12 Neural Limitations on Visual Development in Primates

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Newborn primates see poorly. Their visual capacities improve over time, with a course that varies somewhat depending on the measure used to define visual function and the species studied. Many common measures of vision reach adult levels by the age of about 1 year in macaque monkeys and about 5 years in humans; during the period of maturation, performance typically improves roughly 10- to 30-fold. Figure 12.1 caricatures the effect on vision of two of these measures, spatial resolution and sensitivity to spatial contrast. The panel on the left shows a cityscape as seen by an adult, whereas the panel on the right shows the same scene transformed to represent the view of a newborn infant. The "infant view" has been spatially lowpass-filtered (blurred) and reduced in contrast.

Figure 12.2 shows developmental measurements of spatial resolution (Kiorpes, 1992a; Movshon and Kiorpes, 1988) and contrast sensitivity (Boothe et al., 1988) taken from macaque monkey infants. Figure 12.2*A* shows grating activity data from a group of young monkeys tested cross-sectionally; Figure 12.2*B* shows a series of contrast sensitivity functions measured longitudinally in two representative individual animals. Figure 12.2*B* emphasizes that different animals develop at different rates, so in Figure 12.2*C* we show the range of sensitivity and resolution values measured across a population of six monkeys. Both resolution and sensitivity develop smoothly over the first 6 to 12 months of life. These functions mature somewhat more rapidly when measured electrophysiologically using a visual evoked potential (VEP) technique in monkeys (Skoczenski et al., 1995) and humans (Kelly et al., 1997; Norcia et al., 1990; Chapter 13; see also Peterzell et al., 1995). This discrepancy between techniques is not surprising given that the VEP signal arises from the summed activity of visual cortical neurons. As we discuss later, neurons in infant visual cortex are considerably more mature than behavior would suggest.

We want to understand the processes that limit visual development. In the first part of this chapter we will consider what aspects of visual system organization and function limit performance in newborn infants, and what factors develop to permit attainment of adult level of visual performance. We are also interested in the modifiable mechanisms that are responsible for the altered visual development that occurs when normal vision is disrupted, and in the second part of the chapter we will explore the neural factors responsible for this behavioral plasticity.

Visual input

Many aspects of the eye and the optical and retinal elements involved in the initial encoding of the visual stimulus improve postnatally. The macaque eye grows by about 40% from infancy to adulthood, increasing the magnification of the retinal image (Blakemore and Vital-Durand, 1986a; Williams and Boothe, 1981). The quality of the eye's optics improves over the same span (Williams and Boothe, 1981), increasing the resolution and contrast of the retinal image. Even in the absence of neural changes, the increased retinal magnification would cause a proportionate improvement in visual resolution as long as retinal sampling was held constant. The optical changes are less likely to be important for infant vision, as they primarily affect spatial frequencies well beyond the behavioral resolution limit at any age. So optical factors seem unlikely to account for more than about a 40% change in visual resolution. Retinal changes, however, may be more significant.

Hendrickson and her colleagues have shown that the morphology and distribution of cone photoreceptors undergo marked changes after birth in both humans and monkeys (Hendrickson and Kupfer, 1976; Hendrickson and Yuodelis, 1984; Packer et al., 1990; Yuodelis and Hendrickson, 1986). The foveal concentration of cones that is characteristic of adult retinae is much less marked in neonates; during development, cones migrate toward the center of the fovea. Figure 12.3*A* shows this effect in data from five macaque monkeys aged 1 week to adult. The data in Figure 12.3*A* are plotted in terms of units of visual angle, so they incorporate both the effects of retinal changes and the effects of eye growth (which act in the opposite direction to the increase in retinal cone density created by migration). The combination of these factors changes the linear sampling density of the foveal cone mosaic by about a factor of 3 from 1 week to adulthood. This change is captured in Figure 12.3*A* by plotting the Nyquist frequency of the retinal

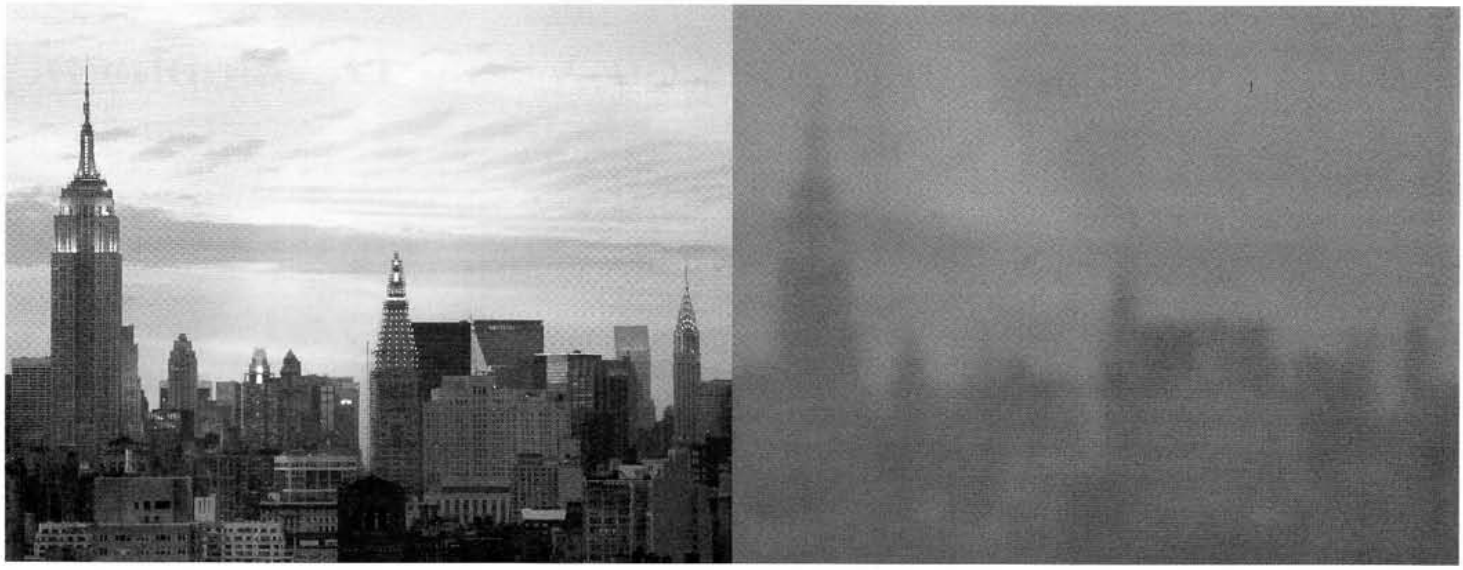

FIGURE 12.1. Simulation of the visual worlds of an adult and young infant primate. To create the simulated image on the right, the image on the left was convolved with a Gaussian, the σ of which was 1°; the image contrast was reduced by a factor of 5. The angular width of the view shown is approximately 10°.

mosaic, the highest spatial frequency that can be accurately reconstructed from samples spaced like foveal cones; this value grows from about 18 cycles/degree at 1 week to about 55 cycles/degree in adulthood. Comparing these values with the behavioral measurements of resolution in Figure 12.2*A* shows that in no case does the spacing of foveal cones seem to impose an important limit on visual resolution. Figure 12.3*A* shows that much of the change in foveal cone density takes place by 4 weeks of age in macaques, but the period over which the photoreceptor array matures to its final adult levels is still somewhat unclear. Peak cone density is approximately 75% of adult density by 6 months of age in monkeys, and only about 50% of adult density by 4 years of age in humans (Hendrickson, 1992, 1993).

