams, such as the perception of global motion and global form, appear to involve collaborative rather than competitive interactions between the eyes after early deprivation. Despite these differences, the sensitive periods for damage seem to be similar after bilateral and unilateral deprivation, with a surprisingly short damage period for global motion and surprisingly long damage periods for acuity, peripheral vision, and asymmetry of OKN, periods which are longer than the period of visually driven normal development.

SYNTHESIS AND CONCLUSIONS

Our results indicate that there are different sensitive periods for different aspects of vision. For example, visual deprivation beginning at 6 months of age prevents the development of normal acuity or peripheral light sensitivity, but has no effect on sensitivity to the global direction of motion, which is affected adversely only by visual deprivation near birth. Our results also indicate that the deleterious effects of visual deprivation are sometimes worse if there was not only deprivation but also uneven competition between the eyes—because the deprivation was unilateral and there was little patching of the nondeprived eye; however, the adverse effects of uneven competition are not seen at all points during development or for all visual abilities. Moreover, the sensitive period for damage can be either considerably longer than the period of normal development (as is the case with acuity)
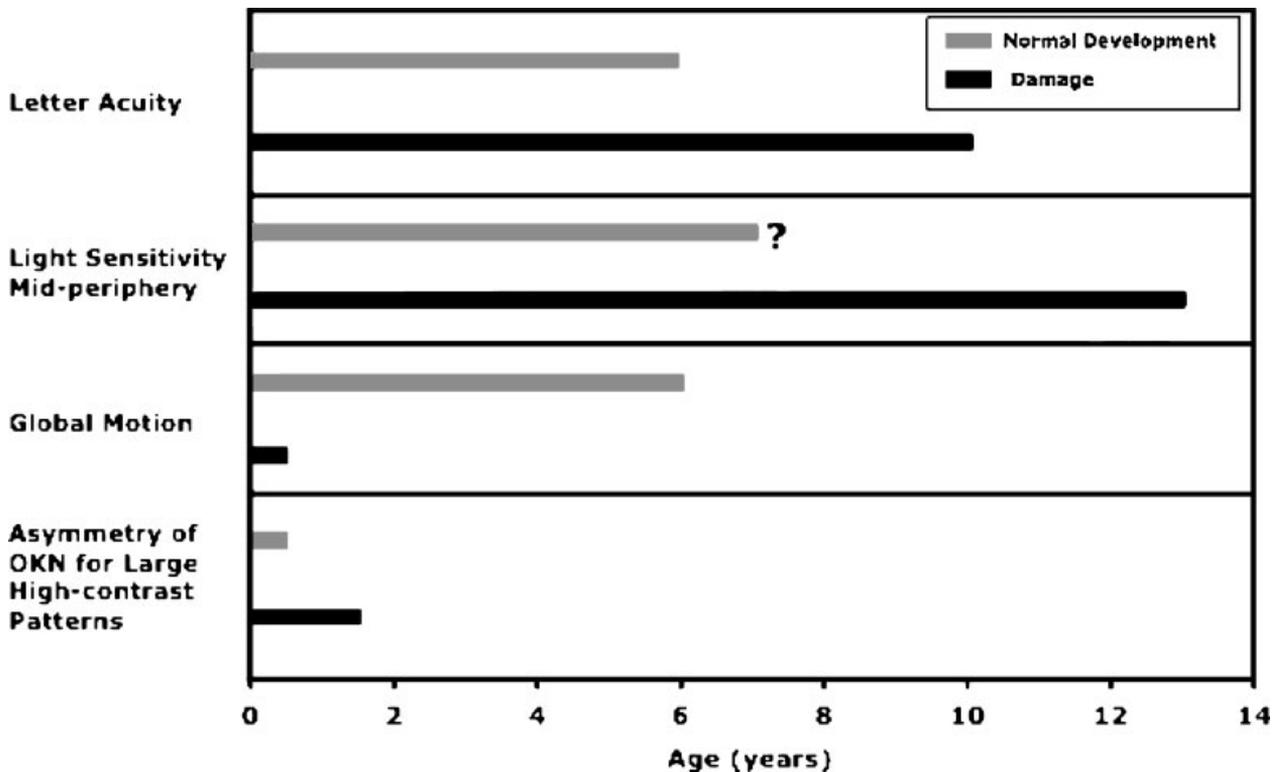
FIGURE 9 Examples of sensitive periods across four aspects of vision. Gray bars represent periods of normal development, and black bars represent sensitive periods for damage. Ages indicating the end of each period are approximate and apply to the conditions described in the text. For convenience, we chose birth as the beginning of each sensitive period for damage, although the actual ages are unknown. The graph illustrates that the period of normal development ends at ages varying from a few months (asymmetry of OKN for large, high-contrast patterns) to 6 or 7 years of age (letter acuity, global motion, and perhaps light sensitivity in the midperiphery—for which 7 years is the youngest age tested beyond infancy). The sensitive period for damage can be considerably longer or shorter than the period of normal development.

