Cold Spring Harbor Symposia on Quantitative Biology

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*Cold Spring Harb Symp Quant Biol* 1996 61: 39-48
Access the most recent version at doi:10.1101/SQB.1996.061.01.007

# Amblyopia: A Developmental Disorder of the Central Visual Pathways

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The primate visual system is organized with remarkable spatial precision. In the central retina, which supports our finest spatial discriminations, signals from each of thousands of photoreceptors are faithfully transmitted into the central visual system along a series of synaptic relays which are so refined that they lose no significant information about spatial precision. This precise order arises during development as a result of visual experience; indeed, visual experience of clearly focused, stable, and binocularly aligned images seems to be required (for review, see Movshon and Kiorpes 1993). If visual experience in early life is abnormal, monkeys and humans commonly develop a disorder of spatial vision called *amblyopia*. Amblyopia has no obvious organic cause. It manifests itself as a deficit in visual acuity that cannot be corrected optically. Amblyopia in humans can be caused by strabismus (misalignment of the eyes), and by other forms of abnormal visual experience such as anisometropia (a difference in the refractive state of the two eyes) and visual deprivation from cataracts, when these conditions are present during infancy and early childhood (see Levi and Carkeet 1993; Movshon and Kiorpes 1993).

The most prominent deficit in amblyopia is in spatial vision, and the condition is commonly characterized by a deficit in spatial resolution, as measured by either Snellen (optotype) acuity or grating acuity. In addition to acuity losses, amblyopes also show decreased contrast sensitivity and visual discrimination ability when tested through their amblyopic eyes. Indeed, studies of human amblyopes often show that the deficits in simple detection tasks (e.g., grating acuity) are relatively small compared to their deficits in visual discrimination (e.g., vernier acuity). Strabismic amblyopes are thought to be particularly severely impaired on a variety of spatial localization tasks like vernier alignment and bisection; they seem to have a distortion of the spatial sense that is not completely captured by measurements of grating acuity. Anisometropic amblyopes, on the other hand, are thought to show localization deficits that are proportional to their deficits in acuity (Levi and Klein 1985). It is, however, difficult to make classification of human amblyopes by the conditions they show at the time of examination, since complete clinical histories are rarely available to verify that these conditions have obtained throughout life. Moreover, we and other investigators have found evidence that strabismus and/or anisometropia may sometimes arise as a *result* of an amblyopia that has a different underlying cause (von Noorden 1980; Almeder et al. 1990; Kiorpes et al. 1993; Kiorpes and Wallman 1995).

To understand the causes, character, and biological basis of amblyopia, it is necessary to study the condition in an animal model. The pioneering work of Wiesel and Hubel (1963a,b; Hubel and Wiesel 1965) on the effects of abnormal early visual experience uncovered many important principles that govern the development of visual function, and the susceptibility of that development to the influence of the visual environment. Their work did not include a detailed analysis of visual function per se and concentrated on forms of visual deprivation that cause large changes in neural function and connectivity. We have developed and studied primate models for strabismic and anisometropic amblyopia. The use of the animal model has the virtue that the visual experience and clinical history of the subjects can be controlled and completely known.

The results of our behavioral experiments reveal that in a series of psychophysical tests, experimentally created amblyopia in monkeys has the same range of characteristics as naturally occurring amblyopia in humans. Physiological recordings show that the neural changes associated with amblyopia are seen in the primary visual cortex but not earlier in the visual pathway. The results suggest that the biological basis of amblyopia is a disruption of the processes responsible for the spatial precision of neuronal connections in the thalamo-cortical pathway.

## METHODS

Our general methods for raising infant monkeys under conditions of abnormal visual experience, testing their visual capacities, and studying the properties of neurons in the visual thalamus and cortex have been described in detail elsewhere (Kiorpes et al. 1987, 1993; Kiorpes 1992a,b; Movshon et al. 1987; Levitt et al. 1994). All rearing and experimental procedures were conducted in compliance with the *NIH Guide for the Care and Use of Laboratory Animals*.

The subjects in these experiments were macaque monkeys, *Macaca nemestrina* or *Macaca mulatta*. The monkeys became amblyopic after a controlled period of abnormal early visual experience, either monocular eyelid closure, surgically created strabismus, or unilateral blur created by instillation of atropine or by extended-wear −10D contact lenses. Control data were obtained from eight monkeys raised normally. Monocular lid closure began within a few days of birth. Esotropic strabismus was induced 3–4 weeks after birth and persisted indefinitely; the size of the deviation was typically 5–25 degrees. Blur-rearing was begun 10–25 days after birth; unilateral defocus was imposed for 7–10 months thereafter.

Human data were obtained as part of the Cooperative Amblyopia Classification Study (McKee et al. 1992; Movshon et al. 1996). The data used here were taken from 251 observers aged 8–40 years. Of these, 67 were normal and 184 were amblyopes with a clinical history of anisometropia and/or strabismus.

## RESULTS

### Characteristics of Experimental Amblyopia in Macaque Monkeys

The spatial capacity of the visual system is commonly measured by the spatial contrast sensitivity function, which relates sensitivity (the inverse of threshold) to the spatial frequency of a sinusoidal grating target. Figure 1A shows the contrast sensitivity functions measured for each eye of a normal monkey (Kiorpes et al. 1993); the functions have a characteristic inverted-U shape. The peak contrast sensitivity of about 100 (corresponding to a contrast threshold of 0.01) is near 3 c/deg, and sensitivity falls to 1 (the lowest possible) slightly above 20 c/deg; this value is the finest spatial frequency resolved by the animal, or its grating acuity.