While photoreceptor migration is taking place, the structure of individual cones is also changing. Initially, their outer segments are short and stubby; but they develop over time to achieve the elongated, slender morphology of adult photoreceptors. This maturation permits the outer segment to capture light efficiently; in the immature retina, a far higher fraction of incident quanta fails to be absorbed by photopigment than in the adult retina (Banks and Bennett, 1988; Brown et al., 1987). Foveal cone outer segments appear generally adult-like by 12 weeks of age in monkeys and 15 months in humans; however, elongation of outer segments continues over the first year in monkeys and beyond 4 years in humans (Hendrickson, 1992, 1993).

The effects of such diverse factors as changes in the size and optical quality of the eye and changes in the morphology and distribution of receptors are critical for the performance of central visual mechanisms, but can be difficult to work out intuitively. They can conveniently be analyzed with the theory of the "ideal observer" (Geisler, 1984, and Chapter 52, Ideal Observer Analysis). An ideal observer model uses the properties of optics and early visual elements to calculate ideal performance given just the early limitations; the cascade of factors is schematically shown in Fig. 12.3*B*. The ideal observer simulates each of the early steps in seeing from the incidence of light at the cornea to its absorption and representation by the photoreceptor array. The ideal observer is internally noise-free; its performance is limited only by the Poisson fluctuations in the number of photons absorbed by photoreceptors. As such, it is not a model of the nervous system; rather, it simulates the performance of a perfect nervous system limited only by the optical and photoreceptor apparatus available. It therefore provides an objective benchmark against which the performance of real, imperfect observers can be measured.

Following the work of Geisler (1984) and Banks and Bennett (1988), we created an ideal observer model for the infant macaque monkey and used it to compare real and ideal performance (Kiorpes et al., 2000b). We modeled ideal performance at three ages: 1 week, 4 weeks, and 24 weeks. To make as accurate a model as possible, we made as many measurements as possible from the same macaque species from which the behavioral data were drawn. The key parameters for the model at the different age points are listed in Table 12.1. The photoreceptor and cone density data and pupil diameters were measured directly from *Macaca nemestrina* monkeys; the other values were taken or estimated from the literature. The structure of the ideal observer model is shown in Figure 12.3*B*. To determine contrast threshold for each of a set of stimulus conditions chosen to be

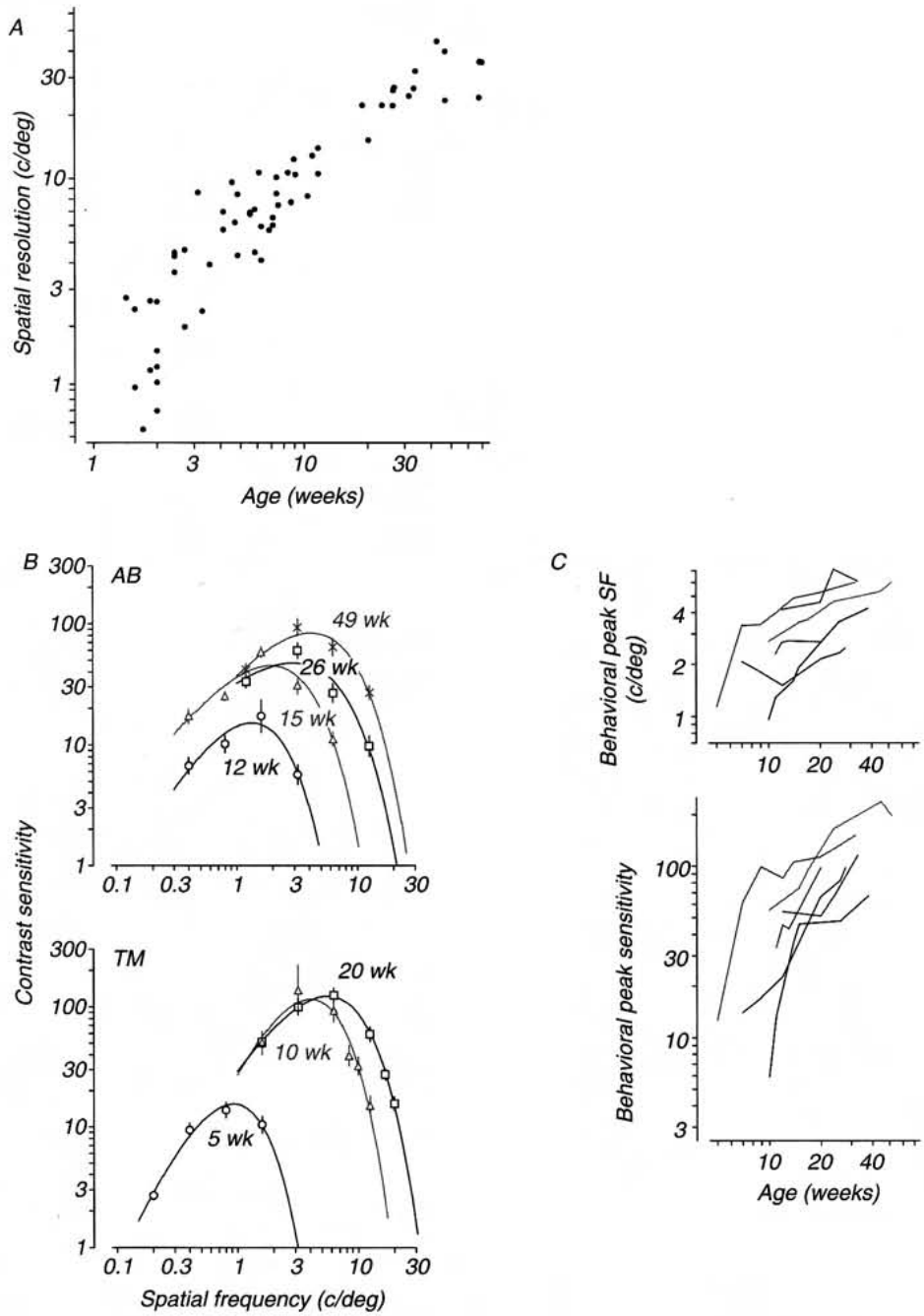

FIGURE 12.2. The development of spatial vision in infant macaque monkeys. *A,* Spatial resolution data from a set of 17 normal infant macaques (taken from Kiorpes, 1992a; Movshon and Kiorpes, 1988). The measure of spatial resolution was grating acuity, the highest spatial frequency at which a grating could reliably be distinguished from a uniform field of the same luminance. Animals younger than 16 weeks were tested using a forced-choice, preferential looking technique. Older animals were tested in a standard two-choice operant discrimination task. *B,* Spatial contrast sensitivity functions, measured using operant techniques, in two infant macaques at a range of ages (as indicated) (data from Boothe et al., 1988). Error bars indicate the standard error of the mean threshold determined by Probit analysis. *C,* The range of rates of development of spatial contrast sensitivity in six infant macaques. Each line represents the course of contrast sensitivity development in an individual monkey. The two plots indicate the horizontal and vertical positions of the peaks of the measured contrast sensitivity functions. (Redrawn from Movshon and Kiorpes, 1988.)