or considerably shorter than the period of normal development (as is the case with global motion). Figure 9 summarizes examples of these various patterns.

Together, the results are consistent with theories that visual input can affect later development by (a) preventing deterioration of existing neural structures; (b) reserving neural networks (via Hebbian competition) for later refinement; (c) allowing a developmental trajectory to start from an optimal state; (d) allowing recovery from earlier deprivation, possibly via the recruiting of alternative pathways; and/or (e) allowing the refinement of previously established structures. Our results indicate that there are timing constraints on each of these mechanisms that are manifested as variations in sensitive periods.

REFERENCES

Atkinson, J. (1979). Development of optokinetic nystagmus in the human infant and monkey infant: An analogue to development in kittens. In R. D. Freeman (Ed.), Developmental neurobiology of vision (pp. 277–287). New York: Plenum Press.

Atkinson, J., & Braddick, O. (1981). Development of optokinetic nystagmus in infants: An indicator of cortical binocularity? In D. G. R. Fisher, A. Monty, & J. W. Senders (Eds.), Eye movements: Cognition and visual perception (pp. 53–64). Hillsdale, NJ: Erlbaum.

Banks, M. S., & Bennett, P. J. (1988). Optical and photoreceptor immaturities limit the spatial and chromatic vision of human neonates. Journal of the Optical Society of America A, 5, 2059–2079.

Banton, T., & Berenthal, B. I. (1996). Infants' sensitivity to uniform motion. Vision Research, 36, 1633–1640.

Bavelier, D., & Neville, H. (2002). Cross-modal plasticity: Where and how? Nature Reviews Neuroscience, 3, 443–452.

Beaver, C. J., Mitchell, E. E., & Robertson, H. A. (1993). Immunohistochemical study of the pattern of rapid expression of c-fos protein in the visual cortex of dark-reared kittens following initial exposure to light. Journal of Comparative Neurology, 333, 469–484.

Berenthal, B. I., & Bradbury, A. (1992). Infant's detection of shearing motion in random dot displays. Developmental Psychology, 28, 1056–1066.

Birch, E. E., & Stager, D. R. (1988). Prevalence of good visual acuity following surgery for congenital unilateral cataract. Archives of Ophthalmology, 106, 40–43.

Birch, E. E., & Stager, D. R. (1996). Critical period for surgical treatment of dense congenital unilateral cataract. Investigative Ophthalmology & Visual Science, 37, 1532–1538.

Birch, E. E., Stager, D. R., Leffler, J., & Weakley, D. (1998). Early treatment of congenital unilateral cataract minimizes unequal competition. Investigative Ophthalmology & Visual Science, 39, 1560–1566.

Birch, E. E., Stager, D. R., & Wright, W. W. (1986). Grating acuity development after early surgery for congenital unilateral cataract. Archives of Ophthalmology, 104, 1783–1787.

Birch, E. E., Swanson, W. H., Stager, D., Woody, M., & Everett, M. (1993). Outcome after very early treatment of dense congenital unilateral cataract. Investigative Ophthalmology & Visual Science, 34, 3687–3699.

