# 15 Neural Development of Cats Raised with Deprivation of Visual Patterns

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This chapter is intended to be a selective and somewhat speculative review of the effects of early visual deprivation on the development of the central visual pathways. Its purpose is to consider some simplifying but hypothetical mechanisms by which the early visual environment can interact with the developing brain. Because most of the relevant data are derived from cats raised with their eyelids sutured closed or in total darkness, the review is limited to these studies.

To achieve focus, consideration is given neither to the large number of observations of the effects of other interesting forms of visual deprivation, such as strabismus, anisometropia, or astigmatism on the development of the central visual pathways, nor to the relatively few studies of visual deprivation on other mammalian species, such as rodents, rabbits, insectivores, carnivores other than the cat, or primates. Also, this chapter is concerned mainly with those permanent abnormalities caused by visual deprivation lasting throughout all or most of the critical period (i.e., that postnatal period during which the developing visual system is susceptible to environmental influences; e.g., refs. 15, 114). Excellent and more comprehensive reviews of the other subjects mentioned above have appeared recently.[13, 95, 177]

It is not at all clear how one relates cats raised with fairly complete visual deprivation (i.e., by lid suture or in total darkness) to the galaxy of clinical disorders of vision thought to result from abnormal early visual environments. Not only do the central visual pathways of cats differ markedly from those of humans, but also clinical disorders homologous to those created by complete visual deprivation are relatively rare. However, the basic mechanisms whereby the visual environment interacts with the immature visual system, as discussed in this chapter, can at least speculatively be related to some of the human disorders. Thus, the concluding portion of the chapter contains a limited consideration of possible relationships between the cat data and certain clinical disorders. Many of the ideas expressed here can be found more fully developed in the review chapter by Sherman and Spear.[225]

## NORMAL VISUAL PATHWAYS

It is beyond the scope of this chapter to describe in detail the central visual pathways of the normal cat. Rather, what follows is a selective account focused upon characteristics studied in visually deprived cats. Most of this will consequently deal with the geniculostriate pathways, although the superior colliculus, cortical area 18, and lateral suprasylvian cortex will be briefly considered. The consideration of central visual pathways begins with retinal ganglion cells. More comprehensive descriptions of the central visual pathways in normal cats can be found in a number of recent reviews (e.g., refs. 151, 192, 198, 204, 225, 252, 266).

### GENERAL TOPOGRAPHY

#### NEURAL CONNECTIONS

Figure 15-1 summarizes some of the connections among the retina, lateral geniculate nucleus, superior colliculus, cortical area 17 (striate cortex), cortical area 18, and lateral suprasylvian cortex in the cat. As already noted, this is not intended as a complete description of the central visual pathways, but rather as a partial survey to provide a background for discussing the effects of early visual deprivation.



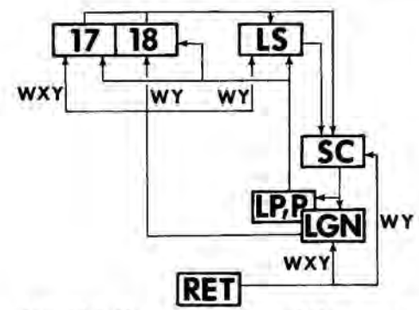


Fig. 15-1 Diagram of some of the connections in the cat's central visual pathways. For simplicity, many pathways have been omitted (e.g., the corticogeniculate pathway and pathways involving the pretectum). RET, retina; LGN, lateral geniculate nucleus; LP,P, lateral posterior and posterior nuclei of the thalamus; SC, superior colliculus; 17, 18, cortical areas 17 and 18; LS, lateral suprasylvian cortex. W, X, and Y refer to the composition of retinofugal and geniculocortical pathways regarding W-, X-, and Y-cells.

The main central targets of the retina are the dorsal division of the lateral geniculate nucleus and the upper three layers of the superior colliculus. Retinal ganglion cells also project to the suprachiasmatic nucleus of the hypothalamus, the ventral division of the lateral geniculate nucleus, the pretectum, and the accessory optic nucleus in the tegmentum.[8, 89, 146, 172, 192] The lateral geniculate nucleus (hereafter, this phrase refers to only the dorsal division) projects to a number of visual cortical areas, including areas 17, 18, and the lateral suprasylvian cortex.[64, 65, 68, 119, 154, 195, 265] These cortical areas (as well as others not shown in Fig. 15-1) are the source of a large corticotectal pathway to the upper layers of the superior colliculus.[63, 68, 135, 252, 277] Finally, cells in the upper layers of the superior colliculus issue axons to several thalamic targets.[68, 75, 87, 119, 178, 195, 252] These thalamic targets include the geniculate C laminae, the lateral posterior nucleus, and the posterior nucleus, and they, in turn, project to the visual cortical areas shown in Figure 15-1.[4, 10, 74-76, 133, 134, 178, 179] These areas are richly interconnected, and a number of further pathways have been omitted from Figure 15-1 for simplicity.

#### LATERAL GENICULATE NUCLEUS

**Lamination**

The cat's lateral geniculate nucleus is a laminated structure that can be divided into three major divisions: the A laminae, the C laminae, and the medial interlaminar nucleus. The A laminae lie dorsal to the C laminae, and the medial interlaminar nucleus is found immediately medial to these divisions. The contralateral retina innervates laminae A, C, C2, and part of the medial interlaminar nucleus, while the ipsilateral retina innervates laminae A1, C1, and most of the remainder of the medial interlaminar nucleus.[79, 94, 146] Only a small portion of the lateral geniculate nucleus—the "geniculate wing" extending rostromedially from the medial interlaminar nucleus—receives overlapping input from both eyes.[79]

**Relay Cells**

Most or all neurons of the lateral geniculate nucleus receive optic-tract input and project to the visual cortex. These neurons are relay cells. Neurons in laminae A and A1 project to cortical areas 17 and 18, and neurons in the C laminae and medial interlaminar nucleus project to nearly all of the known visual cortical areas.[65, 68, 108, 190, 195]

**Interneurons**

In addition to relay cells, it is generally assumed that interneurons also exist in the lateral geniculate nucleus. Estimates of their relative numbers range from less than 5 percent (and perhaps none) to roughly 25 percent (e.g., refs. 153, 163). Attempts to identify interneurons have been based upon negative data, such as the failure of a recorded geniculate neuron to be excited antidromically by electrical stimulation of the visual cortex, or the failure of a geniculate neuron to transport horseradish peroxidase (HRP) retrogradely from a cortical injection site. Unfortunately, it is quite possible that a relay neuron might fail to propagate an antidromic action potential or transport HRP retrogradely (for a detailed discusson of this, see ref. 57).