The visual sensitivity deficit in amblyopia is directly revealed by the contrast sensitivity function. Amblyopic eyes typically show reduced sensitivity to contrast; the loss is typically greatest at moderate and high spatial frequencies. The actual pattern of contrast sensitivity loss varies among individuals but does not vary by etiology: Similar contrast sensitivity deficits are seen in strabismic and anisometropic amblyopes.

Figures 1B and 1C show contrast sensitivity measurements for two amblyopic monkeys, one strabismic and one anisometropic (Kiorpes et al. 1993). In each case, the contrast sensitivity function for the amblyopic eye is shifted down and to the left of the function for the fellow eye, indicating losses in both sensitivity and spatial resolution. The contrast sensitivity of the fellow eye is similar to that of a normal monkey's eye.

Amblyopia is a disorder of development, and spatial vision in amblyopes is in many ways similar to spatial vision in normal infants. The contrast sensitivity function in young monkeys reveals that the infant visual system is less sensitive to contrast and can resolve only relatively low spatial frequencies compared to the adult. Similarly, the amblyopic eye resolves lower spatial frequencies and is less sensitive to contrast than the fellow eye. Figure 1D shows a comparison of contrast sensitivity in the same infant monkey at the ages of 5 weeks and 20 weeks (Boothe et al. 1988). Comparing these data with those of amblyopes (Fig. 1B,C) suggests (and a quantitative analysis of infant and amblyope contrast sensitivity data confirms) that the performance of the amblyopic eye resembles the performance of the eyes of young normal monkeys (Kiorpes 1992a,b, 1996).

As Figure 1D suggests, during the development of spatial contrast sensitivity, the peak of the function moves up and to the right; this happens without important changes in the overall shape of the function (Movshon and Kiorpes 1988). Figure 2 shows that the positions of these contrast sensitivity peaks in young normal animals (Fig. 2A) are similar to those observed in older amblyopes, either strabismic (Fig. 2B) or anisometropic (Fig. 2C).

Grating acuity is the highest spatial frequency that can be resolved at 100% contrast; that is, it is the spatial frequency at which the spatial contrast sensitivity functions in Figure 1 fall to a value of 1. Vernier acuity is another indicator of spatial visual performance and is usually measured by determining the smallest detectable offset between a pair of abutting colinear lines or edges. We studied the development of grating acuity and vernier acuity in normal monkeys and in monkeys with strabismus (Kiorpes and Movshon 1989; Kiorpes 1992a,b). The development of acuities both in normal animals and in the fellow eye of amblyopes follows a regular time course that appears roughly linear when plotted as a function of the logarithm of age. Amblyopia seems to slow the developmental time course for these acuities, rather than arresting development at a particular time or causing a deterioration of visual performance after maturation is complete. In addition, in normal monkeys and humans, vernier acuity is relatively poorer near birth and therefore shows a greater postnatal change than does grating acuity (Shimojo et al. 1984; Kiorpes and Movshon 1989).

In human amblyopes, vernier acuity—a measure of spatial discrimination performance and position sensitivity—is relatively more disrupted than is grating acuity, which is a measure of spatial resolution and sensitivity (Levi and Klein 1985). Figure 3A examines this in amblyopic monkeys by comparing the interocular ratio of vernier acuity and grating acuity for the two eyes. Virtually all the data lie above the diagonal, showing that vernier acuity losses are larger than grating acuity losses. In humans, Levi and Klein (1985) reported that this effect was larger for strabismic than for anisometropic amblyopes, but Figure 3A shows that there is no important difference between the losses shown by the two kinds of monkey amblyopes.

This pattern of a superordinate loss in vernier acuity can be accounted for in terms of the differences in de-