Blakemore, C. (1988). The sensitive periods of the monkey visual cortex. In G. Lennerstrand, G. K. von Noorden, & C. C. Campos (Eds.), Strabismus and amblyopia: Experimental basis for advances in clinical management (pp. 219–234). New York: Plenum Press.

Blakemore, C. (1990). Vision: Coding and efficiency. In C. Blakemore (Ed.), Maturation of mechanisms for efficient spatial vision. Cambridge, England: Cambridge University Press.

Blakemore, C., Garey, L., & Vital-Durand, F. (1978). The physiological effects of monocular deprivation and their reversal in the monkey's cortex. Journal of Physiology, 283, 223–262.

Blakemore, C., & Vital-Durand, F. (1983). Visual deprivation prevents the postnatal maturation of spatial contrast sensitivity neurons of the monkey's striate cortex. Journal of Physiology (London), 345, 40p.

Boothe, R. G., Dobson, V., & Teller, D. Y. (1985). Postnatal development of vision in human and nonhuman primates. Annual Review of Neuroscience, 8, 495–545.

Bowering, M. E. R. (1992). The peripheral vision of normal children and of children treated for cataracts. (Doctoral dissertation, McMaster University, 1992). Dissertation Abstracts International, 54/02, 752.

Bowering, E. R., Maurer, D., Lewis, T. L., & Brent, H. P. (1993). Sensitivity in the nasal and temporal hemifields in children treated for cataract. Investigative Ophthalmology & Visual Science, 34, 3501–3509.

Bowering, E. R., Maurer, D., Lewis, T. L., & Brent, H. P. (1997). Constriction of the visual field of children after early visual deprivation. Journal of Pediatric Ophthalmology & Strabismus, 34, 347–356.

Bowering, E. R., Maurer, D., Lewis, T. L., Brent, H. P., & Riedel, P. (1996). The visual field in childhood: Normal development and the influence of deprivation (Developmental Cognitive Neuroscience Rep. No. 96.1 MRC Cognitive Development Unit, London, U.K.).

Braddick, O. (1996a). Binocularity in infancy. Eye, 10, 182–188.

Braddick, O. (1996b). Motion processing: Where is the nasal-temporal asymmetry? Current Biology, 6, 250–253.

Braun, J. J., & Gault, F. P. (1969). Monocular and binocular control of horizontal optokinetic nystagmus in cats and rabbits. Journal of Comparative and Physiological Psychology, 69, 12–16.

Brown, A., & Yamamoto, M. (1986). Visual acuity in newborn and preterm infants measured with grating acuity cards. American Journal of Ophthalmology, 102, 245–253.

Candy, R. T., & Banks, M. S. (1999). Use of an early nonlinearity to measure optical and receptor resolution in the human infant. Vision Research, 39, 3386–3398.

Catalano, R. A., Simon, J. W., Jenkins, P. L., & Kadel, G. L. (1987). Preferential looking as a guide for amblyopia therapy in monocular infantile cataracts. Journal of Pediatric Ophthalmology & Strabismus, 24, 56–63.

Courage, M., & Adams, R. (1990). Visual acuity assessment from birth to three years using the acuity card procedure: Cross-sectional and longitudinal samples. Optometry & Vision Science, 67, 713–718.

Crawford, M. L. (1988). Electrophysiology of cortical neurons under different conditions of visual deprivation. In G. Lennerstrand, G. K. von Noorden, & C. C. Campos (Eds.), Strabismus and amblyopia: Experimental basis for advances in clinical management (pp. 207–218). New York: Plenum Press.

Crawford, M. L. J., de Faber, J.-T., Harwerth, R. S., Smith, E. L., & von Noorden, G. K. (1989). The effects of reverse monocular deprivation in monkeys: II. Electrophysiological and anatomical studies. Experimental Brain Research, 74, 338–347.

Crawford, M. L. J., Pesch, T. W., von Noorden, G. K., Harwerth, R. S., & Smith, E. L. (1991). Bilateral form deprivation in monkeys. Investigative Ophthalmology & Visual Science, 32, 2328–2336.

Daw, N. W. (1998). Critical periods and amblyopia. Archives of Ophthalmology, 116, 502–505.