### Visual Cortex

All areas of the neocortex are comprised of six layers parallel to the pial surface. These are numbered I to VI from the pial surface to the white matter. The relationship between this lamination scheme and the pathways to and from the cortex is best understood for area 17. The other cortical areas probably have similar relationships.

Input from the lateral geniculate nucleus terminates mainly in layer IV of the neocortex, but smaller projections to layers I, III, V, and VI are also evident.[154, 157, 195] Although layers II, III, and V receive little or no geniculate input, many neurons with somata in these layers nonetheless appear to be directly postsynaptic to geniculate axons, presumably because these cortical neurons have dendrites that venture into layers I, IV, or VI (e.g., ref. 25). Projections from the lateral posterior and posterior nuclei of the thalamus terminate mainly in layer I. Efferent projections include corticocortical pathways, mainly from layer III; corticotectal pathways from layer V; and corticogeniculate pathways from layer VI.[68, 90, 107, 166, 168, 185, 271]

The functional unit of the visual cortex seems to be a column running vertically through the layers.[3, 112, 203] Ocular dominance in layer IV of areas 17 and 18 seems arranged in a patchy fashion compatible with this columnar organization. Parallel bands roughly 500 μm wide exist in layer IV, and each has inputs from a set of geniculate laminae related to one eye.[206, 207]

### Superior Colliculus

The superior colliculus, like the lateral geniculate nucleus, is a laminated structure. The upper three layers are purely visual while the lower four layers are polysensory.[73, 130, 258] This chapter does not deal with these lower, polysensory layers. The upper layers receive two major visual inputs via the brachium of the superior colliculus. These are the retinotectal and corticotectal pathways. The former contains fibers predominantly from the contralateral nasal retina while the latter derives from a variety of visual cortical areas (e.g., ref. 252). Efferents from these upper layers project to thalamic targets, principally to the posterior and lateral posterior nuclei but also to the C laminae of the lateral geniculate nucleus (see above). This projection forms a link in a major extrageniculate visual pathway to the cerebral cortex—the retino-tecto-thalamo-cortical pathway.

## RETINAL GANGLION CELLS

### Morphological Cell Classes

Most morphological classification schemes of the cat's retinal ganglion cells are based on Golgi-impregnated material. Cajal, in the late nineteenth century, used such material to describe many morphological classes of mammalian ganglion cells, a scheme that he also applied to the cat (see the excellent translation of this body of work in ref. 191). More recently, Boycott and Wässle[21] lumped these morphological types of ganglion cell into three main groups, called *alpha, beta,* and *gamma* cells, and this scheme has attracted considerable attention. Alpha cells have the largest somata and relatively few dendrites that extend over a large distance. These few dendrites usually show considerable branching. Beta cells have intermediate-sized somata and a small but dense dendritic arbor. Gamma cells have the smallest somata, but their dendritic arbors are as extensive as are those of alpha cells, although less dendritic branching occurs. Also, considerable overlap in soma sizes was noted between beta and gamma cells.

There is reason to suspect that this classification scheme may not be complete, a point made by Boycott and Wässle.[21] For instance, these authors tentatively described a fourth class of retinal ganglion cells, which they called *delta* cells, that in many ways seem to have morphological properties intermediate between those of alpha and beta cells. These cells have slightly larger somata and denser dendritic arbors than do typical gamma cells. Furthermore, the classification scheme of Boycott and Wässle is based on a view of the cells in flat-mounted retinas, and does not take into account the distribution of dendrites within the sublaminae of the inner plexiform layer. Cajal (see translation in ref. 191) described many different ganglion-cell classes based on these distribution patterns (see also ref. 51). Finally, it must be emphasized that Golgi impregnation techniques are capricious and often quite selective for certain cell types. It is possible that other morphological classes of retinal ganglion cells are refractory to elucidation by this approach. For instance, Leventhal et al.[160, 161] retrogradely filled with HRP a class of ganglion cells (*epsilon* cells) not described in Golgi impregnated material. These have medium-sized somata (like beta cells) but an extensive, sparse dendritic arbor (like gamma cells).



### Physiological Cell Classes

Two complimentary schemes of classification for cat retinal ganglion cells are recognized. These are the ON and OFF center classes and the W-, X-, and Y-cell classes.*

#### ON and OFF Center Cells

Kuffler[144] first pointed out the antagonistic, center/surround organization of receptive fields for cat retinal ganglion cells, which he divided into two groups. One is represented by ON center cells. Their receptive fields have a small, circular, central region in which the onset of light excites the cell while the cessation of light inhibits the cell. Surrounding this is an annular region with the reverse properties: here the onset of light inhibits and cessation excites the cell. OFF center cells have a mirror-image arrangement. Such a cell is excited by the cessation of light in the center or the onset of light in the surround, and inhibited by the onset of light in the center and the cessation of light in the surround. Until recently (see description of W-cells below) all or virtually all of the cat's retinal ganglion cells were thought to fall into one of these two classes.

#### W-, X-, and Y-Cells

In a seminal paper, Enroth-Cugell and Robson[49] described the classification of retinal ganglion cells into X- and Y-cells from recordings made in the optic tract. More recently, a third class, W-cells, has also been described among retinal ganglion cells.

Relatively little is known about W-cells (e.g., refs. 32, 33, 267–269). These cells seem to form a fairly heterogeneous group that, upon further investigation, might prove to be comprised of several cell classes lumped together (e.g., ref. 192). Many W-cells display the aforementioned center/surround organization in their receptive fields, but many do not. Among the latter are W-cells having fields with diffuse regions sensitive to the onset and cessation of light, those with fields selective for the direction of stimulus movement, and others. Compared to X- and Y-cells, W-cells have more slowly conducting axons, poor responsiveness and sensitivity to visual targets, and often larger, more diffuse receptive fields.

Much more is known about X- and Y-cells. These have receptive fields with a center/surround organization. The initial distinction made by Enroth-Cugell and Robson[49] between X- and Y-cells was based on the linearity of spatial summation within the receptive field, but since then, many studies have enlarged the number of distinguishing physiological properties for these cells.[26, 31, 59, 97, 98, 106, 147, 241, 242, 261]

Compared to Y-cells, X-cells display more linear response properties to visual stimuli; more slowly conducting axons; generally better spatial acuity (i.e., sensitivity to fine spatial detail); generally poorer temporal resolution (i.e., sensitivity to fast temporal changes); smaller receptive-field centers; and more tonic or sustained responsiveness to an appropriate standing contrast, such as a small bright spot produced in the center of an ON center cell or a dark spot for an OFF center cell.