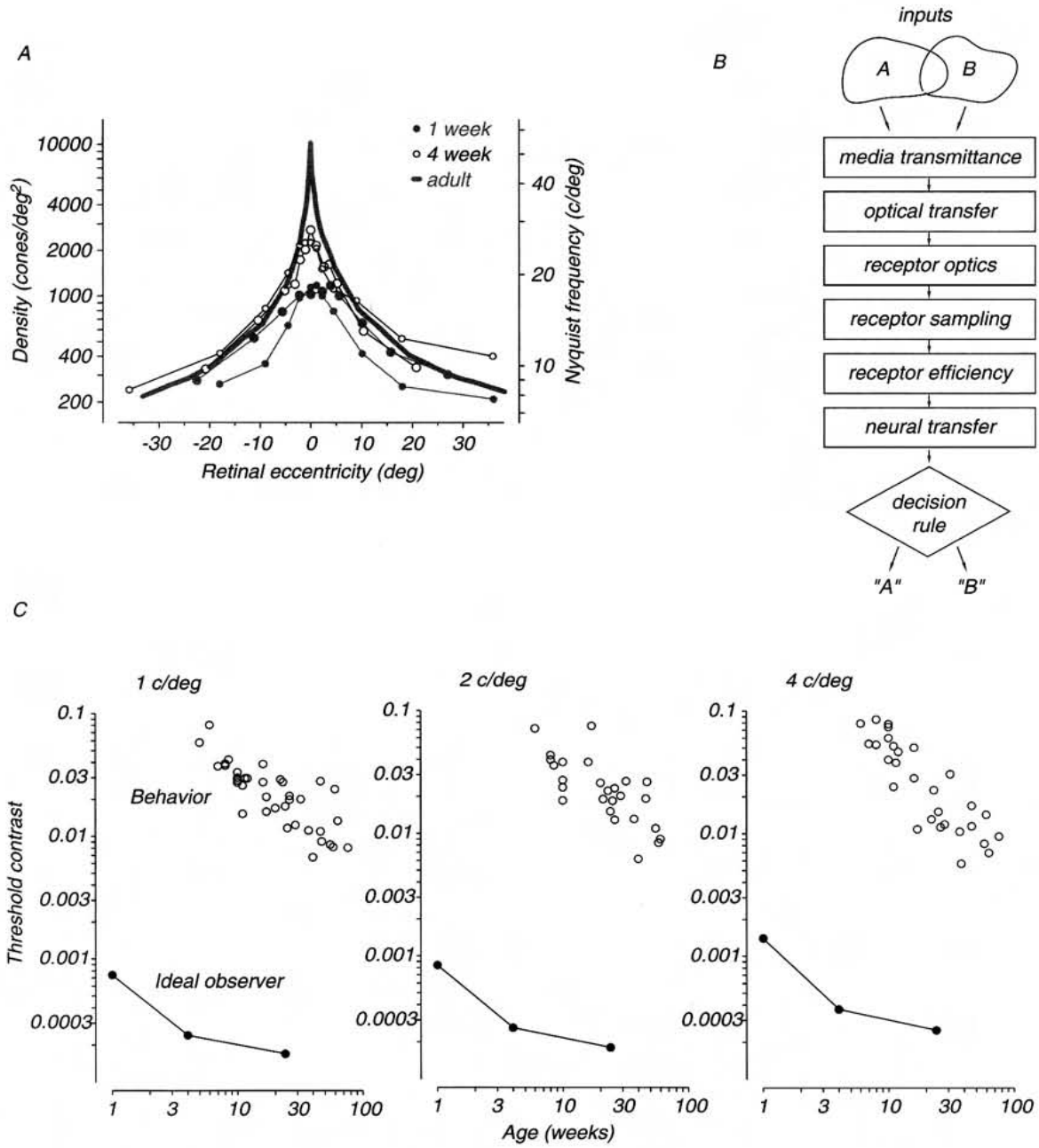

FIGURE 12.3. Assessing the influence of retinal development on spatial vision. *A*, Cone density along the horizontal meridian of the visual field in five macaque monkeys, aged 1 week to adult. Density is expressed on the left ordinate in units of areal density in visual space, and on the right ordinate as the Nyquist frequency of a perfect hexagonal array. The Nyquist frequency is the highest spatial frequency that can be accurately reconstructed from a given set of sample points. (Unpublished measurements by C. Henry, M. J. Hawken, J. A. Movshon, and L. Kiorpes). *B*, A schematic illustration of the stages of analysis in an ideal observer model (after Geisler, 1984). See text for details. *C*, Comparison of contrast thresholds for macaques and for the macaque ideal observer model (Kiorpes et al., 2000b). Simulated thresholds for the ideal observer are shown as solid symbols connected by lines. Real thresholds, measured behaviorally in 13 macaques, are shown as open symbols (data from Kiorpes and Movshon, 1998).

TABLE 12.1

Key parameters for macaque ideal observer simulations

	1 Week	4 Weeks	24 Weeks
Line spread function width at half height (min arc)	2.25	1.69	1.33
Pupil diameter (mm)	4.8	5.3	6
Posterior nodal distance (mm)	10.91	11.84	13.52
Cone density (cone/mm^2)	37268	110374	202905
Outer segment diameter (μm)	1.94	2.09	1.79
Outer segment length (μm)	13.6	31.8	40.0

comparable to conditions used to gather data from monkeys, we simulated responses to a stimulus and a blank (inputs A and B). We filtered the inputs by the transfer function for the eye, sampled the stimulus using the measured photoreceptor mosaic, incorporated Poisson photon noise, computed the likelihood of a stimulus or blank, and chose the more likely ("A" or "B"). We repeated this process 1000 times for each condition, compiled the resulting data into psychometric functions, and analyzed them exactly as we analyze behavioral data. The results of these simulations for gratings of three spatial frequencies at the three chosen ages are shown in Figure 12.3*C* as filled points connected by lines. Comparable behavioral measurements are shown as isolated open symbols.

The first point to note is that the absolute sensitivity of the ideal observer is at least 100 times higher than the monkeys'; in other words, the animals' quantum efficiency was no better than 1%. This value is comparable to that determined in humans (Banks and Bennett, 1988; Geisler, 1984; Pelli, 1990) and reflects the fact that observers do not seem to be capable of using all the information available in the pattern of photoreceptor quantum absorptions. However, ideal observer simulations are nonetheless useful for comparing *relative* performance, here given by the relative shapes of the trends for real and ideal observers. Developmental changes in sensitivity shown by the ideal observer are largely confined to the first 4 postnatal weeks, whereas the bulk of the change measured behaviorally takes place after 4 weeks. Therefore, very little of the change in contrast threshold beyond 4 weeks can be accounted for by changes in the visual periphery in macaque monkeys. Banks and Bennett (1988) performed a similar analysis in human infants, arguing that peripheral factors play a somewhat more prominent role in the development of contrast sensitivity. Our conclusions differ from theirs for two reasons: first, photoreceptors in infant monkeys are somewhat more mature than in human infants; second, we used a more realistic calculation to estimate the way that photopigment absorptions depend on outer segment morphology. In any case, our conclusions and Banks and Bennett's differ only in detail, and suggest that the great bulk of postnatal development in contrast sensitivity depends on neural factors and not on optical and retinal maturation.

Subcortical visual structures

Largely for technical reasons, little is known about the development of the physiological organization of retinal ganglion cell receptive fields. In cats, Rusoff and Dubin (1977) reported the presence of adult-like center responses within a week of eye opening in kittens; however, receptive field surrounds were weak compared to adult surrounds. Because the optical quality of the kitten eye is poor (Bonds and Freeman, 1978), the maturity of retinal neural circuits is not easy to assess from these data. There have been no studies of ganglion cell receptive fields in infant monkeys.

The primary recipients of information from the retina, the lateral geniculate nucleus (LGN) and superior colliculus (SC), have been studied in infant primate, as has the nucleus of the optic tract (NOT), which receives a small but direct input from the retina (Kourouyan and Horton, 1997; Telkes et al., 2000).

The organization of the optokinetic system, whose visual inputs come through the NOT and the dorsal terminal nucleus of the accessory optic system, is qualitatively adult-like between 5 and 12 weeks after birth (Distler et al., 1999), but there is little quantitative information available on neuronal sensitivity or receptive field organization in these structures. The functional organization and receptive field properties of neurons in newborn monkey SC are remarkably mature (Wallace et al., 1997). Topographic organization is adult-like in the neonate, as are many receptive field properties. However, receptive field sizes—particularly for neurons with receptive fields near the fovea—are larger in the newborn than in the adult. Visual responses are also more sluggish throughout the SC, and visual latencies are significantly longer than in adults. Wallace et al. (1997) have argued that the retinotectal input is the primary determinant of SC response properties in infants, with little contribution from corticotectal projections. They have suggested that the immaturities of SC response properties may be explained by postnatal maturation of retinotectal myelination and changes in the retina itself. This conclusion is based on the assumption that the properties of cortical receptive fields in infants are quite immature; however, as documented later in this chapter, neurons in the primary visual cortex are surprisingly mature in infants. Thus it is equally plausible that the visual responses of SC neurons in infants primarily reflect the properties of afferent input from cortex, as they do in adults (Schiller et al., 1974).