Daw, N. W. (2003). Critical periods in the visual system. In B. Hopkins & S. P. Johnson (Eds.), Neurobiology of infant vision (pp. 43–103). Westport, CT: Praeger.

Daw, N. W., Fox, K., Sato, H., & Czepita, D. (1992). Critical period for monocular deprivation in the cat visual cortex. Journal of Neurophysiology, 67, 197–202.

Dobson, V., Schwartz, T. L., Sandstrom, D. J., & Michel, L. (1987). Binocular visual acuity of neonates: The acuity card procedure. Developmental Medicine & Child Neurology, 29, 199–206.

Elman, J. L., Bates, E. A., Johnson, M. H., Karmiloff-Smith, A., Parisi, D., & Plunket, K. (1996). Rethinking innateness. A connectionist perspective on development. Cambridge, MA: MIT Press.

Ellemberg, D., Lewis, T. L., Dirks, M., Maurer, D., Ledgway, T., Guillemot, J.-P., & Lepore, F. (2004). Putting order into the development of sensitivity to global motion. Vision Research, 44, 2403–2411.

Ellemberg, D., Lewis, T. L., Liu, C. H., & Maurer, D. (1999). The development of spatial and temporal vision during childhood. Vision Research, 39, 2325–2333.

Ellemberg, D., Lewis, T. L., Maurer, D., Brar, S., & Brent, H. P. (2002). Better perception of global motion after monocular than after binocular deprivation. Vision Research, 42, 169–179.

Ellemberg, D., Lewis, T. L., Maurer, D., & Brent, H. P. (2000). Influence of monocular deprivation during infancy on the later development of spatial and temporal vision. Vision Research, 40, 3283–3295.

Ellemberg, D., Lewis, T. L., Maurer, D., & Brent, H. P. (2001). The role of visual input in setting up spatial filters in the human visual system. Proceedings of the Society for Imaging Science and Technology (pp. 421–425). Springfield, VA: Society for Imaging Science & Technology.

Fahle, M., & Schmid, M. (1988). Naso-temporal asymmetry of visual perception and of the visual cortex. Vision Research, 28, 293–300.

Fantz, R., Ordy, J., & Udelf, M. (1962). Maturation of pattern vision in infants during the first six months. Journal of Comparative and Physiological Psychology, 55, 907–917.

Fine, I., Wade, A., Brewer, A., May, M., Goodman, D., Boynton, G., Wandell, B., & MacLeod, D. (2003). Long-term deprivation affects visual perception and cortex. Nature Neuroscience, 6, 915–916.

Garey, L. J., & De Courten, C. (1983). Structural development of the lateral geniculate nucleus and visual cortex in monkey and man. Behavioral Brain Research, 10, 3–13.

Gunn, A., Cory, E., Atkinson, J., Braddick, O., Wattam-Bell, J., Guzzetta, A., & Cioni, G. (2002). Dorsal and ventral stream sensitivity in normal development and hemiplegia. Neuroreport, 13, 843–847.

Harris, L. R., Lepore, F., Guillemot, J.-P., & Cynader, M. (1980, Oct. 3). Abolition of optokinetic nystagmus in the cat. Science, 210, 91–92.

Harwerth, R. S., Smith, E. L., Boltz, M. L. J., Crawford, M. L. J., & von Noorden, G. K. (1983a). Behavioral studies on the effect of abnormal early visual experience in monkeys: Spatial modulation sensitivity. Vision Research, 23, 1501–1510.

Harwerth, R. S., Smith, E. L., Boltz, M. L. J., Crawford, M. L. J., & von Noorden, G. K. (1983b). Behavioral studies on the effect of abnormal early visual experience in monkeys: Temporal modulation sensitivity. Vision Research, 23, 1511–1517.

Harwerth, R. S., Smith, E. L. III., Duncan, G. C., Crawford, M. L. J., & von Noorden, G. K. (1986, April 11). Multiple sensitive periods in the development of the primate visual system. Science, 232, 235–238.

Harwerth, R. S., Smith, E. L. III., Paul, A. D., Crawford, M. L. J., & von Noorden, G. K. (1991). Functional effects of bilateral form deprivation in monkeys. Investigative Ophthalmology & Visual Science, 32, 2311–2327.