X- and Y-cells also have different spatiotemporal properties, as illustrated by contrast sensitivity functions. These functions plot the contrast of the sine-wave grating needed to evoke a threshold response from the cell over a range of spatial and temporal frequencies.† Figure 15-2 schematically

*For reasons set forth by Rowe and Stone,[198] this review follows the noncommittal, and most common, terminology of W-, X-, and Y-cells to indicate these neuron classes. Other terminology has appeared for these classes. It is not always clear that cell groups identified by different names represent completely isomorphic classification schemes. With this qualification, the following terms are generally interchangeable: *transient, brisk-transient, Group I, phasic, homogeneous,* or *nonlinear* for Y-cells; *sustained, brisk-sustained, Group II, tonic, heterogeneous,* or *linear* for X-cells; and *sluggish, sluggish-sustained,* or *sluggish-transient* for W-cells.[31-33, 49, 59, 97, 106, 261]

†Square-wave gratings, which are simply alternating stripes of equally spaced, dark and light regions, will be more familiar to most readers. If a photometer were passed across the stripes, it would register a square wave luminosity profile. A sine-wave grating is similar in all respects, except that its luminosity profile is described by a sine wave. Four variables of such gratings are usually altered: contrast, spatial frequency, temporal frequency,

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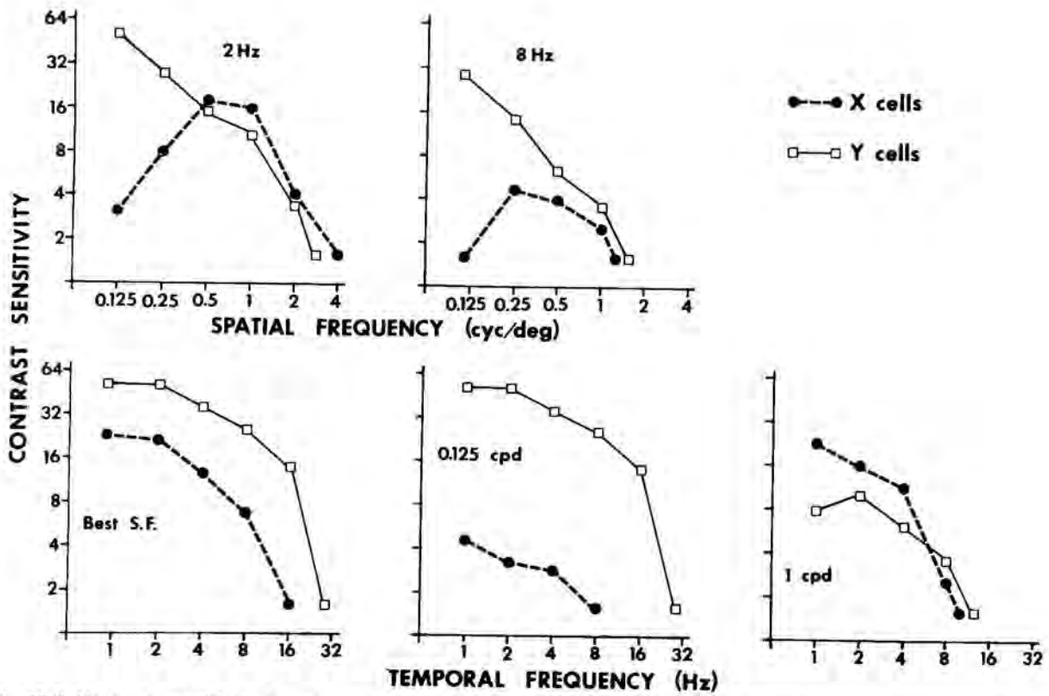


Fig. 15-2 Contrast sensitivity functions for geniculate X- and Y-cells in the cat. Each function represents the contrast sensitivity to counterphased, sine-wave gratings averaged for 10 X- and 10 Y-cells, each with a receptive field between 5 and 10 degrees from the area centralis. The top row shows spatial functions obtained at 2 and 8 Hertz. The bottom row shows temporal functions obtained at the best spatial frequency (i.e., the spatial frequency to which the neuron is most sensitive), and at the same lower (0.125 cycles per degree) or higher (1 cycle per degree) spatial frequency. As noted in the text, the most dramatic differences in contrast sensitivity between these cell classes occurs at lower spatial frequencies. Here, Y-cells are relatively sensitive while X-cells are not (for details, see ref. 147). The Y-cell contrast sensitivity functions represent a composite of linear and nonlinear response components. So and Shapley[242] have recently described the sensitivity of each of these components for Y-cells.

shows typical contrast sensitivity functions for X- and Y-cells. Except at the highest spatial frequencies, Y-cells generally exhibit better contrast sensitivity than do X-cells. The contrast sensitivity for X-cells peaks at some moderate spatial frequency and falls off at lower and higher frequencies. For Y-cells, the spatial function shows little or no sensitivity loss for low spatial frequencies and a monotonic decrease for higher ones. The temporal contrast sensitivity functions appear qualitatively similar for X- and Y-cells, and absolute sensitivity depends upon the spatial frequency of the stimulus (see Fig. 15-2). Thus the most dramatic difference between X- and Y-cells shown by this analysis is in their sensitivity to lower spatial frequencies: here, Y-cells are relatively sensitive and X-cells are not. This rather dramatic difference in sensitivity to lower spatial frequencies is reconsidered below.

and spatial phase angle. Contrast is defined as $(L_{max} - L_{min})/(L_{max} + L_{min})$ where $L_{max}$ and $L_{min}$ are, respectively, the maximum and minimum luminance values across the grating. Contrast is typically changed without changing the mean luminance, which is $\frac{1}{2}(L_{max} + L_{min})$. Spatial frequency is the number of stimulus cycles per degree of visual angle. Temporal frequency (in cycles per second or Hertz) represents temporal changes in the grating. This is achieved either by drifting the grating and calculating temporal frequency from the product of spatial frequency (cycles per degree) and speed of drift (degrees per second), or by counterphasing the grating such that brighter areas gradually become darker and vice-versa, usually in a sinusoidal manner. In both forms of temporal modulation, the average luminance remains constant throughout. The spatial phase angle refers to the position of the grating. A 180-degree phase shift indicates displacement of the grating perpendicular to its orientation by one half of a spatial cycle, a 90-degree phase shift by one quarter, and so forth. The theoretical advantages of sine-wave gratings are discussed in detail elsewhere (e.g., ref. 204). Briefly, Fourier's theorem states that any complex waveform can be created by the superposition of appropriate sine waves properly selected for phase, spatial frequency, and amplitude or contrast (Fourier synthesis); and, conversely, that such a waveform can be described in terms of its component sine waves (Fourier analysis). Black and white visual scenes can be described as complex waveforms for which light intensity is plotted as a function of distance across the scene. Such a scene can be synthesized and analyzed in terms of its component sine-wave gratings. In this context, the sine-wave grating is a fundamental visual stimulus to which the responses can be measured.