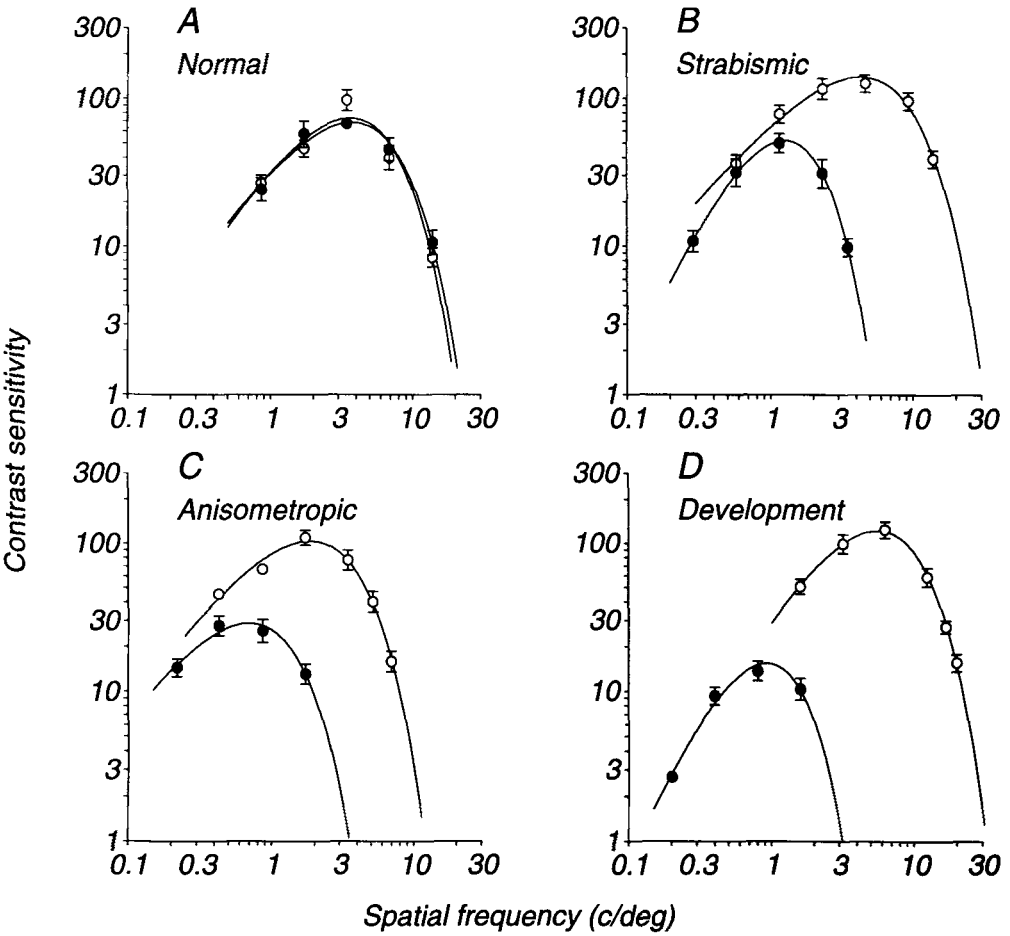


**Figure 1.** Contrast sensitivity functions measured in four monkeys. (*A*) Data from a normally reared monkey, viewing monocularly; the filled and open symbols show data taken from each eye. (*B*, *C*) Data from two amblyopic monkeys, one strabismic and one anisometropic. Filled symbols show data from the amblyopic eye, open symbols show data from the fellow eye. (*D*) Longitudinal data from one normally reared monkey, measured at the ages of 5 weeks and 20 weeks (*filled* and *open* symbols, respectively).

velopment of the two acuities. In normal animals, vernier acuity is relatively less mature in infants and develops to a greater extent than grating acuity during maturation. The relatively greater disruption of vernier acuity may then be a consequence of the relative immaturity of the visual system, rather than a peculiar deficit in positional acuity. Figure 3B compares the values of grating and vernier acuity for several kinds of monkey observers. Developmental data for normal monkeys are shown by the pluses. If these two acuities developed in lock-step, then the data would lie together along a line of unit slope, but evidently they do not. The filled symbols in Figure 3B show that the data for amblyopic monkeys lie near the data for young normal monkeys, further reinforcing the notion that the disorder in amblyopia can be understood as a failure of normal developmental processes to run their course.

### Comparison of Amblyopia in Monkeys and Humans

Our experimentally amblyopic monkeys show many patterns of visual loss that are also characteristic of human amblyopia. To examine this impression quantitatively, we compared our monkey data directly with human data from the Cooperative Amblyopia Classification Study, a recently completed large-scale prospective study of human subjects (McKee et al. 1992; Movshon et al. 1996). We confined our comparison to data from a subset of the subjects in that study: normals, and amblyopes with a documented clinical history of strabismus, anisometropia, or both.

Figure 4 uses the same format as Figure 3 and adds to the monkey data previously shown four additional human data sets: normal observers, "pure" strabismics, "pure" anisometropes, and strabismic-anisometropic observers ("strab/aniso"). Figure 4A shows a comparison of the relative losses in vernier and grating acuity, as in Figure 3A. Almost all the human observers, like the monkeys, show a greater interocular difference in vernier acuity than in grating acuity. In contrast to some earlier reports (see e.g., Levi and Klein 1985), there is no apparent difference in this pattern of loss among the different groups of human amblyopes; this is of course the pattern seen in the

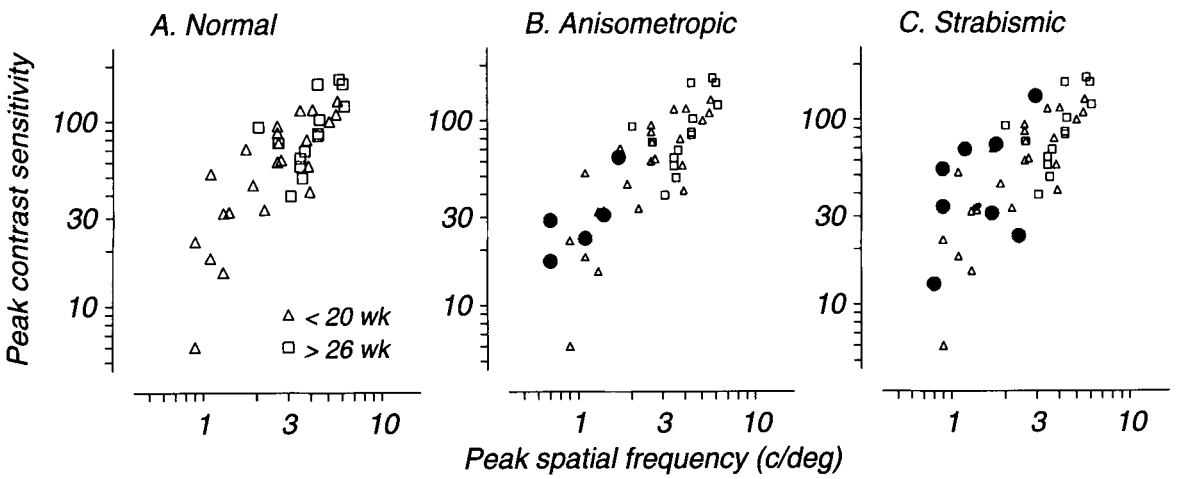


**Figure 2.** Results of a quantitative analysis of contrast sensitivity data showing how the curve shifts with age and with amblyopia. The relationship between peak spatial frequency and peak contrast sensitivity for normal infants (*triangles*) and adults (*squares*) is shown in *A*. The same data are plotted along with data from strabismic (*B*) and anisometropic (*C*) amblyopes. The data from amblyopes are similar to those from young normal monkeys.