The development of receptive field properties of LGN cells in Old-World primates has been studied more extensively than SC and NOT (Blakemore and Vital-Durand,

1986a; Hawken et al., 1997; Movshon et al., 1997). Like SC neurons, LGN cells in newborn monkeys often respond sluggishly to visual stimuli, and they have longer latencies than are found in adults. Blakemore and Vital-Durand (1986a) have found visual latencies to be mature by about 10 weeks of age. There is an overall improvement in visual responsiveness and spatial resolution in both parvocellular and magnocellular layers of the LGN over the first postnatal year in macaque monkeys, and Blakemore and Vital-Durand reported a sevenfold improvement in the visual resolution of LGN cells over this period. Moreover, Hawken and colleagues (1997) have demonstrated that the overall envelope of neuronal contrast sensitivity shows a profile much like that of behavioral development, with contrast sensitivity and spatial resolution developing concurrently. They found an early rapid development of contrast sensitivity over the first 2 months, followed by a more gradual progression to adult levels by about 8 months of age. Taken together, these studies suggest that the development of LGN spatial properties matches behavioral development, and that the properties of LGN cells or their afferents set an important limit on vision during development (Movshon and Kiorpes, 1993). Our own results (Movshon et al., 1997), however, present a somewhat different picture.

To compare behavioral development to physiological changes in LGN responses, we recorded from LGN cells in 1-week-, 4-week-, and 24-week-old macaque monkeys, and made quantitative measurements of their responses to spatial targets. For comparison with behavioral measurements, we concentrated on two aspects of LGN responses: sensitivity to contrast and sensitivity to spatial frequency. The results are shown in Figure 12.4, which places the data from the LGN in direct comparison with the behavioral data from Figure 12.2*C*. The shaded range and left-hand ordinates on each plot represent the changes in the position of the peak of the contrast sensitivity function (CSF) measured behaviorally. The symbols and right-hand ordinates represent the results of our LGN recordings. Each symbol represents the geometric mean (± the standard deviation of the distribution) of measurements from our whole population of LGN cells. The filled symbols show data from magnocellular neurons, whereas the open symbols represent data from parvocellular neurons. The upper plot shows values of the characteristic spatial frequency—this is the spatial frequency at which the response of the receptive field (RF) center mechanism, inferred from a fitted difference-of-Gaussians model, falls to $1/e$ of its peak (Enroth-Cugell and Robson, 1966; Linsenmeier et al., 1982). The lower plot shows values of responsivity, the slope of the initial linear segment of the contrast-response function, measured with optimal drifting grating targets (Linsenmeier et al., 1982). There is an improvement in both the sensitivity and spatial resolution of LGN cells between birth and 6 months, but a comparison

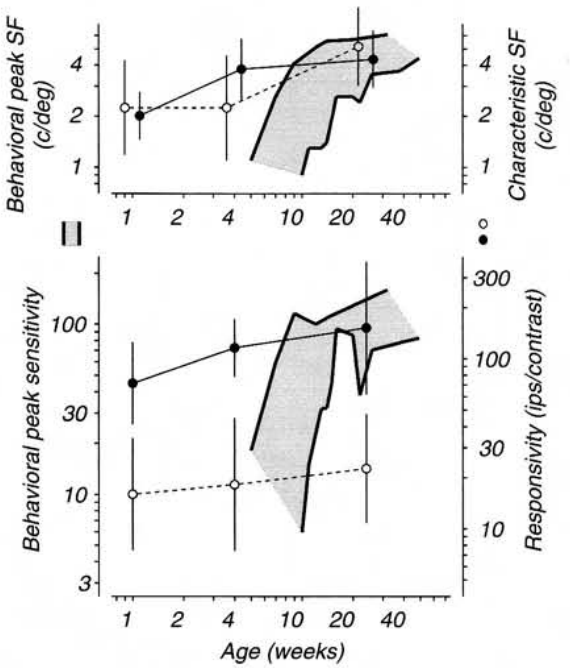

FIGURE 12.4. Comparison of behavioral contrast sensitivity development with the development of spatial contrast sensitivity in LGN neurons. The gray zone in each part of the figure represents (using the left-hand ordinates) the range between the slowest and fastest development in a population of six monkeys tested longitudinally (Boothe et al., 1988). The upper plot shows the development of the spatial frequency at which peak contrast sensitivity was observed; the lower plot shows the development of the peak contrast sensitivity value. The symbols and lines represent (using the right-hand ordinates) population data obtained from 355 LGN neurons recorded from 10 monkeys aged 1 to 24 weeks. Each symbol represents the geometric mean of the measured values of characteristic spatial frequency and responsivity in impulses per second (IPS) for parvocellular (*open circles*) and magnocellular (*filled circles*) neurons (see text for details). The error bars indicate ±1 SD to convey a sense of the span of the underlying distribution. Note that the right- and left-hand ordinates are arbitrarily shifted so that the data sets meet at adult levels; no absolute relationship is implied.

of the physiological and behavioral data shows that the magnitude of the change is far too small to account for the observed behavioral changes. Moreover, although the physiological changes are, by most measures, largely complete by the age of 4 weeks, most behavioral changes occur later. We conclude that developmental changes in LGN response properties—and, by inference then, in the retinal afferents to LGN—are modest and do not account for behavioral change. In fact, the changes in LGN cell properties are similar to those expected of an ideal macaque observer (Fig. 12.3*C*), which as we have discussed is also an inadequate account of behavioral development. Our results differ from those presented in earlier reports (Blakemore and Vital-Durand, 1986a; Hawken et al., 1997) primarily in that we found far more adult-like spatial receptive fields in our youngest animals than they did. The difference may be

attributable to the different anesthetic techniques used. (Our studies used opiate anesthesia, whereas those of Blakemore and his colleagues used a combination of N_2O and barbiturates.)

Visual cortex

The primary visual cortex (V1) has long been known to show considerable postnatal modifiability by visual experience; moreover, the development of visual cortical response properties is seriously disrupted by visual deprivation. There is compelling evidence that normal vision is required for normal cortical development, and that abnormal vision can distort cortical development. This has led to the widespread view that the visual cortex is very immature at birth and that its development is actively "instructed" by visual input. An alternative view is that visual experience is not required to instruct development, but is merely "permissive," allowing the normal sequence of developmental events to take place (for reviews, see Movshon and Kiorpes, 1990; Movshon and Van Sluyters, 1981). A crucial piece of evidence that distinguishes these views is the status of the visual cortex in very young animals. If, as initially claimed, the visual cortex of neonates is responsive to visual stimuli and contains at least some neurons with adult-like selectivity (Hubel and Wiesel, 1963), it would seem unlikely that visual experience served as a strong instructor for development. If, however, the neonatal visual cortex contains few neurons with adult-like responses, the argument for a strong active role for visual experience in visual development is much more plausible (Blakemore and Van Sluyters, 1975; Pettigrew, 1974). This debate initially centered on development in kittens, but the same differences of view have been recapitulated in the literature on development in monkeys (Blakemore, 1990; Blasdel et al., 1995; Chino et al., 1997; Movshon and Kiorpes, 1993; Wiesel and Hubel, 1974).