## Structure/Function Correlations for Single Neurons

Boycott and Wässle[21] proposed that alpha, beta, and gamma cells are the structural counterparts of, respectively, Y-, X-, and W-cells. This was based upon indirect evidence linking axon diameter to conduction velocity and the size of the dendritic arbor to the receptive-field size.

Subsequent supporting evidence for this correspondence is based on the distribution and central projections of alpha, beta, and gamma cells as inferred from soma size alone. The best evidence is that of Cleland et al.,[34] who were able to correlate the position of nearly every (but not every) recorded Y-cell in a limited patch of retina with a large soma, presumably belonging to an alpha cell. The relationship between beta and X-cells and gamma and W-cells is less secure and more controversial, since there is considerable overlap in their soma sizes.[60, 160, 161, 186] Kelly and Gilbert[136] noted that cells with somata in the size range for beta cells project to regions associated with X-cell projections (lamina A and A1 of the lateral geniculate nucleus), while cells with somata in the gamma cell range project to regions associated with W-cell projections (the superior colliculus). However, Leventhal et al.[160, 161] recently demonstrated epsilon cells that project to regions of the lateral geniculate nucleus associated with W-cells (see below), and which have somata in the beta cell range, and it is still not clear what physiological class is represented by delta cells.[21]

It should be recognized that these structure/function correlations rest on indirect data, and there is some reason to question certain aspects of this hypothesis. As noted above, the morphological classification scheme of Boycott and Wässle[21] is probably incomplete, as these authors have already noted. Also, most of the correlations are made between Nissl-stained material and physiological data, and this necessitates an assumption (reasonable to be sure) about the soma size relationship between Golgi-impregnated and Nissl-stained neurons. In general, the relationship between alpha and Y-cells seems fairly secure, largely because of the heroic experiments of Cleland et al.,[34] but the correspondence among beta, gamma, delta, epsilon, W-, and X-cells is still a matter of some uncertainty.

## Central Projections of W-, X-, and Y-Cells

### W-Cells

The vast majority of optic-tract axons that project to the superior colliculus (i.e., retinotectal axons) are W cells.[60, 99] W cells also innervate the lateral geniculate nucleus. These retinogeniculate axons terminate mainly in the C laminae,[290] but some appear to innervate the medial interlaminar nucleus.[46, 79, 160]‡ There is no evidence of W-cell input to laminae A and A1 (see Fig. 15-3).

### X-Cells

X-cells do not project to the superior colliculus,[60, 99] and their projection is limited exclusively, or nearly so, to the A laminae of the lateral geniculate nucleus,[31, 106, 290] although limited X-cell input to lamina C and the medial interlaminar nucleus has also been described[46, 290] (but see ref. 142). The X-cell projections thus seem fairly well focused onto the A laminae of the lateral geniculate nucleus, and no region outside these laminae receives substantive retinofugal X-cell inputs (see Fig. 15-3).

‡Morphological evidence suggests a fine-fibered[79] retinal input from ganglion cells classified as epsilon[160] to a narrow strip of cells located near the borders of the pulvinar and medial interlaminar nucleus. This presumably represents a W-cell pathway. Some authors have described this as direct pathway from the retina to the pulvinar (e.g., ref. 160). However, Guillery et al.[79] argue that the terminal zone is more properly considered an extension of the lateral geniculate nucleus, and they have termed this extension the *geniculate wing*.

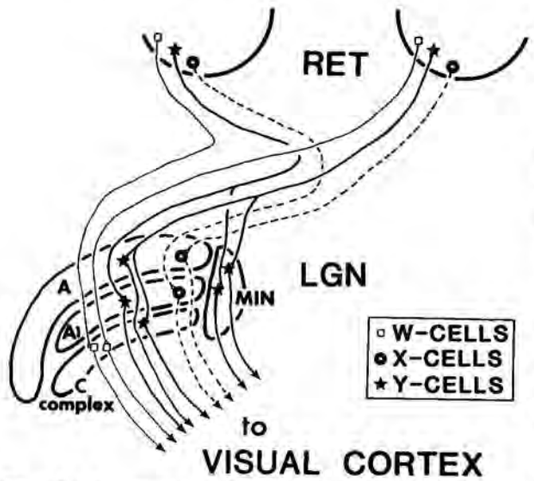


Fig. 15-3 Schematic diagram of the retino-geniculo-cortical pathways in the cat. Three parallel and independent pathways are shown, representing the W-, X-, and Y-cell pathways. RET, retina; LGN, lateral geniculate nucleus. The geniculate subdivisions are indicated for lamina A (A), lamina A1 (A1), laminae C, C1, and C2 (C complex), and the medial interlaminar nucleus (MIN). As illustrated, Y-cells can be found in each of these subdivisions. X-cells are limited exclusively or nearly so to the A laminae, and W-cells are likewise mainly limited to the C laminae.

**Y-Cells**

Y-cells project via branching axons to both the superior colliculus and the lateral geniculate nucleus,[20, 99] although W-cells vastly outnumber Y-cells in the retinotectal pathway.[99] Within the lateral geniculate nucleus (see Fig. 15-3), Y-cells project to the A laminae, the dorsal tier of lamina C, and to the medial interlaminar nucleus.[31, 46, 106, 142, 290] Bowling and Michael[20] found that single optic-tract axons from Y-cells branch to innervate all of these separate geniculate targets as well as the superior colliculus.