monkey amblyopes as well. Figure 4A does show in humans that individuals with both strabismus and anisometropia tend to be more profoundly amblyopic than those with only one condition; we have not attempted to make this distinction in the monkey data since we classify the animals by the condition we created experimentally. However, we have shown that strabismic animals with more profound amblyopia tend also to develop anisometropia later in life (Kiorpes and Wallman 1995). These monkeys would therefore appear as combined strabismics/anisometropes and would have more severe amblyopias like their human counterparts.

Figure 4B shows the relationship between grating and vernier acuity, as in Figure 3B. Again, the data from monkeys and humans overlap almost completely, excepting only that normal humans achieve values of both grating and vernier acuity that slightly exceed those observed in monkeys. The more profound amblyopia in human strab/anisos is again evident. Thus, both in the pattern of relative interocular differences and in the pattern of relative vernier and grating acuity losses, the monkey data show the same pattern as the human data, and the ranges of the data for humans and monkeys overlap almost completely.

Experimentally strabismic and experimentally anisometropic monkeys are excellent models with which to study the factors that affect the development of amblyopia. In our experimental populations, approximately two-thirds of the monkeys raised with either anisometropia or strabismus subsequently developed amblyopia. This is very close to the prevalence of amblyopia in humans with naturally occurring strabismus or anisometropia, which is typically 40–60%. Strabismic animals that adopted a unilateral (as opposed to alternating) pattern of fixation were most likely to develop amblyopia; a similar association is found in humans. Additionally, the younger the age at which the abnormal visual conditions were imposed, the more likely it was that amblyopia developed (Kiorpes et al. 1989).

### Neuronal Changes in Amblyopia

The goal of creating an animal model is to permit an exploration of the neurobiological changes that underlie the condition. There are a number of possibilities. Since amblyopia usually affects one eye, it is natural to wonder whether its effects are seen in the normally monocular portions of the visual pathway, the retina and lateral geniculate nucleus (LGN). Following monocular visual deprivation, Wiesel and Hubel (1963a,b) showed that there were large qualitative changes in the pattern of binocular inputs to cortical neurons but found little discernible effect on the response properties of neurons in the LGN.

We quantitatively examined the spatiotemporal properties and contrast sensitivity of 254 LGN neurons in five monkeys that were deprived of vision from the time of birth by suturing closed the lids of one eye (Levitt et al. 1989). This rearing creates an amblyopia so profound that the deprived eye is effectively left without any spatial vision at all, although rudimentary sensitivity to luminance differences remains (Harwerth et al. 1983). Like Wiesel and Hubel, we found no important differences in visual responsiveness or sensitivity between groups of LGN neurons driven by the deprived and non-deprived eye. There were some subtle differences, the most obvious being that the contrast gain of magnocellular and parvocellular neurons driven by the deprived eye was on average about 20% lower than that of comparable neurons driven by the non-deprived eye. In almost all respects the data for neurons driven by the two eyes were identical, and the few anomalies are far too subtle to account for the complete loss of visual capacity in the deprived eyes.