Hoffmann, K.-P. (1986). Visual inputs relevant for the optokinetic nystagmus in mammals. Progress in Brain Research, 64, 75–84.

Hoffmann, K.-P. (1989). Functional organization in the optokinetic system of mammals. In H. Rahman (Ed.), Progress in zoology: Neuronal plasticity and brain function (pp. 261–271). New York: Fisher.

Hubel, D. H., & Wiesel, T. N. (1963). Receptive fields of cells in striate cortex of very young, visually inexperienced kittens. Journal of Neurophysiology, 26, 994–1002.

Hubel, D. H., & Wiesel, T. N. (1970). The period of susceptibility to the physiological effects of unilateral eye closure in kittens. Journal of Physiology, 206, 419–436.

Hubel, D. H., Wiesel, T. N., & LeVay, S. (1977). Plasticity of ocular dominance columns in monkey striate cortex. Philosophical Transactions of the Royal Society of London B, 278, 377–409.

Huttenlocher, P. R. (1979). Synaptic density in human frontal cortex—Developmental changes and effects of aging. Brain Research, 163, 195–205.

Huttenlocher, P. R. (1984). Synapse elimination and plasticity in developing human cerebral cortex. American Journal of Medical Deficiency, 88, 488–496.

Huttenlocher, P. R., & Dabholkar, A. S. (1997). Regional differences in synaptogenesis in human cerebral cortex. Journal of Comparative Neurology, 387, 167–178.

Huttenlocher, P. R., & De Courten, C. (1987). The development of synapses in striate cortex of man. Human Neurobiology, 6, 1–9.

Huttenlocher, P. R., De Courten, C., Garey, L. J., & Van Der Loos, H. (1982). Synaptogenesis in human visual cortex—Evidence for synaptic elimination during normal development. Neuroscience Letters, 33, 247–252.

Jacobson, S. G., Mohindra, I., & Held, R. (1983). Binocular vision from deprivation in human infants. Documenta Ophthalmologica, 55, 237–249.

Jeffrey, B., Birch, E., Stager, D., & Weakley, D. (2001). Early binocular visual experience may improve binocular sensory outcomes in children after surgery for congenital unilateral 9 cataract. Journal of the American Association of Pediatric Ophthalmology & Strabismus, 5, 209–216.

Jeffrey, B. G., Wang, Y.-Z, & Birch, E. E. (2004). Altered global shape discrimination in deprivation amblyopia. Vision Research, 44, 167–177.

Jones, K. R., Spear, P. D., & Tong, L. (1984). Critical periods for effects of monocular deprivation: Differences between striate and extrastriate cortex. Journal of Neuroscience, 4, 2543–2552.

Katz, L. C., & Shatz, C. J. (1996, Nov. 15). Synaptic activity and the construction of cortical circuits. Science, 274, 1132–1138.

Kiorpes, L., & Movshon, J. A. (1998). Peripheral and central factors limiting the development of contrast sensitivity in macaque monkeys. Vision Research, 38, 61–70.

Krementizer, J. P., Vaughan, H. G., Kurtzberg, D., & Dowling, K. (1979). Smooth-pursuit eye movements in the newborn infant. Child Development, 50, 442–448.

Kugelberg, U. (1992). Visual acuity following treatment of bilateral congenital cataracts. Documenta Ophthalmologica, 82, 211–215.

Le Grand, R., Mondloch, C. J., Maurer, D., & Brent, H. P. (2001). Early visual experience and face processing. Nature, 410, 890. Correction: 2001, 412, 786.

Le Grand, R., Mondloch, C. J., Maurer, D., & Brent, H. P. (2003). Expert face processing requires visual input to the right hemisphere during infancy. Nature Neuroscience, 10, 1108–1112. Correction: 2003, 12, 1329.

LeVay, S., Wiesel, T. N., & Hubel, D. H. (1980). The development of ocular dominance columns in normal and visually deprived monkeys. Journal of Comparative Neurology, 191, 1–51.