### Distribution of W-, X-, and Y-Cells

It is difficult to establish the distribution of W-, X-, and Y-cells across the retina. Physiological estimates are plagued by uncontrolled electrode sampling biases,[60] and while one can determine the distribution of Nissl-stained somata, it is not completely clear how these somata relate to W-, X-, and Y-cells (see the section on structure function correlations for single neurons). The Nissl-stained material offers an additional problem of interpretation, since various workers do not yet agree on the total number of retinal ganglion cells present in such material.[115, 117, 118, 263, 264]

With these qualifications in mind, the following tentative conclusions can be drawn.[34, 60, 186, 197, 263] The density of X-cells peaks sharply at the area centralis, whereas W- and Y-cells exhibit a much flatter distribution. Thus, the relative proportion of X-cells decreases with eccentricity from the area centralis. W-cells do show a slight density increase along the visual streak (a horizontal region of increased ganglion-cell density passing through the area centralis), and Y-cell density peaks slightly in or near the area centralis. Relative numbers of these cell types are based upon the soma size distributions from Nissl-stained material. It is thought that Y-cells comprise only about 5 to 10 percent of the retinal ganglion-cell population, while X- and W-cells comprise the remainder in roughly equal numbers. It is curious that such a small number of Y-cells has such a widespread retinofugal distribution and such a large number of X cells funnels its output nearly exclusively to the A laminae of the lateral geniculate nucleus.

## LATERAL GENICULATE NUCLEUS

### Neuronal Response Properties

With few subtle exceptions, neurons of the cat's lateral geniculate nucleus exhibit receptive-field properties that are indistinguishable from those of retinal ganglion cells.[26, 109, 131, 242] This seems consistent with the observation that each geniculate neuron receives optic-tract input from one or very few retinal ganglion cells of the same functional class.[31] Thus, geniculate neurons can be classified as ON or OFF and W-, X-, or Y-cell, and their properties are virtually identical to those described in the section on physiological cell classes for these classes of retinal ganglion cells.[26, 31, 106, 147, 242] Also, given the retinogeniculate projections of W-, X-, and Y-cells outlined in the section on the central projections of these cells, the location of these cells within the lateral geniculate nucleus is as follows: W-cells are mainly limited to the C laminae, although some can be found in the medial interlaminar nucleus; X-cells are mainly limited to the A laminae; and Y-cells are found in the A laminae, the upper part of lamina C, and the medial interlaminar nucleus.



Each geniculate neuron has an excitatory receptive field for one (dominant) eye, and the dominant eye can be determined by the laminar location of the geniculate neuron. Most geniculate neurons also exhibit a weak, inhibitory receptive field for the other (nondominant) eye.[201] X-cells are inhibited by the Y-cell pathway,[235] and there is some evidence that Y-cells can be inhibited by the X-cell pathway.[106]

### Structure/Function Correlations for Single Neurons

Several investigators have proposed structural correlates for geniculate W-, X-, and Y-cells based on indirect evidence.[152, 290] Recently, Friedlander et al.[56, 57] and Stanford et al.[255] were able to establish these relationships with a direct approach. These authors recorded intracellularly from a geniculate neuron, studied its response properties to identify it as a W-, X-, or Y-cell, iontophoresed HRP into the same neuron, and by subsequent histochemistry were able to obtain morphological data from the physiologically identified neuron. Although the W-, X-, and Y-cell classes each exhibit considerable morphological heterogeneity, each also has characteristic morphological features distinct from the others.

**W-Cells**

W-cells were studied in the C laminae.[255] They have small- to medium-sized somata and thin, sinuous dendrites oriented parallel to the laminar borders. Clustered appendages can be found on the dendrites of some W-cells. Finally, for most W-cells, a rather thin axon can be traced into the optic radiations, and some of these axons emit collateral branches with terminals as they pass through the perigeniculate nucleus. Neurons of the perigeniculate nucleus, in turn, project down into the lateral geniculate nucleus.[1] This seems to form a feedback circuit, and many interneuronal functions can be ascribed to perigeniculate neurons.[47, 242]

**X-Cells**

X-cells were found only in the A laminae.[56, 57] These cells also have small- to medium-sized somata and thin, sinuous dendrites, but the dendritic orientation is perpendicular to the lamination. No dendrite of any X-cell was seen to cross a laminar border. Most X-cells also display a rich array of complex, stalked appendages all along the dendritic tree, and many X-cells exhibit collateral innervation of the perigeniculate nucleus as their intermediate-sized axons proceed toward the optic radiations. In many ways, X-cells resemble W-cells rotated by 90 degrees around an anteroposterior axis.

A rather surprising finding of Friedlander et al.[57] is the presence of some X-cells identified as geniculocortical relay neurons with morphological features previously thought to represent interneurons. Thus, one should question the existence of purely intrageniculate interneurons (see the section on relay cells) and also consider the possibility that geniculate interneurons are located entirely in the perigeniculate nucleus. It is nonetheless likely that at least some interneurons are located entirely within the lateral geniculate nucleus.

**Y-Cells**

Y-cells were studied in the A and C laminae.[56, 57] These neurons have large somata and thick, relatively straight dendrites arranged in a spherically symmetrical arbor. Every Y-cell identified as a relay neuron has at least some dendrites that cross laminar borders. Most Y-cells have few, simple dendritic appendages, but for some of these neurons, clustered appendages can be found at dendritic branch points. Y-cells have thick axons, and nearly all of these provide collateral innervation of the perigeniculate nucleus.

### Distribution of W-, X-, and Y-Cells

The location of W-, X-, and Y-cells within the divisions of the lateral geniculate nucleus has already been described in the section on the neuronal response properties of the lateral geniculate nucleus. The relative proportions of these cells is a question of some debate. Wilson et al.[290] have speculated that W-cells represent only about 15 percent of neurons in the nucleus, but relevant data for W-

cells are sparse and indirect. In the A laminae, most electrophysiological recordings result in X- to Y-cell ratios of roughly 1 to 2:1.[106, 241, 290] It has been argued that this reflects a strong electrode sampling bias in favor of the larger Y-cells, and that the actual geniculate X- to Y-cell ratio is similar to the retinal value of 5 to 10:1 (e.g., ref. 241).

However, Friedlander et al.[57] challenged these assumptions. These authors compared the soma size distribution of HRP-injected neurons with that actually available (based on Nissl-stained material in the same and adjacent sections). No evidence of electrode sampling biases based on soma size was seen, and the relative ratio of X- to Y-cells in the A laminae was inferred to be less than 2:1. Since geniculate Y-cells occur frequently outside of the A laminae and X-cells do not, it is likely that the overall ratio of geniculate X- to Y-cells approaches 1:1. This is a much lower ratio than suggested for the retina, and the possible significance of this is considered below.