To revisit these questions and to explore the relationship between the development of physiological response properties of V1 cells and behavioral visual development, the authors recorded from cells in macaque monkeys, aged 1 week, 4 weeks, 16 weeks, and adult (Movshon et al., 1999, 2000), and made quantitative measurements of the animals' responses to spatial stimuli. We studied a variety of response properties at each age point, including receptive field size and spatial frequency tuning, selectivity for orientation and direction of motion, and selectivity for stimulus area as an indication of the strength of receptive field surrounds. Figure 12.5 shows the development of six derived measures that summarize these developmental data. In each case, the algebraic or geometric mean value for the measure is given (± the standard deviation of the distribution; details of the analyses are given in the figure legend).

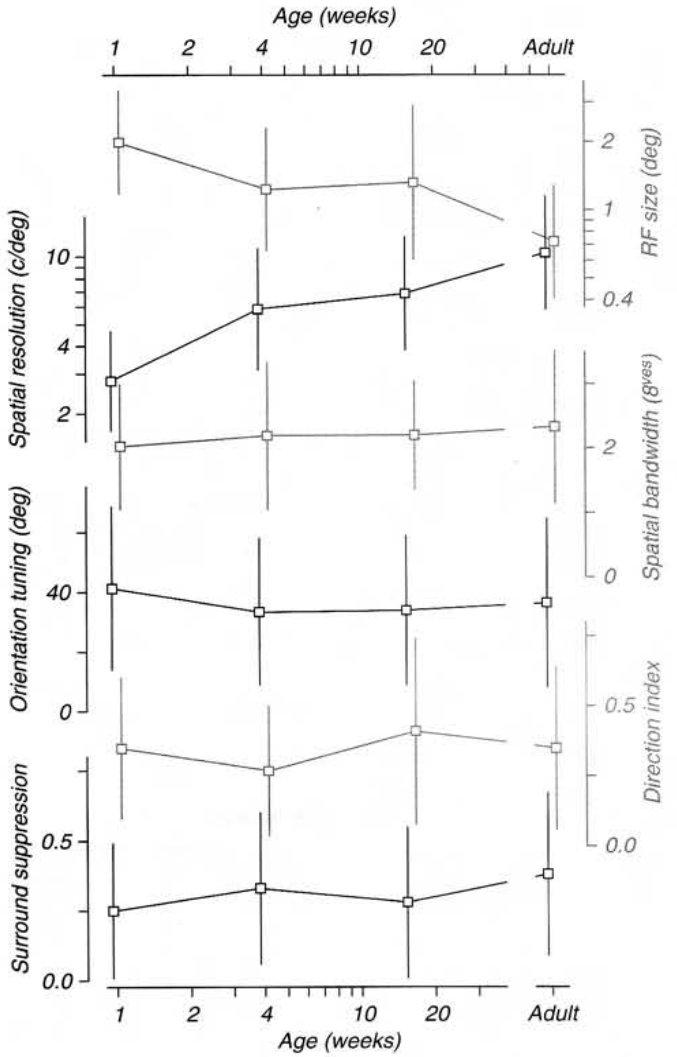

FIGURE 12.5. Development of the receptive field (RF) properties of V1 neurons in macaques (from Movshon et al., 1999, 2000). Each panel of the plot represents the development of a particular receptive field property in a study of 453 V1 neurons representing the central 5° of the visual field, recorded from 11 animals at the indicated ages. Each point represents the mean or the geometric mean, as appropriate, of the values measured for all neurons recorded at a particular age; the error bars indicate ±1 SD to convey a sense of the span of the underlying distribution. In sequence from the top, the parameters displayed are *receptive field size*, defined as the size of an otherwise optimal patch of grating that elicited at least 95% of the maximum response (Cavanaugh et al., 2002); *spatial resolution*, defined as the highest spatial frequency at which the cell gave a response of at least 10% of its maximum; *spatial bandwidth*, defined as the ratio between the highest and lowest spatial frequencies giving at least half-maximal response, expressed in octaves; *orientation tuning*, defined as the change in orientation from the peak that causes the response to fall by one half; *direction index*, defined as $1\text{-}np/p$, where p is the response to an optimal grating moving in the preferred direction and np is the response to the same grating moving 180° from the preferred; *surround suppression*, defined as the fractional reduction in response resulting from the enlargement of an optimal-size patch of grating to cover the full screen (Cavanaugh et al., 2002).

The two upper graphs in Figure 12.5 show the development of the spatial scale of V1 receptive fields by plotting receptive field size and spatial resolution for grating stimuli as a function of age. Both measures suggest that, from the age of 1 week to adulthood, receptive fields shrink on average by about a factor of 3, a value comparable to that seen for similar measures in LGN cells (see Fig. 12.4). The four lower graphs in Figure 12.5 show the development of four indices of receptive field selectivity. These show that, with remarkable consistency, the spatial structure of V1 receptive fields remains constant during development. None of the parameters that measure receptive field structure—selectivity for spatial frequency and orientation, selectivity for direction of movement, or strength of neuronal surround suppression—varies at all with age. In some other respects, V1 neuronal properties are immature in infants. For example, peak response magnitudes and sensitivity to rapid stimulus change are substantially less in 1-week-old animals than in adults; however, the visual effects of these changes are, to some degree, ameliorated by the curious fact that responses in 1-week-old animals are substantially more reliable than in adults (Rust et al., 2002).

The simplest picture that emerges from these data is that the receptive fields of visual cortex neurons gradually reduce in size during development, without changing any of their other spatial properties. The degree to which they do this seems to be identical to the rate at which the receptive fields of LGN cells change size and the spacing between foveal cones decreases, but this is substantially slower than the rate at which behavioral changes take place. Figure 12.6*A* compares the evolution of several spatial properties during development. The graph plots visual acuity (from Fig. 12.2*A*), along with the development of spatial resolution of LGN and V1 cells and with the development of the cone mosaic as indicated by the Nyquist frequency. Changes in behavioral acuity are more extensive than changes in any of the neural properties plotted, and all these neural properties seem to develop in step, as evidenced by their parallel progressions across the plot.

The comparison shown in Figure 12.6*A* suggests that the changes in V1 spatial properties simply follow changes at the periphery. One explanation, articulated by Wilson (1988), is illustrated in Figure 12.6*B* (see also Brown et al., 1987; Peterzell et al., 1993; and Peterzell and Teller, 1996). Cortical receptive fields can be considered to be a map of connections directly back to the mosaic of cones whose signals drive them. As noted earlier, cones in infant retina are spaced widely (*top left*), and the receptive fields of cortical neurons (given in cross-section, *middle*) are correspondingly broad. This corresponds to a selectivity for relatively low spatial