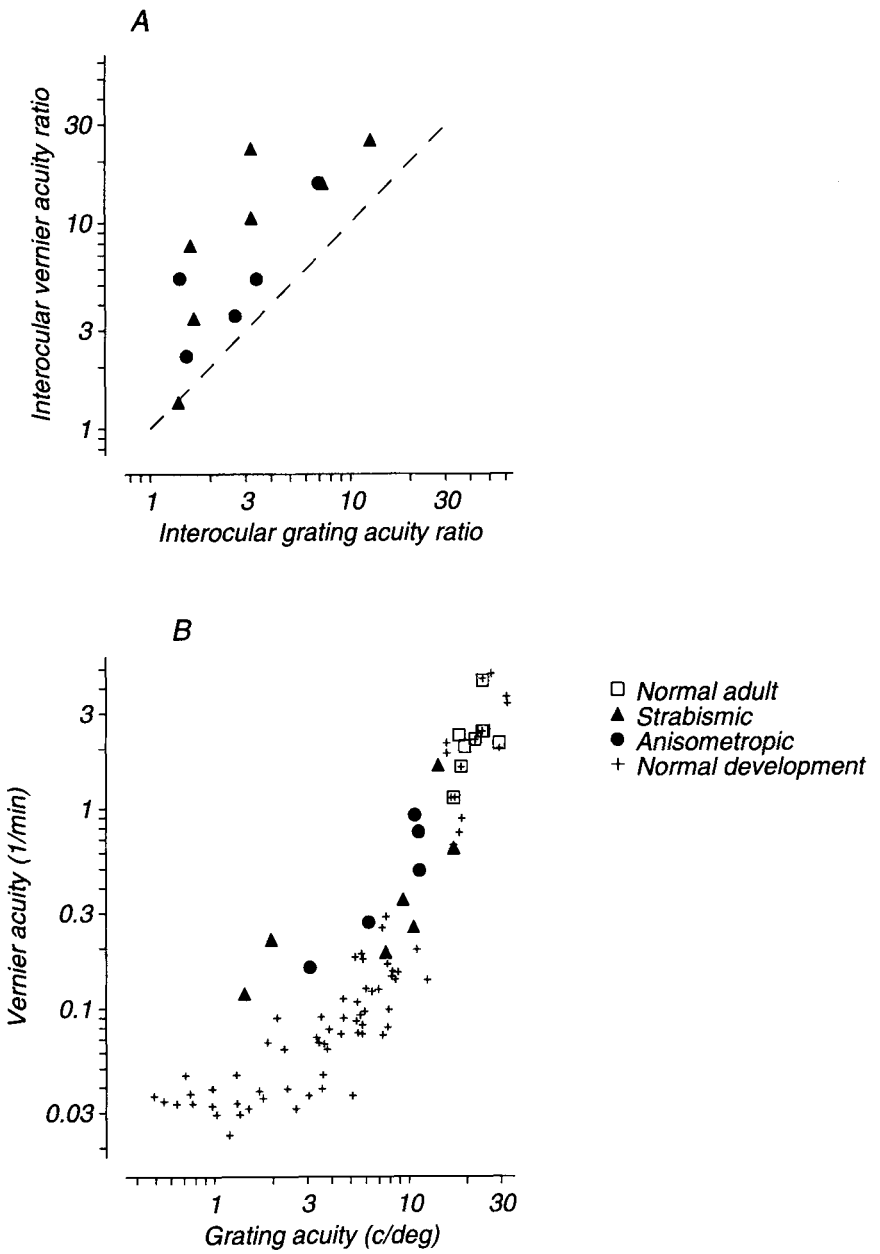


**Figure 3.** (*A*) Comparison of the magnitude of the vernier and grating acuity deficits for strabismic (*triangles*) and anisometropic (*circles*) amblyopes. The ratio of the vernier acuity values for the two eyes of each monkey is plotted against the ratio of the grating acuity values. In most cases, the vernier acuity deficit is larger than the grating acuity deficit (the data lie mostly above the dashed line, which represents a 1:1 relationship). (*B*) Relationship between vernier acuity and grating acuity in amblyopic monkeys as compared to that during normal development. The normal developmental data (*pluses*) are from animals ranging in age from near birth to 1 year. The performance of the amblyopes resembles that of young normal monkeys, although the data from two severe strabismic amblyopes deviate from the function.

We made similar measurements of the properties of 76 neurons from one monkey that was raised with unilateral blur; again there were no differences in the properties of cells driven by the two eyes (Movshon et al. 1987).

Visual deprivation is a crude manipulation that produces very profound changes in the central visual pathways. Monocular deprivation functionally disconnects the deprived eye from the cortex, so that few neurons there show any influence of visual signals arising in the deprived eye (Wiesel and Hubel 1963b; Hubel et al. 1977; LeVay et al. 1980). This suggests a second possible explanation for amblyopia: Perhaps a smaller-than-normal proportion of cortical neurons can be activated through the amblyopic eye, leading to its reduced visual capacity.

We studied the functional binocular connections and spatiotemporal properties of neurons in the pri-