### Projections of W-, X-, and Y-Cells

#### W-Cells

Geniculate W-cells have a wide distribution to the visual cortex, often via branching axons, and include all of the cortical areas considered in Figure 15-1.[65, 190] The laminar input to the cortex is best understood in area 17. Here, W-cells terminate in layers I, III, and IV.[154, 157]

#### X-Cells

X-cells distribute exclusive or nearly so to area 17.[86, 171, 265] Most of the termination is limited to the ventral half of layer IV, but some X-cells also project to layer VI.[25, 52, 69, 157] The terminal distribution within layer IV is sufficiently small to be limited to a single ocular dominance column.[52]

#### Y-Cells

Y-cells from the A laminae distribute to areas 17 and 18. Most or all of these project to both areas via branching axons.[65, 265] Y-cells in the C laminae and medial interlaminar nucleus seem to have a wide cortical distribution, including all of the areas shown in Figure 15-1.[65, 195] Again, multiple projections of single cells via branching axons probably occur. In area 17, Y-cells project to the dorsal half of layer IV and to layer VI.[25, 52, 69, 157] The distribution within layer IV of single Y-cell axons is large and discontinuous, and each Y-cell axon probably innervates several ocular dominance columns related to the same eye.[52]

## VISUAL CORTEX

### Cortical Area 17

#### Simple and Complex Cells

In a classical receptive-field study of striate-cortex neurons, Hubel and Wiesel[110] found that practically all such cells could be placed into either simple or complex categories. Simple and complex cells can be found in any cortical layer, although there is a tendency for simple cells to be found in layers IV and VI, and complex cells in layers II, III, V, and VI.[67, 110] Other, rather infrequent categories have also been described, but one of these, the hypercomplex cell, is thought to be a variant of simple or complex cells.[67, 193, 194, 288]

Simple and complex cells share certain features. Most striking is their stimulus specificity. Both types are sensitive to the orientation of elongated targets, and often also to the direction of moving targets, quite unlike the nonselective properties of geniculate neurons. Additionally, both simple and complex cells tend to have binocular receptive fields, presumably due to the convergence of inputs from appropriate geniculate laminae. The relatively few monocular cells include many simple cells in layer IV[207] and cells located in the representation of the area centralis.[2]

Simple and complex cells can be distinguished by the following criteria.[110, 227, 287] First, simple cells exhibit summation within the receptive field, whereas complex cells do not. That is, a stimulus that fills a simple-cell field maximally excites the cell, whereas the best stimulus for a complex cell is smaller than its field. Second, simple cells usually have separate ON and OFF discharge zones, while in complex cells, these zones are superimposed. Third, at matched eccentricities, simple cells have smaller fields, are more sensitive to stimulus orientation, and prefer more slowly moving targets than do complex cells. Finally, simple cells have inhibitory or suppressive receptive-field regions that flank the discharge center, while complex cells display no such inhibition.



#### Columnar Organization

These cells of the striate cortex seem to be functionally organized into "columns" that run across layers, with each column containing both simple and complex cells.[67, 112] Cells encountered along an electrode penetration perpendicular to the layering, and thus within a single column, share a number of functional attributes, such as the preferred orientation for a target. As one proceeds across columns, one sees a gradual, monotonic shift in preferred orientation. Such a gradual shift has recently been demonstrated with metabolic labelling.[3, 203] Furthermore, columnar organization seems to be a basic plan of the neocortex.[174]

#### Structure/Function Correlations for Single Neurons

The neocortex contains two basic morphological neuron types, pyramidal and stellate cells, although other types have been described.[182, 230] Pyramidal cells have large somata shaped more or less like pyramids, with long apical dendrites ascending often to the pial surface, and an array of basal dendrites arrayed roughly parallel to the layering. Stellate cells have less extensive dendrites with a wide variety of dendritic arborizations. Pyramidal cells are found mainly in layers II, III, V, and VI, while stellate cells tend to concentrate in layer IV. Nonetheless, both cell types can be found in all layers.

Attempts have been made to relate these structural cell types to simple and complex cells. Because pyramidal and complex cells on the one hand, and stellate and simple cells on the other, seem to have similar distributions among the layers of the striate cortex, it seemed possible that pyramidal cells were complex and stellate cells were simple. Kelly and Van Essen[137] first obtained direct evidence for these possible relationships with intracellular Procion yellow marking of physiologically identified cells. These authors found most complex and simple cells to be pyramidal and stellate, respectively, but exceptions were noted. Recently, similar studies have generally confirmed this, but have emphasized the lack of a precise structure/function correlation based on the above morphological and physiological classes.[69, 162]

### Cortical Area 18

#### Receptive Fields

Neurons of area 18 are basically arranged into simple and complex classes with laminar and columnar organization similar to those in area 17.[44, 112, 176, 184] However, compared to the receptive fields in area 17, those in area 18 tend to be larger and prefer faster-moving targets. Probably related to this is the preference of area 18 cells, relative to those in area 17, for targets of lower spatial and higher temporal frequencies.

#### Effects of Area-17 Lesions

Area 18 receives two well-defined visual inputs, among others: one from striate cortex and one from the lateral geniculate nucleus. Studies of receptive-field properties of area 18 after acute lesions to area 17,[44] or with reversible inactivation of area 17 by cooling[208] have demonstrated a surprising general lack of change in these receptive-field properties (see, however, ref. 42). It thus seems that geniculocortical inputs to area 18 are sufficient to provide these cortical cells with nearly normal receptive-field properties. The function of the input from area 17 has yet to be elucidated.

### Lateral Suprasylvian Cortex

#### Receptive Fields

Neurons in the lateral suprasylvian cortex tend to have large, binocular receptive fields and are briskly responsive to stimulus motion but poorly responsive to stationary targets. These cells typically display direction, but not orientation, selectivity.[28, 113, 238, 243, 276]

#### Effects of Lesions to Areas 17 and 18

The lateral suprasylvian cortex receives at least three separate visual inputs. These originate from areas 17 and 18, from the geniculate C laminae and medial interlaminar nucleus, and from the posterior and lateral posterior nuclei of the thalamus. Inputs from the C laminae and probably from the posterior

and lateral posterior nuclei represent retino-tecto-thalamo-cortical pathways. Ablation of areas 17 and 18 markedly alters the receptive-field properties of cells in the lateral suprasylvian cortex. Most of these cells postoperatively lose their direction selectivity and sensitivity to stimulation of the ipsilateral eye, and they become sensitive to stationary targets, with poor responsiveness to moving stimuli.