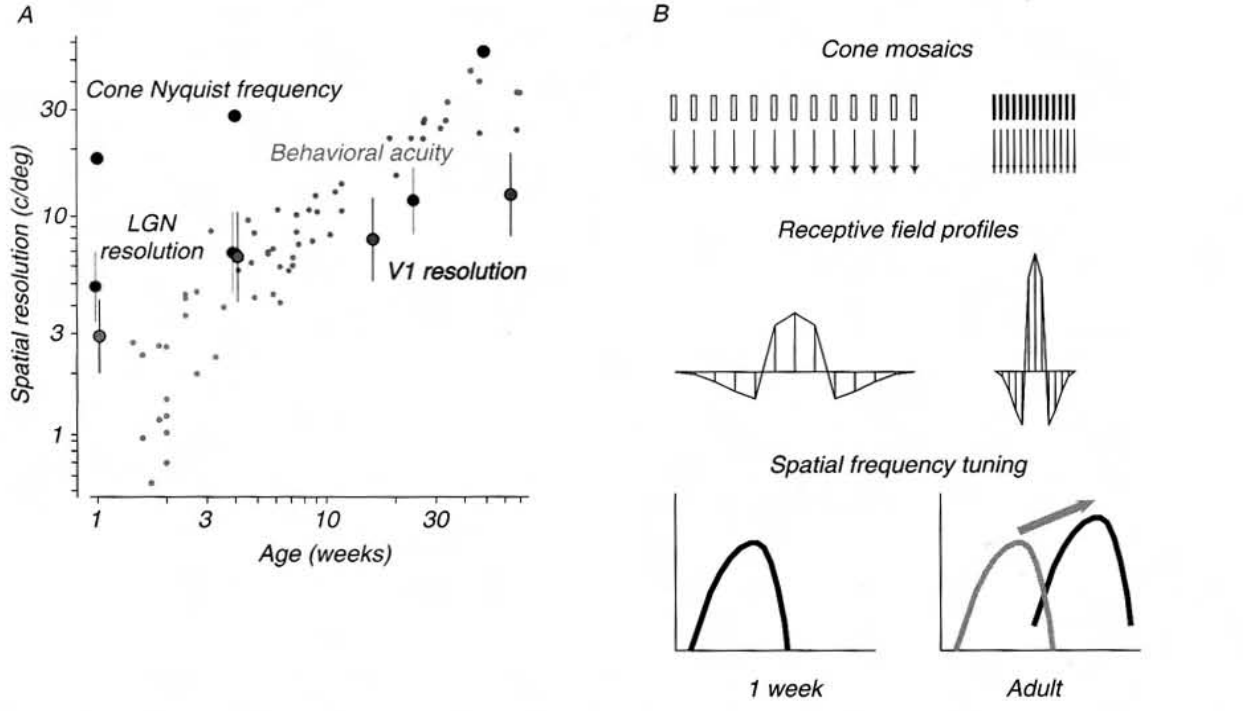

FIGURE 12.6. Relative development of different elements of spatial vision. *A*, The development of grating acuity (from Fig. 12.2*A*) is compared to three measures of neural development: Nyquist frequency (taken from the peak values of the cone density distributions in Fig. 12.3*A*); the spatial resolution of neurons in the LGN (average of P and M cells, from Fig. 12.4); and the spatial resolution of neurons in V1 (from Fig. 12.5). *B*, A conceptual account of how cortical receptive field development would result from migration of cones; see text for details.

frequencies (*bottom*). Let us suppose that cortical receptive fields—*as defined by their connections to cones*—are unchanged during development. Now as the cones migrate toward the center of the fovea and become more tightly packed (*top right*), cortical receptive fields shrink in proportion (*middle right*), and neurons consequently develop a preference for higher spatial frequencies without changing the shape of their tuning curves (*bottom right*). Because of the changes in cone outer segment morphology (discussed earlier), the sensitivity of individual cones increases slightly during development, leading to a slight increase in contrast sensitivity, which, in turn, leads to the slight upward shift in the tuning curve (*bottom right*). Our finding that the resolution of V1 and LGN cells change at a rate similar to the change in peak density of cone photoreceptors, combined with the complete stability of neuronal selectivity for orientation and spatial frequency during development (see Fig. 12.5), suggests that cortical receptive field properties passively follow the retina as it develops. We earlier developed the argument that retinal changes are too small and happen too early in development to explain behavioral development; it follows, then, that postnatal changes at the level of the visual cortex also fail to account for the normal course of behavioral development.

The results of direct investigation of neonatal monkey cortex argue against the notion that visual experience is strongly instructive and instead support the idea that normal visual experience is simply permissive to normal visual development. The other important piece of the puzzle is to identify what specific changes take place in the face of abnormal visual experience.

Abnormal visual experience and amblyopia

It seems paradoxical that V1 receptive field development passively follows peripheral organization, which is not influenced by visual experience in primates (Blakemore and Vital-Durand, 1986b; Hendrickson et al., 1987; Levitt et al., 2001; Movshon et al., 1987), whereas decades of evidence has accumulated for experience-dependent plasticity in V1. Most studies of the effect of visual experience on development in primates have used monocular or binocular deprivation to manipulate visual experience (Baker et al., 1974; Blakemore, 1990; Blakemore and Vital-Durand, 1986b; Horton, 1984; LeVay et al., 1980; von Noorden and Crawford, 1978; Wiesel, 1982; Wiesel and Hubel, 1974). This kind of deprivation typically devastates spatial vision, reducing contrast sensitivity and resolution so severely that in some cases blindness results (Harwerth et al., 1983; von Noorden, 1973; von Noorden et al., 1970). The most obvious consequence of monocular deprivation is a dramatic loss of influence of the deprived eye over cells in the visual cortex, evident physiologically and anatomically, even when the deprivation lasts for as short a period as 1 week. Physiologically, cortical binocularity is lost, and most neurons can be influenced only through the nondeprived eye. Anatomically, there is a nearly complete takeover of deprived eye territory by the nondeprived eye.

The obvious correlation between the loss of cortical influence by the deprived eye and the loss of vision has been interpreted to mean that visual function is determined by the number of cortical neurons influenced by a given eye; changes in this balance during development lead to changes in vision. None of these studies has quantified the spatial, temporal, or contrast response properties of deprived cortex, as there are few responsive cells to study. It may be that experience-dependent plasticity in primate V1 is restricted to the balance of inputs from the two eyes, and does not affect the spatial properties of individual neurons. But data on the effects of binocular deprivation suggest that cortical receptive field properties can be altered by experience (Blakemore, 1990). We wanted to establish whether cortical receptive field properties could be influenced by abnormal visual experience that was less radical than complete form deprivation, and we have therefore studied visual behavior and cortical organization in animals raised in a way that creates more modest and experimentally tractable visual deficits.

Visual disorders that occur in early childhood, such as strabismus (crossed eyes) and anisometropia (monocular defocus), are associated with *amblyopia*, literally meaning "blunted" vision. Visual acuity and contrast sensitivity in the amblyopic eyes of monkeys and humans are reduced, but not nearly so severely as they are following visual deprivation (Blakemore and Vital-Durand, 1981; Harwerth et al., 1983; Kiorpes, 1992b, 1996, 2001; Kiorpes et al., 1987; Kiorpes et al., 1993; Kiorpes and Movshon, 1996; Levi and Carkeet, 1993; Smith et al., 1985). Figure 12.7*A* shows the development of spatial resolution in each eye of a population of strabismic monkeys (Kiorpes, 1992b) and compares it to the development of resolution in normal monkeys tested monocularly. Resolution in the fellow (nondeviating) eyes develops normally, but resolution development in the strabismic eyes lags. Figure 12.7*B* illustrates losses in contrast sensitivity for three monkeys, each made experimentally amblyopic by a different technique. Normally, contrast sensitivity is similar for both eyes of an individual (*upper left panel, TJ*). The other three panels show contrast sensitivity for each eye in monkeys in which the development of amblyopia followed experimentally produced strabismus, blur created by extended wear of a defocusing contact lens (anisometropia), or blur created by chronic instillation of atropine. Contrast sensitivity functions for the amblyopic eyes, regardless of the origin of amblyopia, are shifted to lower sensitivity and lower spatial frequencies. If we compare the functions obtained from amblyopic eyes with functions from young normal animals (Fig. 12.2*B*). There is