Levi, D. M. (2005). Perceptual learning in adults with amblyopia: A reevaluation of critical periods in human vision. Developmental Psychobiology, 46, 223–233.

Lewis, T. L., Ellemberg, D., Maurer, D., & Brent, H. P. (2000). Changes in spatial vision during middle childhood in patients treated for congenital cataract. Investigative Ophthalmology & Visual Science, 41, S726.

Lewis, T. L., Ellemberg, D., Maurer, D., Wilkinson, F., Wilson, H. R., Dirks, M., & Brent, H. P. (2002). Sensitivity to global form in GLASS patterns after early visual deprivation in humans. Vision Research, 42, 939–948.

Lewis, T. L., & Maurer, D. (1992). The development of the temporal and nasal visual fields during infancy. Vision Research, 32, 903–911.

Lewis, T. L., Maurer, D., & Blackburn, K. (1985). The development of young infants' ability to detect stimuli in the nasal visual field. Vision Research, 25, 943–950.

Lewis, T. L., Maurer, D., & Brent, H. P. (1985). Optokinetic nystagmus in children treated for bilateral cataracts. In R. Groner, G. W. McConkie, & C. Menz (Eds.), Eye movements and human information processing (pp. 85–105). Amsterdam: North-Holland.

Lewis, T. L., Maurer, D., & Brent, H. P. (1989). Optokinetic nystagmus in normal and visually deprived children: Implications for cortical development. Canadian Journal of Psychology, 43, 121–140.

Lewis, T. L., Maurer, D., & Brent, H. P. (1995). Development of grating acuity in children treated for unilateral or bilateral congenital cataract. Investigative Ophthalmology & Visual Science, 36, 2080–2095.

Lewis, T. L., Maurer, D., Chung, J. Y. Y., Holmes-Shannon, R., & Van Schaik, C. S. (2000). The development of symmetrical OKN in infants: Quantification based on OKN acuity for nasalward versus temporalward motion. Vision Research, 40, 445–453.

Lewis, T. L., Maurer, D., Smith, R. J., & Haslip, J. K. (1992). The development of symmetrical optokinetic nystagmus during infancy. Clinical Vision Sciences, 7, 211–218.

Lewis, T. L., Maurer, D., Tytla, M. E., Bowering, E., & Brent, H. P. (1992). Vision in the "good" eye of children treated for unilateral congenital cataract. Ophthalmology, 99, 1013–1017.

Lloyd, I. C., Dowler, J. G., Kriss, A., Speedwell, L., Thompson, D. A., Russell-Eggitt, I., & Taylor, D. (1995). Modulation of amblyopia therapy following early surgery for unilateral congenital cataracts. British Journal of Ophthalmology, 79, 802–806.

Lundvall, A., & Kugelberg, U. (2002). Outcome after treatment for congenital bilateral cataract. Acta Ophthalmologica Scandanavia, 80, 593–597.

Magnusson, G., Abrahamsson, M., & Sjöstrand, J. (2002). Changes in visual acuity from 4 to 12 years of age in children operated for bilateral congenital cataracts. British Journal of Ophthalmology, 86, 1385–1398.

Maurer, D., & Lewis, T. L. (1993). Visual outcomes after infantile cataract. In K. Simons (Ed.), Early visual development: Normal and abnormal (pp. 454–484). New York: Oxford University Press.

Maurer, D., & Lewis, T. L. (1998). Overt orienting toward peripheral stimuli: Normal development and underlying mechanisms. In J. E. Richards (Ed.), Cognitive neuroscience of attention: A developmental perspective (pp. 51–102). Mahwah, NJ: Erlbaum.

Maurer, D., & Lewis, T. L. (2001a). Visual acuity and spatial contrast sensitivity: Normal development and underlying mechanisms. In C. Nelson & M. Luciana (Ed.), Handbook of developmental cognitive neuroscience (pp. 237–250). Cambridge, MA: MIT Press.

Maurer, D., & Lewis, T. L. (2001b). Visual acuity: The role of visual input in inducing postnatal change. Clinical Neuroscience Research, 1, 239–247.