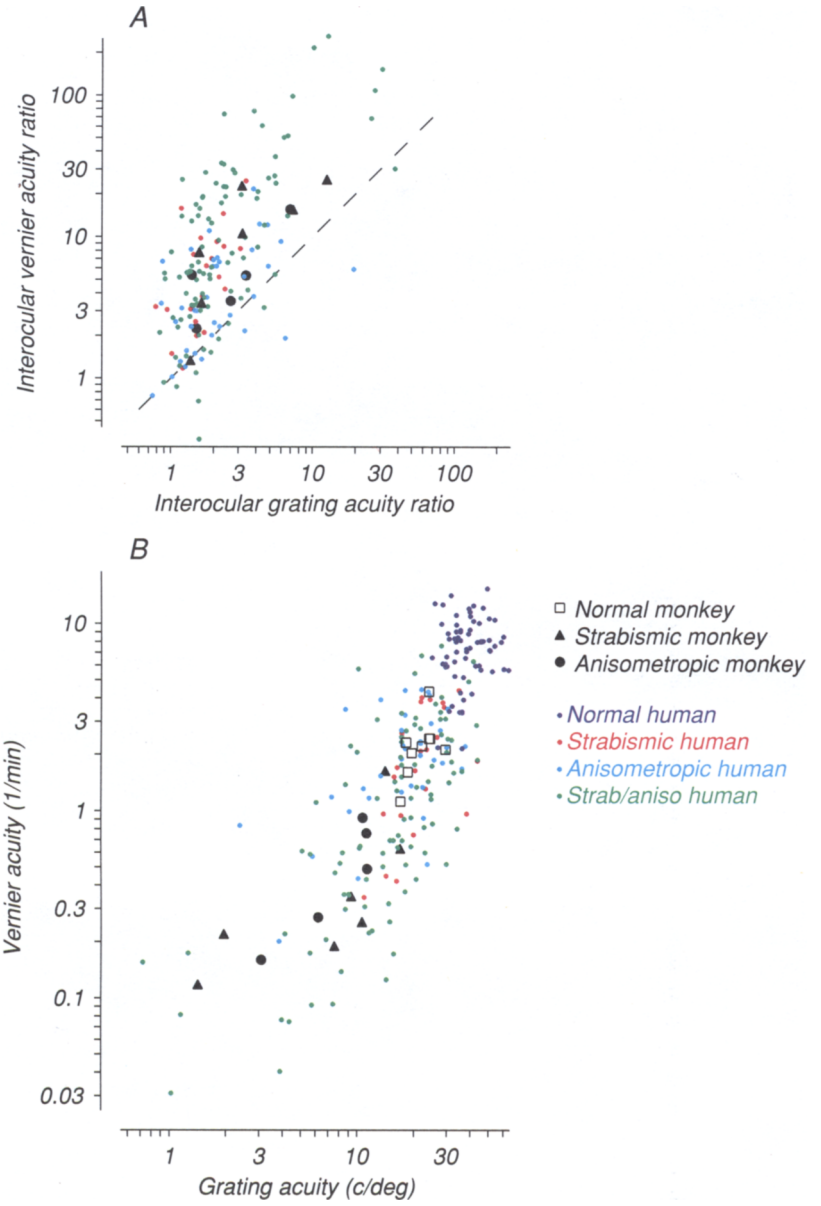


**Figure 4.** Comparison between monkey and human amblyopia. The format of *A* is the same as Fig. 3A; the format of *B* is the same as Fig. 3B; the monkey data are as shown in those figures. The human data are from 221 subjects classified as indicated in the legend. There is good correspondence between the human and monkey data, although normal humans have finer acuity than normal monkeys (*B*).

mary visual cortex of monkeys made amblyopic by either simulated anisometropia or strabismus. Figure 5 compares the distributions of cortical eye dominance for neurons recorded from these animals with data from normal monkeys, and with data from monocularly deprived monkeys (Hubel et al. 1977). Figure 5A shows the pattern of eye dominance found in 394 neurons recorded from normally reared monkeys. About 70% of cortical neurons are binocularly activated. Figure 5B shows the eye dominance of 600 neurons recorded in the cortex of eight monocularly deprived monkeys (Hubel et al. 1977; LeVay et al. 1980). The deprivation virtually disconnects the deprived eye from the cortex. Figure 5C shows the eye dominance of 316 neurons recorded from four amblyopic monkeys raised with unilateral blur produced by atropine (Movshon et al. 1987). Although the number of binocular neurons in these monkeys is somewhat reduced, there is little evidence of a wholesale shift in cortical eye dominance away from the blurred eye. Figure 5D shows the eye dominance of 225 neurons recorded from two amblyopic monkeys raised with esotropic strabismus (J.A. Movshon et al., unpubl.). Although almost all binocular neurons are lost in these

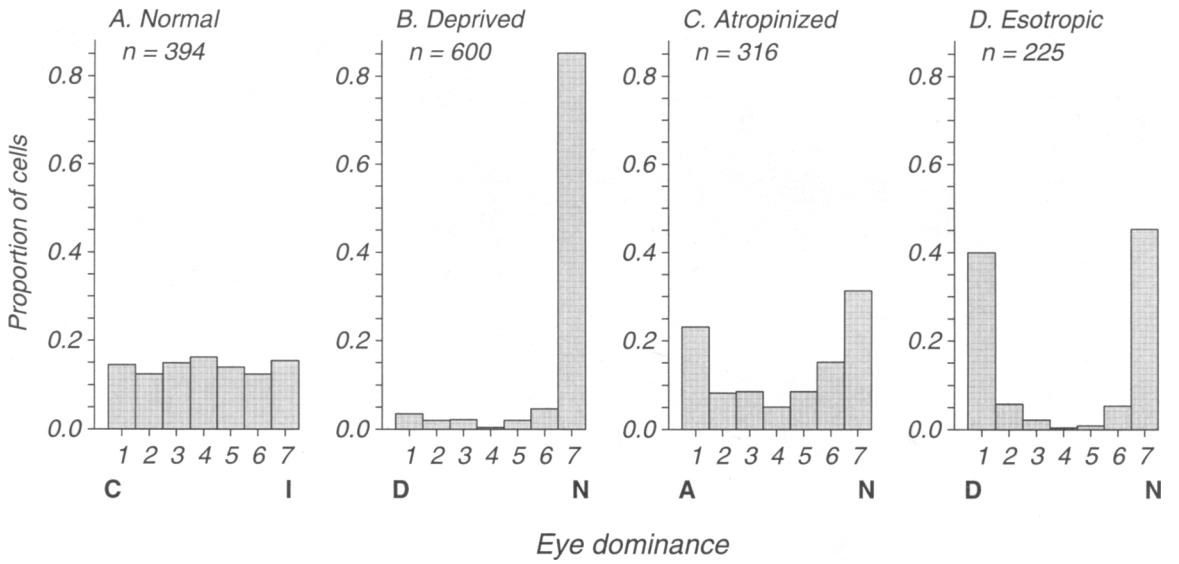


**Figure 5.** Eye dominance distributions for neurons recorded from the primary visual cortex of four groups of monkeys. The eye dominance scale is based on the traditional 7-point scale, in which groups 1 and 7 represent monocularly driven neurons, group 4 represents neurons equally driven from the two eyes, and groups 2, 3, 5, and 6 represent graded degrees of relative binocularity. (*A*) Data from 394 neurons recorded from normally reared animals. The scale goes from complete dominance by the contralateral eye (group 1, **C**) through complete dominance by the ipsilateral eye (group 7, **I**). (*B*) Data from 600 neurons recorded from eight monocularly deprived animals by Hubel et al. (1977) and LeVay et al. (1980). The data are combined so that the deprived eye (**D**) corresponds to group 1 and the non-deprived eye (**N**) corresponds to group 7. (*C*) Data from 316 neurons recorded from four atropine-treated monkeys by Movshon et al. (1987). The data are combined so that the atropinized eye (**A**) corresponds to group 1 and the untreated eye (**N**) corresponds to group 7. (*D*) Data from 225 neurons recorded from two esotropic strabismic monkeys (J.A. Movshon et al., unpubl.). The data are combined so that the surgically deviated eye (**D**) corresponds to group 1 and the non-deviated eye (**N**) corresponds to group 7. In all atropinized and esotropic monkeys, the treated eye was the amblyopic eye.