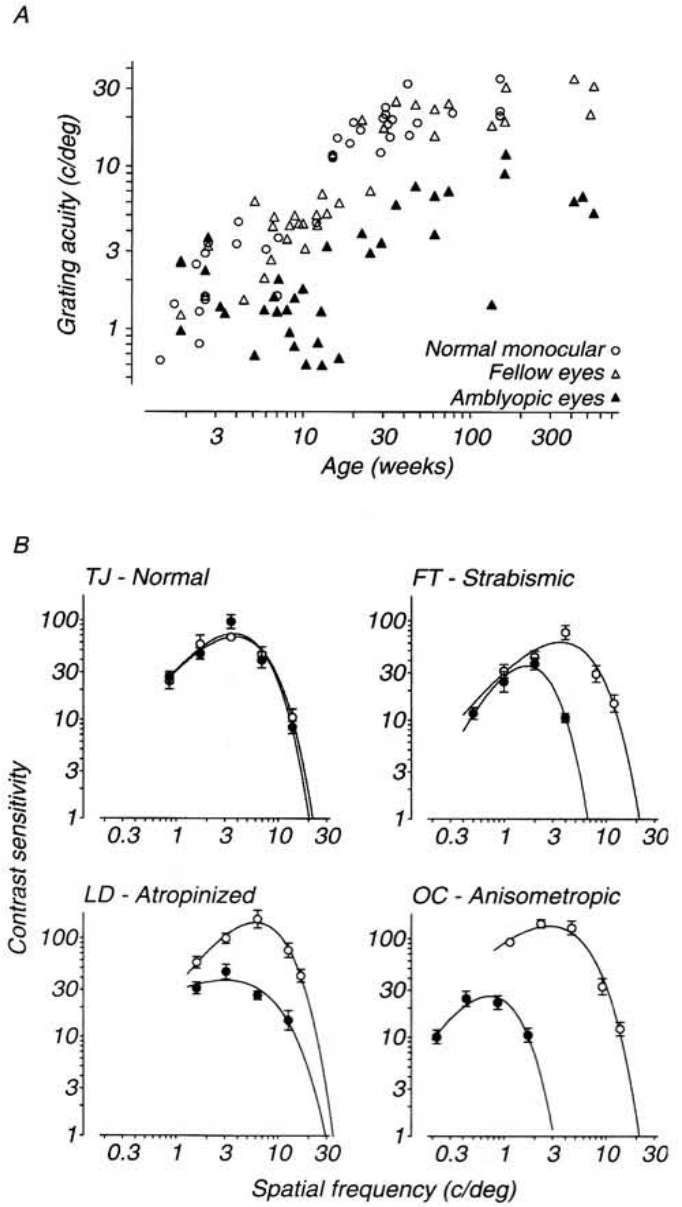

FIGURE 12.7. Spatial vision in amblyopic monkeys. *A*, Spatial resolution data obtained longitudinally from a set of six strabismic infant macaques (data from Kiorpes, 1992b). Data taken monocularly from each eye of the strabismic animals (triangles) are compared with monocular data taken from normal animals (circles; compare to Fig. 12.2*A*). The measure of spatial resolution was grating acuity, the highest spatial frequency at which a grating could be distinguished reliably from a uniform field of the same luminance. Animals younger than 16 weeks were tested using a forced-choice, preferential looking technique. Older animals were tested using a standard two-choice operant discrimination task. *B*, Monocular spatial contrast sensitivity functions for each eye of four macaque monkeys (one normal and three amblyopic), measured using operant techniques (data from Kiorpes et al., 1987, 1998).

a distinct similarity; this similarity is also evident when other visual functions are measured (Kiorpes, 1992b; Levi and Carkeet, 1993).

To explore the neuronal correlates of amblyopia, we analyzed the responses of V1 neurons in amblyopic monkeys (Kiorpes et al., 1998; Movshon et al., 1987). We studied selectivity for orientation, spatial frequency, drift rate, and contrast response properties of neurons driven by each eye, as well as binocular organization. In all types of amblyopic monkeys, there was a disruption of the binocular organization of V1 neurons. Figure 12.8*A* presents V1 eye dominance distributions from normal monkeys and from four groups of monkeys with amblyopia. Monocularly deprived monkeys were found to show the most marked loss of input from the amblyopic eye. The other three groups of amblyopic monkeys each showed substantial losses in binocular neurons, but in none of these groups was there a complete loss of cortical input from the amblyopic eye. Because all the animals in these groups had behaviorally documented amblyopia, this finding indicates that a loss of neurons influenced by the amblyopic eye is not sufficient to account for amblyopia. Thus it is important to evaluate the quality of the visual signals carried by the neurons driven by each eye.

In strabismic and anisometropic amblyopia, the spatial organization of receptive fields driven by the amblyopic eye is degraded. The distributions of preferred spatial frequency and spatial resolution are shifted to lower spatial frequencies relative to those for cells driven by the fellow eye. However, there is no consistent elevation in contrast threshold for neurons driven by the amblyopic eye. The combined results of two studies (Kiorpes et al., 1998; Movshon et al., 1987) are shown in Figure 12.8*B*, which summarizes and compares the behavioral and physiological findings for contrast sensitivity and peak spatial frequency in amblyopia. In each panel, the measures plotted are the interocular ratios of spatial frequency and contrast sensitivity. For behavior, these values are taken from the peaks of the contrast sensitivity functions (e.g., Fig. 12.7*B*). For physiology, the values are the geometric means of the values measured for populations of neurons driven by each eye. A comparison of the upper two panels shows that the range of behavioral deficits is large, whereas the range of physiological deficits is relatively smaller. Nonetheless, both measures show correlated losses in peak contrast sensitivity and peak spatial frequency. The same data are reorganized in the two lower panels to make a direct comparison of behavioral and physiological losses in peak spatial frequency and peak contrast sensitivity. There is a strong correlation between behavioral and physiological loss for peak spatial frequency ($r = 0.60$), although the physiological deficit is consistently smaller than the behavioral one. The relationship for contrast sensitivity is weaker ($r = 0.37$), and does not achieve statistical