Maurer, D., Lewis, T. L., Brent, H. P., & Levin, A. V. (1999, Oct. 1). Rapid improvement in the acuity of infants after visual input. Science, 286, 108–110.

Maurer, D., & Mondloch, C. (2004). Neonatal synesthesia: A re-evaluation. In L. Robertson & N. Sagiv (Eds.), Attention on synesthesia: Cognition, development and neuroscience (pp. 193–213). Oxford, England: Oxford University Press.

Mayer, D. L., Beiser, A. S., Warner, A. F., Pratt, E. M., Raye, K. N., & Lang, J. M. (1995). Monocular acuity norms for the Teller acuity cards between ages one month and four years. Investigative Ophthalmology & Visual Science, 36, 671–685.

Mayer, D. L., & Dobson, V. (1982). Visual acuity development in infants and young children as assessed by operant preferential looking. Vision Research, 22, 1141–1151.

Mayer, D. L., Moore, B., & Robb, R. M. (1989). Assessment of vision and amblyopia by preferential looking tests after early surgery for unilateral congenital cataracts. Journal of Pediatric Ophthalmology & Strabismus, 26, 61–68.

McCulloch, D., & Skarf, B. (1994). Pattern reversal visual evoked potentials following early treatment of unilateral congenital cataract. Archives of Ophthalmology, 112, 510–518.

Mioche, L., & Perenin, M. (1986). Central and peripheral residual vision in humans with bilateral deprivation amblyopia. Experimental Brain Research, 62, 259–272.

Miranda, S. B. (1970). Visual abilities and pattern preferences of premature and full-term neonates. Journal of Experimental Child Psychology, 10, 189–205.

Mitchell, D. E. (1988). The extent of visual recovery from early monocular or binocular visual deprivation in kittens. Journal of Physiology, 395, 639–660.

Mitchell, D. E. (1991). The long-term effectiveness of different regimens of occlusion on recovery from early monocular deprivation in kittens. Philosophical Transactions of the Royal Society of London [Biology], 333, 51–79.

Mitchell, D. E., Beaver, C., & Ritchie, P. (1995). A method to study changes in eye-related columns in the visual cortex of kittens during and following early periods of monocular deprivation. Canadian Journal of Physiology and Pharmacology, 73, 1352–1363.

Mitchell, D. E., & Gingras, G. (1998). Visual recovery after monocular deprivation is driven by absolute rather than relative visually evoked activity levels. Current Biology, 8, 1179–1182. Erratum:R897.

Movshon, J. A., & Kiorpes, L. (1993). Biological limits on visual development in primates. In K. Simons (Ed.), Early visual development: Normal and abnormal (pp. 296–305). New York: Oxford University Press.

Mower, G. (1994). Differences in the induction of Fos protein in cat visual cortex during and after the critical period. Molecular Brain Research, 21, 47–54.

Murphy, K., & Mitchell, D. (1987). Reduced visual acuity in both eyes of monocularly deprived kittens following a short or long period of reverse occlusion. Journal of Neuroscience, 71, 526–536.

Naegele, J. R., & Held, R. (1982). The postnatal development of monocular optokinetic nystagmus in infants. Vision Research, 22, 341–346.

Naegele, J. R., & Held, R. (1983). Development of optokinetic nystagmus and effects of abnormal visual experience during infancy. In M. Jeannerod & A. Hein (Eds.), Spatially oriented behavior (pp. 155–174). New York: Springer-Verlag.

Oram, M. W., & Perrett, D. (1996). Integration of form and motion in the anterior superior temporal polysensory area (STPa) of the macaque monkey. Journal of Neurophysiology, 76, 109–129.

Pasik, T., & Pasik, P. (1964). Optokinetic nystagmus: An unlearned response altered by section of chiasma and corpus callosum in monkeys. Nature, 203, 609–611.

Rauschecker, J. (1995). Compensatory plasticity and sensory substitution in the cerebral cortex. Trends in Neuroscience, 18, 36–43.

Roy, M. S., Lachapelle, P., & Lepore, F. (1989). Maturation of the optokinetic nystagmus as a function of the speed of stimulation in full-term and preterm infants. Clinical Vision Sciences, 4, 357–366.