## SUPERIOR COLLICULUS

In many ways, the receptive fields of collicular neurons in the upper three layers seem to resemble those of lateral suprasylvian cortex cells. These collicular cells tend to have large, binocular receptive fields that prefer moving stimuli with direction, but not orientation, selectivity.[196, 259]

Hoffmann[99] described three visual inputs to the superior colliculus (see Fig. 15-4). These include the W-cell direct (retinotectal) pathway, the Y-cell direct (retinotectal) pathway, and the Y-cell indirect (retino-geniculo-cortico-tectal) pathway. The corticotectal neuron has been identified as a complex cell in layer V that receives monosynaptic geniculocortical input from Y-cells[99, 185, 237] (but see ref. 86).

Removal of cortical areas 17 and 18 changes the collicular receptive fields in the same general way that this ablation changes the fields of the lateral suprasylvian cortex. The collicular fields become dominated by the contralateral eye, lose their direction selectivity, and become more sensitive to stationary stimuli and less sensitive to moving ones.[196, 283]

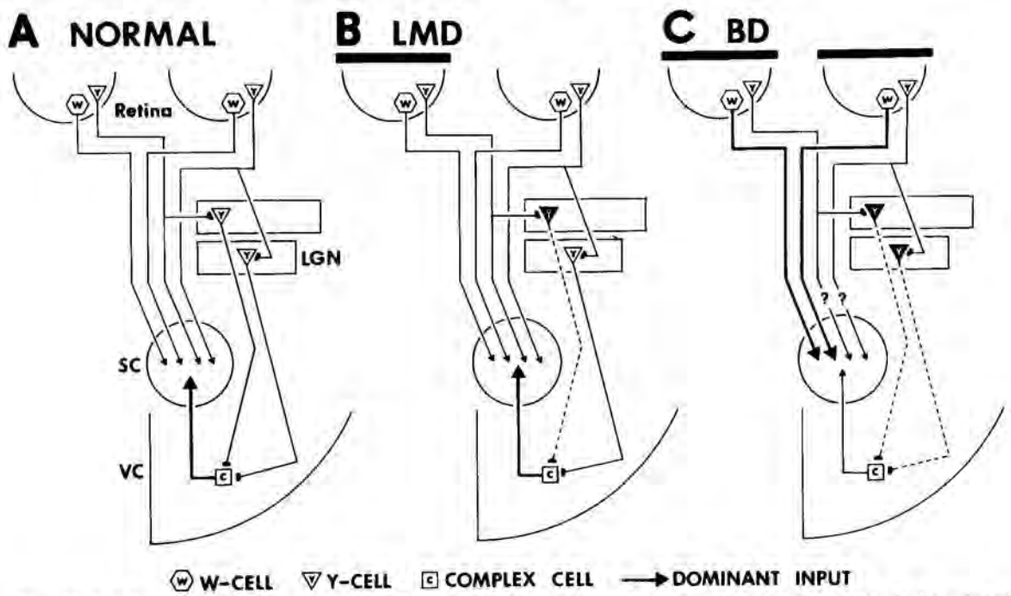


Fig. 15-4 Schematic diagram of visual pathways to the superior colliculus in normal, monocularly sutured, and binocularly sutured cats. (A) Normal pathways. Three pathways have been described:[99] the W-cell retinotectal pathway, the Y-cell retinotectal pathway, and the Y-cell indirect (retino-geniculo-cortico-tectal) pathway involving geniculate Y-cells and cortical complex cells. X-cell participation in collicular innervation has not yet been reported. The dominant input appears to be corticotectal. (B) Pathways in a (left) monocularly sutured cat.[102] The nondeprived pathways and the W- and Y-cell retinotectal pathways from the deprived eye seem normal. The indirect Y-cell pathway from the deprived eye is quite abnormal, apparently because of the abnormal development of Y-cells in deprived geniculate laminae. The dominant input appears to be corticotectal, from the nondeprived eye. (C) Pathways in a binocularly sutured cat.[103] The W-cell retinotectal pathway develops normally, but it is not clear whether this is also true for the Y-cell retinotectal pathway. The Y-cell indirect pathway fails completely to develop, apparently because of poor development of deprived geniculate Y-cells. The dominant input appears to be (W-cell) retinotectal. LGN, lateral geniculate nucleus; SC, superior colliculus; VC, visual cortex. (Hoffmann K-P, Sherman SM: Effect of early binocular deprivation on visual input to cat superior colliculus. J Neurophysiol 38:1049, 1975.)



## FUNCTIONAL ORGANIZATION OF THE CENTRAL VISUAL PATHWAYS

Most detailed hypotheses regarding the functional organization of the visual system have concentrated on geniculostriate pathways (e.g., refs. 110, 112, 151, 266). However, it should be emphasized that bilateral lesions to cortical areas 17 and 18 produce a cat with surprisingly good visual performance.[7, 149, 253] Consequently, most of the information available and most of the concepts regarding functional organization relate to portions of the cat's visual system, such as the geniculostriate pathways, that do not seem essential to reasonable visual capacity (see the section on speculative conclusions).

### SERIAL VERSUS PARALLEL PROCESSING

One of the most important and unanswered questions about the geniculocortical pathways concerns the formation of cortical simple and complex cells from geniculate inputs. Two main hypotheses have been advanced to explain this. These represent serial and parallel processing (see ref. 266 for a review of these hypotheses).

#### Serial Processing

Hubel and Wiesel[110, 112] suggested the concept of a single neural chain from the retina through the lateral geniculate nucleus to the visual cortex. Hierarchy within the chain is inferred from receptive-field complexity. From such an analysis, these authors proposed that a fairly homogeneous population of retinal ganglion cells innervates an equally homogeneous population of geniculate neurons; these geniculate neurons innervate cortical simple cells; simple cells innervate complex cells; complex cells innervate hypercomplex cells; and so forth. The naming of neurons suggests their hierarchical location (e.g., ref. 198). This hypothesis has the great virtue of providing a simplifying theoretical framework for rather complicated data, and it has served as a dramatically productive basis for further investigation of the visual system. Before this theory was offered, notions about the central visual pathways were so rudimentary and confused that useful, specific hypotheses were seldom generated for experimental validation.

Many aspects of this theory of serial processing still seem valid, but others do not. One shortcoming is that the theory does not incorporate the parallel inputs to the visual cortex represented by W-, X-, and Y-cells, for the obvious reason that Hubel and Wiesel[110, 112] generated their hypothesis before Enroth-Cugell and Robson[49] first described X- and Y-cells. Also, some recent evidence seems incompatible with the specific hierarchical placement of neurons in the striate cortex. For example, complex cells respond to various stimuli to which simple cells are rather insensitive,[84, 175] and can be orthodromically and monosynaptically stimulated from the optic radiations as frequently as can simple cells.[23-25, 105, 265] Finally, pharmacological evidence suggests that the inputs to many complex cells do not have orientation selectivity, and therefore cannot be simple cells.[231, 232]

#### Parallel Processing

Stone and his colleagues proposed a parallel processing hypothesis for the organization of the geniculocortical pathways.[105, 106, 262, 265, 266] The serial and parallel processing hypotheses are substantially different but not mutually exclusive. Parallel processing suggests that W-, X-, and Y-cells represent three parallel and functionally independent pathways from the retina through the lateral geniculate nucleus to and through the visual cortex. Each of these pathways analyzes somewhat different aspects of the visual scene (see also below), and the three types of analyses are integrated at some as yet undefined central structure.