animals, each eye's signals control approximately the same number of neurons. Since the animals whose data are shown in Figure 5C and D were all amblyopic, it appears that amblyopia can occur without significant changes in the eye dominance of cortical neurons, although strabismus can cause such changes in some cases (Eggers et al. 1984).

If the *number* of cortical neurons driven by each eye is not changed by amblyopia, perhaps some of their other properties are altered. Because amblyopia is, as we have discussed, a deficit of spatial vision, we studied the spatial properties of the receptive fields of cortical neurons in monkeys raised with strabismus and unilateral blur. Figure 6 shows that the spatial resolution and sensitivity of neurons in the portions of the visual cortex that represent the central visual field are indeed altered in amblyopia. Figure 6A plots the optimal spatial frequency and peak contrast sensitivity of 255 neurons from the four amblyopic monkeys raised with unilateral blur (Movshon et al. 1987). Figure 6B shows in similar format the data for 204 neurons from the two amblyopic monkeys raised with experimental strabismus. It is evident in each part of this plot that the neurons driven through the treated eye had, on average, lower contrast sensitivity and lower peak spatial frequencies than neurons driven through the untreated eye; the magnitude of the effects is between 30% and 41%, and is similar for the two groups of monkeys. We conclude that the visual neuronal disorder associated with amblyopia that arises earliest in the visual process is this modification of the receptive field properties of cortical neurons. As we consider in more detail below, this may not be the only neuronal abnormality in these animals, but it is arguably the most important for understanding the visual resolution and sensitivity losses associated with amblyopia. These changes must arise from a failure of afferent neurons to make their normal precisely patterned connections.

## DISCUSSION

The results of our experiments on amblyopic monkeys lead to three main conclusions:

1. Strabismus and simulated anisometropia, when present in the first few months of a monkey's life, create a visual anomaly that seems to be indistinguishable from human amblyopia.
2. Neurophysiological recordings from these monkeys show that there are no significant changes in the visual properties of neurons in the thalamus (and, by deduction, in the retina). The first important changes are seen in the primary visual cortex, V1.
3. Both behaviorally and neurophysiologically, the am-