Sherman, S. M. (1973). Visual field deficits in monocularly and binocularly deprived cats. Brain Research, 49, 25–45.

Simons, K. (1983). Visual acuity norms in young children. Survey of Opthalmology, 28, 84–92.

Singer, W. (1988). Neuronal mechanisms of deprivation amblyopia. In G. Lennerstrand, G. K. von Noorden, & C. C. Campos (Eds.), Strabismus and amblyopia: Experimental basis for advances in clinical management (pp. 259–274). New York: Plenum Press.

Swindale, N. V., Vital-Durand, F., & Blakemore, C. (1981). Recovery from monocular deprivation in the monkey: III. Reversal of anatomical effects in the visual cortex. Proceedings of the Royal Society of London B, 213, 435–450.

Teller, D. Y., Succop, A., & Mar, C. (1993). Infant eye movement asymmetries: Stationary counterphase gratings elicit temporal-to-nasal optokinetic nystagmus in two-month-old infants under monocular test conditions. Vision Research, 33, 1859–1864.

Thompson, D. A., Møller, H., Russell-Eggitt, J., & Kriss, A. (1996). Visual acuity in unilateral cataract. British Journal of Ophthalmology, 80, 794–798.

Tschopp, C., Safran, A. B., Viviani, P., Reicherts, M., Bulllinger, A., & Mermoud, C. (1998). Automated visual field examination in children aged 5–8 years: Part II. Normative values. Vision Research, 38, 2211–2218.

Tytla, M. E., Lewis, T. L., Maurer, D., & Brent, H. P. (1991). Peripheral contrast sensitivity in children treated for congenital cataract [Abstract]. Investigative Ophthalmology & Visual Science, 32, 961.

Tytla, M. E., Maurer, D., Lewis, T. L., & Brent, H. P. (1988). Contrast sensitivity in children treated for congenital cataract. Clinical Vision Sciences, 2, 251–264.

Vaegan, M., & Taylor, D. (1979). Critical period for deprivation amblyopia in children. Transactions of the Ophthalmological Society (UK), 99, 432–439.

van Hof-van Duin, J. (1978). Direction preference of optokinetic responses in monocularly tested normal kittens and light-deprived cats. Archives Italiennes de Biologie, 116, 471–477.

van Hof-van Duin, J., & Mohn, G. (1984). Vision in the preterm infant. In H. F. R. Prechtl (Ed.), Continuity of neural functions from prenatal to postnatal life (pp. 93–115). Philadelphia: Lippincott.

van Hof-van Duin, J., & Mohn, G. (1985). The development of visual functions in preterm infants. Ergebaisse der Experimentellen Medizin, 46, 350–361.

van Hof-van Duin, J., & Mohn, G. (1986). Visual field measurements, optokinetic nystagmus and the visual threatening response: Normal and abnormal development. Documenta Ophthalmologica Proceedings Series, 45, 305–316.

Wattam-Bell, J. (1992). The development of maximum displacement limits for discrimination of motion direction in infancy. Vision Research, 32, 621–630.

Wattam-Bell, J. (1994). Coherence thresholds for discrimination of motion direction in infants. Vision Research, 34, 877–883.

Wiesel, T. N., & Hubel, D. H. (1963). Single cell responses in the striate cortex of kittens deprived of vision one eye. Journal of Neurophysiology, 26, 1003–1017.

Wiesel, T. N., & Hubel, D. H. (1965). Comparison of the effects of unilateral and bilateral eye closure on cortical unit responses in kittens. Journal of Neurophysiology, 28, 1029–1040.

Wilson, H. R. (1988). Development of spatiotemporal mechanisms in infant vision. Vision Research, 28, 611–628.

Wilson, H. R. (1993). Theories of infant visual development. In K. Simons (Ed.), Early visual development: Normal and abnormal (pp. 560–572). New York: Oxford University Press.

Youdelis, C., & Hendrickson, A. (1986). A quantitative and qualitative analysis of the human fovea during development. Vision Research, 26, 847–855.