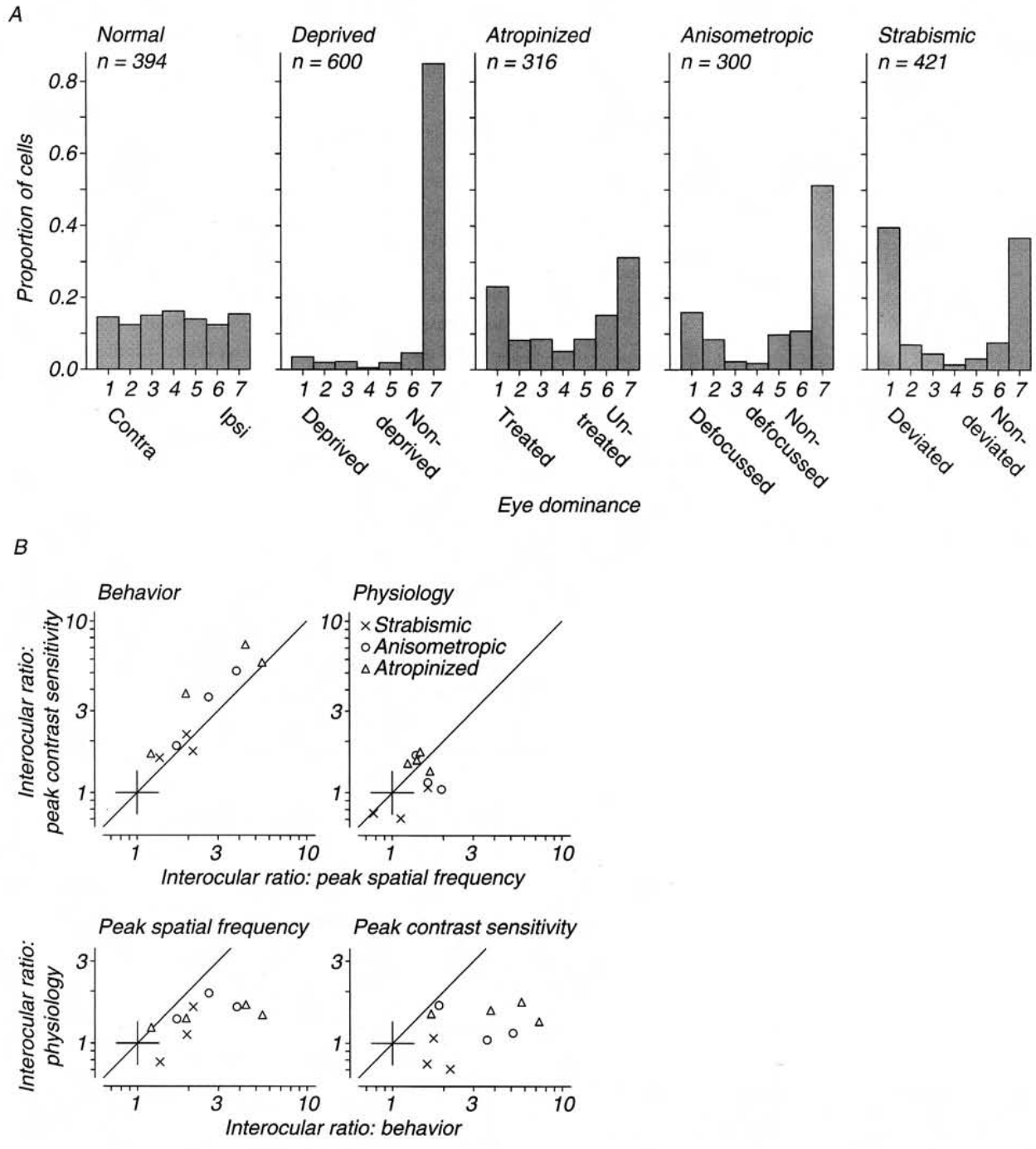

FIGURE 12.8. Physiological measurements of spatial vision in amblyopes. *A*, Distributions of cortical eye dominance obtained from five populations of macaque monkeys. The eye dominance scale is that of Hubel and Wiesel (1962), but only for the normal animals is the eye assignment based on group 1 being contralateral and group 7 being ipsilateral. The distributions for the other four groups are keyed so that the amblyopic eye corresponds to group 1 in all cases. The data for normal subjects and for the three right-hand groups of amblyopes are from Kiorpes et al. (1998) and Movshon et al. (1987). The data for the monocularly deprived animals are from LeVay et al. (1980). *B*, Comparisons of physiological and behavioral data for 10 amblyopic monkeys studied by Kiorpes et al. (1998) and Movshon et al. (1987). Each axis represents the ratio of the indicated performance value between the amblyopic and fellow eye. For behavioral measures, the values compared are the peak spatial frequency and the peak contrast sensitivity from data like those shown in Fig. 12.7*B*. For physiological measures, the values compared are the geometric means of measured values for populations of cells tested monocularly through the amblyopic and fellow eyes.

significance. There was also no consistent effect of amblyopia on overall visual responsiveness, orientation tuning, or temporal tuning.

Thus, neuronal correlates of amblyopia are evident in the spatial properties of cells in V1, but the observed deficits do not fully explain the spatial losses in amblyopia—that is, the physiological losses are relatively small compared to the behavioral ones. A qualitative account of the visual loss in amblyopia might be constructed by combining the losses in spatial sensitivity with the alterations in eye dominance and binocularity (Fig. 12.8*A*), but we are aware of no quantitative model that supports this conjecture.

It is notable that, just as vision in an amblyopic eye resembles the vision of a younger normal eye, so, too, do the properties of cortical neurons driven by the amblyopic eye resemble the properties of neurons driven by a younger normal eye. However, this similarity is unlikely to reflect similar mechanisms in the two cases. We have already argued that the properties of developing cortical neurons are largely determined by the development of the foveal cone mosaic, but there is no reason to believe that retinal development is abnormal in amblyopic animals. LGN cell responses are quantitatively very similar in normal and amblyopic eyes (Blakemore and Vital-Durand, 1986b; Levitt et al., 2001). The disruption of cortical receptive fields in amblyopia must, therefore, result from changes in intracortical or intercortical circuits and not from degraded peripheral inputs. The changes observed are consistent with a broadening and blurring of the structure of cortical receptive fields, reminiscent of the far more extensive changes reported to result from complete binocular form deprivation (Blakemore, 1990). Like our data on V1 development, these results seem to favor a permissive view of the role of the environment in development, but with the added feature that not only visual experience, but *the right kind* of visual experience is required for normal development. In the animals raised with blurred vision in one eye, our experiments can be seen as a selective case of visual deprivation in which cells preferring the highest spatial frequencies are the most penalized by the experience of continuously blurred vision. Perhaps it is only natural that these cells would be the ones most affected, or even lost, resulting in distributions of preferred frequency that are shifted in the way that we have observed (Kiorpes et al., 1998; Movshon et al., 1987). But this account is incomplete—it does not suggest an explanation for the effects of strabismus, which does not cause image blur or the consequent loss of high spatial frequency stimulation.

It seems significant that the relationship between cortical signals and behavioral responses is consistent across development and amblyopia, even if the relationship is quantitatively imperfect. It is therefore natural to wonder about the course of development and the effects of visual experience in cortical areas outside V1.

Extrastriate cortex

We have until now considered the development of and effects of abnormal visual experience on the structure and function of the visual pathway, up to and including the primary visual cortex, V1. But in primates, there is a very extensive collection of cortical areas outside V1, which in aggregate involve about three times as much cortical tissue as V1 (Felleman and Van Essen, 1991). The functional properties of neurons in these areas and their relationship to behavior are a very active focus of study (see, for example, Chapter 34, Ventral and Dorsal Cortical Processing Streams; Chapter 78; Chapter 81; and Chapter 103), yet little attention has been paid to the way that they change during development or after abnormal visual experience. The visual responsiveness of extrastriate areas has been documented using 2-deoxyglucose autoradiography (Bachevalier et al., 1991; Distler et al., 1996). These measurements show that higher cortical areas are relatively delayed in their development compared to V1, and moreover that the development of the ventral "form" areas occurs over a longer time course than the development of dorsal "motion" areas. This general distinction is confirmed by the observation that neurons in inferotemporal visual areas do not appear to be visually responsive until about 6 months of age in macaques, whereas neurons in the dorsal area MT are responsive in much younger monkeys (Rodman et al., 1993). Anatomical experiments suggest that the normal connections of extrastriate cortical areas are probably present around the time of birth, and are organized approximately as in adults (e.g., Barone et al., 1996; Coogan and Van Essen, 1996), although some refinement certainly continues postnatally (e.g., Barone et al., 1995). Indeed, there is some evidence that higher-order areas have exuberant corticocortical connections that are later lost (Rodman and Consuelos, 1994; Webster et al., 1995). Although normal connections are present in infancy, synaptogenesis continues throughout the cortex for many weeks after birth (Rakic et al., 1986), and immunocytochemical studies reveal substantial changes in the distribution of various chemical markers during the first months of life (e.g., Conde et al., 1996; Hendrickson et al., 1991).

Behavioral data on the development of complex visual functions and the influence of amblyopia suggest that functions dependent on the action of extrastriate areas may develop more slowly than simpler acuity and contrast detection tasks in both monkeys and humans. For example, contour integration ability develops over a protracted

time course in comparison to simple grating acuity (Kiorpes et al., 2000a, 2001; Kovacs et al., 1999). Contour integration ability is also susceptible to disruption in amblyopia (Chandna et al., 2001; Hess et al., 1997; Kovacs et al., 2000; Kozma et al., 2000).

These findings lead to our concluding conjecture that a complete picture of the factors that limit visual development and vision after abnormal experience will not be obtained until we have an account of extrastriate cortical development. There is modest evidence that the binocularity and response properties of neurons in V4 are affected in amblyopia (Movshon et al., 1987), and we have argued that changes in binocular organization in area MT following strabismus show that an independent mechanism of cortical binocular plasticity operates during development in this area (Kiorpes et al., 1996). Also, disruption of binocular organization has recently been reported in several extrastriate cortical areas in amblyopic cats (Schroder et al., 2002).

Our analysis of the relationship between visual neuronal function and visual behavior in normal and abnormal development suggests that neuronal properties up to V1 offer only an incomplete account. Neither the changes in V1 neuronal properties during development nor the effects of amblyopia on those properties are quantitatively concordant with the behavioral changes we observe. If the answer does not lie at or before the level of the primary visual cortex, it seems clear that it must lie beyond.

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