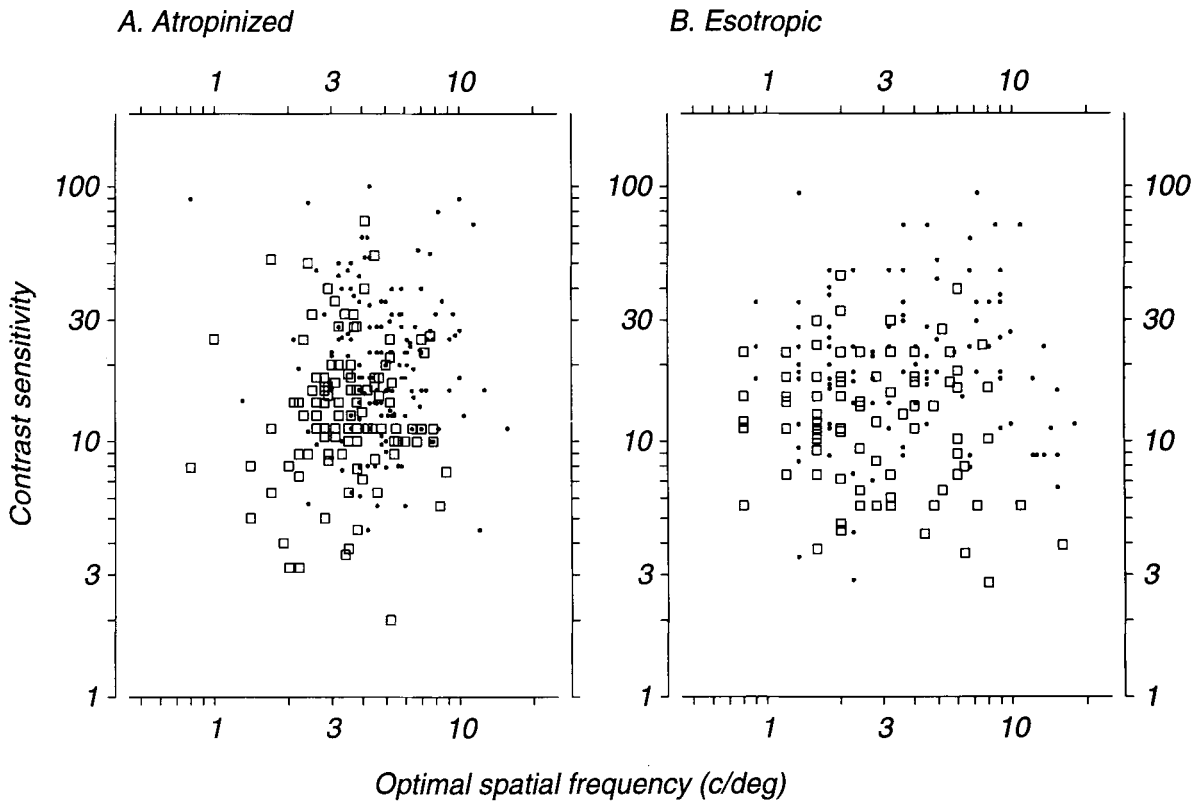


**Figure 6.** Scatter plots showing the optimal spatial frequency and peak contrast sensitivity of neurons recorded from the representation of the central visual fields in the primary visual cortex of two groups of amblyopic monkeys. Each point represents the two values for a single neuron. Small points represent data for neurons dominated by (and tested through) the untreated eye, and large squares represent data for neurons dominated by (and tested through) the treated eye. (*A*) Data from 255 neurons from four atropine-treated monkeys (Movshon et al. 1987). The geometric mean optimal spatial frequency is 31% lower for neurons driven through the treated eye, and the geometric mean contrast sensitivity is 35% lower. (*B*) Data from 204 neurons from two esotropic strabismic monkeys (J.A. Movshon et al. unpubl.). The geometric mean optimal spatial frequency is 30% lower for neurons driven through the treated eye, and the geometric mean contrast sensitivity is 41% lower.

blyopic eye functions as though its spatial contrast sensitivity has been shifted both down to lower sensitivities and leftward to lower spatial frequencies.

It is interesting to consider how the reduction in spatial resolution and sensitivity might arise biologically. The receptive field structure of neurons in the primary visual cortex is quite heterogeneous. However, those neurons with the highest spatial resolution have receptive fields whose spatial structure consists of subregions only 1–2 min arc in width, which suggests that their main inputs arise from only a few photoreceptors (Hawken and Parker 1991). These inputs are presumably relayed through neurons in the parvocellular layers of the LGN, whose receptive fields are comparably tiny (Blakemore and Vital-Durand 1986). Our measurements of neuronal properties in amblyopic monkeys show that these afferent neurons in the LGN are still present and normal in function, but they are absent in parts of the cortex controlled by the amblyopic eye. Because cortical eye dominance does not change overall, we do not believe that these neurons are lost. Rather, it seems that their connections with afferents from the LGN are disrupted, so that they receive inputs from neurons whose receptive fields are dispersed over a substantial region of the retina. This results in cortical receptive fields whose structures are "blurred." The subregions of the receptive fields are larger, leading to a leftward shift in their spatial contrast sensitivity. It is also conceivable that the regions are also less perfectly segregated from one another than in normal animals, leading to partial cancellation of signals from different regions and a reduction in contrast sensitivity.

If we assume that the usual highly precise topographic representation of the visual field (Blasdel and Fitzpatrick 1984) is not altered in the cortex of amblyopic monkeys, we can make simple calculations to estimate the extent of the spatial disruption. The peak of local cortical magnification in monkeys is around 10 mm/deg (i.e., movement of 1 mm on the cortical surface causes an average movement of the location of visual receptive fields of 0.1 deg; Tootell et al. 1988; Wässle et al. 1990). The spatial blurring of visual receptive fields can be calculated from data like those shown in Figure 6 to be of the order of 0.1 deg, corresponding

to a local misrouting of signals over distances of approximately 1 mm. Interestingly, this is the approximate extent of the terminal arborizations of parvocellular LGN afferents to the cortex in neonatal monkeys; perhaps this is the reason that visual cortical receptive fields in neonates show the same reduced spatial resolution as do neurons in amblyopic adults (Blakemore and Vital-Durand 1983; Blasdel and Lund 1983). In the course of normal development with clear, binocularly aligned images, these connections prune down to their adult size of approximately 0.1 mm (Blasdel and Lund 1983; Blasdel and Fitzpatrick 1984). We may suppose that the altered visual conditions that create amblyopia interfere with this pruning, so that afferents from the LGN are randomly misrouted by a distance on the order of 0.5–1 mm in the adult amblyopic visual cortex.

It may be that this misrouting is the basis for the changes seen in the visual sensitivity of amblyopic cortical neurons, and for the abnormal performance of amblyopes themselves. It is important to note, however, that the magnitude of the changes in sensitivity and spatial resolution seen in the neuronal populations (Fig. 6) are probably too small to account for the whole of the visual losses seen in behavioral measurements (Fig. 1). It is also not obvious that these changes can account for the extraordinary loss of vernier acuity seen in some amblyopes (Figs. 3,4) (Levi and Klein 1985). The primary visual cortex is of course only the first in a complex pathway of visual cortical areas (Felleman and Van Essen 1991), and it would be naive to assume that it is the *only* area whose development can be modified by the visual environment. Indeed, we have recently shown that the binocular connections of neurons in MT, an extrastriate visual area, can also be modified by strabismus (Kiorpes et al. 1996). It is thus likely that neurons in other areas are also affected in amblyopia, and we may suppose that a comprehensive account of the biological basis of amblyopia will require examination of the changes in these areas as well as in the primary visual cortex.

## ACKNOWLEDGMENTS

The research described in this paper was supported by grants from the National Eye Institute (EY-02017 and EY-05864) and by the Howard Hughes Medical Institute. These experiments would not have been possible without the contributions of Howard Eggers, Martin Gizzi, Daniel Kiper, Dennis Levi, Jonathan Levitt, Suzanne McKee, Lawrence O'Keefe, Murray Sherman, Peter Spear, and Chao Tang. We are also grateful to Patricia Adler, Michael Gorman, and Jasmine Allen Siegel for their expert technical assistance.

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