The most compelling evidence for this comes from electrical activation of the inputs to the visual cortex.[23-25, 85, 86, 105, 237, 265] Response latency measures for cells in cortical areas 17 and 18 suggest that virtually every neuron that responds to optic-chiasm stimulation can be placed within either the X- or Y-cell pathway without intermixing or convergence between these pathways. W-cell inputs to cortical neurons generally cannot be identified in this manner. Strong receptive-field similarities have also been noted between X- or Y-cells and respective classes of striate-cortex cells.[30, 158]

#### Conclusions

Serial and parallel processing should be regarded as hypotheses rather than tenets. It is presently unclear which, if either, is correct. Perhaps the

geniculocortical pathways are organized into consistent heirarchical pathways, but also that three of these pathways exist in parallel for W-, X-, and Y-cells. The specific relationship of simple and complex cells either to each other or to geniculate W-, X-, and Y-cells remains to be determined.

## Functional Role of Various Cell Types

Another, most important question concerns the role of the various neuron types and pathways in vision. We are far from any genuine answer to this question, but a number of speculations can be considered. These speculations rest upon a number of unsupported assumptions and should not be mistaken for well-accepted tenets. Nevertheless, they are considered below as a useful theoretical framework for the effects of early visual deprivation.

### Serial Processing

As outlined above, the functional implication of the serial processing scheme as proposed by Hubel and Wiesel[110, 112] is relatively straightforward. As the hierarchy within the retino-geniculo-cortical pathways is ascended, neurons become increasingly selective for stimulus parameters. Patterns in the visual scene can thus be inferred from the pattern of responsive cells at the top of the hierarchy.

### W-, X-, and Y-Cells

The presence of W-, X-, and Y-cells suggests that the three separate retino-geniculo-cortical pathways analyze somewhat different aspects of the visual scene. Most suggestions regarding these specific analyses stem from receptive-field differences among W-, X-, and Y-cells.

The functional significance of W-cells is the most difficult to assess, probably because the least is known about this neuron type. Moreover, what little is known about these cells suggests little in the way of their having an important role in the conscious visual perception of stimuli near threshold (i.e., for targets of low contrast, high spatial frequency, or high temporal frequency). W-cells appear to represent only a small proportion of the geniculocortical pathways,[290] they seem to influence cortical cells only rarely,[23-25] and their responsiveness and sensitivity to most visual targets is generally quite poor.[32, 33, 267, 269, 290] Furthermore, in terms of a specific functional role, little is generally attributed to W-cells (cf. ref. 266); however, as we learn more about these cells, this state of affairs could change radically.

Much more specific roles have been proposed for X- and Y-cells. A common proposal is based on the smaller fields, linear spatial summation, preference for slowly moving or stationary targets, and concentration near the representation of the area centralis of X-cells relative to Y-cells (see the section on the distribution of W-, X-, and Y-cells). On the basis of these differences, it is often suggested that X-cells analyze spatial patterns and Y-cells analyze temporal patterns (e.g., refs. 122, 145, 266). Other hypotheses for the functions of X- and Y-cells have also been generated.[151]

The study of spatial and temporal contrast sensitivity functions for geniculate X- and Y-cells has also led to another, quite different hypothesis.[147, 218-220] These spatiotemporal functions reveal a dramatic difference between X- and Y-cells only in response to low spatial frequencies, to which Y-cells are relatively sensitive and X-cells are not (see Fig. 15-2 and the section on W-, X-, and Y-cells). This seems inconsistent with a specific spatial role for X-cells and a temporal one for Y-cells. Instead, psychophysical experiments indicate that the low spatial frequencies to which Y-cells are most sensitive are quite important and even sufficient for excellent form vision, and that the higher spatial frequencies to which X-cells are sensitive provide greater detail and raise visual acuity.[70, 71, 91, 92, 126] It therefore seems reasonable to speculate that Y-cells perform the basic form analysis, while X-cells add to this an analysis of fine spatial details. Again, no specific role can yet be postulated for the rather insensitive W-cells.

Two independent lines of evidence tend to support this view of the X- and Y-cell roles. First, Berkley and Sprague[7] and Lehmkuhle et al.[149] showed that a cat with cortical area 17 completely removed and with some additional loss of area 18 displays remarkably good visual behavior. For most visual tasks, there is practically no pre- and postoperative difference in such an animal. Only at the higher spatial frequencies is a postoperative deficit revealed, and then with a resultant acuity loss of only 20 to 25 percent. Because geniculocortical X-cells project exclusively or nearly so to area 17, while Y-cells (and W-cells) additionally project to numerous extrastriate cortical regions, a cat without significant cortical representation of the X-cell pathway displays a visual deficit only for fine spatial details among the visual capacities tested. The remaining Y-cell (and W-cell) pathways are thereby sufficient for excellent form vision. However, it has not yet been demonstrated that Y-cells are *necessary* for good form vision, nor is it obvious that X-cells alone might not also be sufficient for reasonable visual capacity (see ref. 149).

The second line of related evidence comes from anatomical studies that suggest a tremendous emphasis on Y-cells relative to X-cells in the central visual pathways.[57] For one thing, the X- to Y-cell ratio seems lower for the lateral geniculate nucleus than for the retina. For another, although retinogeniculate and geniculocortical X-cells display a fairly focused distribution, the corresponding Y-cells diverge considerably to innervate much more tissue.[20, 52, 85, 86, 265] Geniculate X-cells innervate only area 17, while Y-cells innervate areas 17, 18, 19, and the lateral suprasylvian cortex (see the section on projections of W-, X-, and Y-cells). Thus the few retinal Y-cells dominate the visual cortex, as compared to the limited influence of the more numerous retinal X-cells (see Fig. 15-5). Perhaps because sensitivity to low spatial frequencies is so important to basic form analysis, much cortex must be devoted to this function, while few peripheral elements (retinal Y-cells) are necessary. Analysis of the less important high spatial frequencies requires

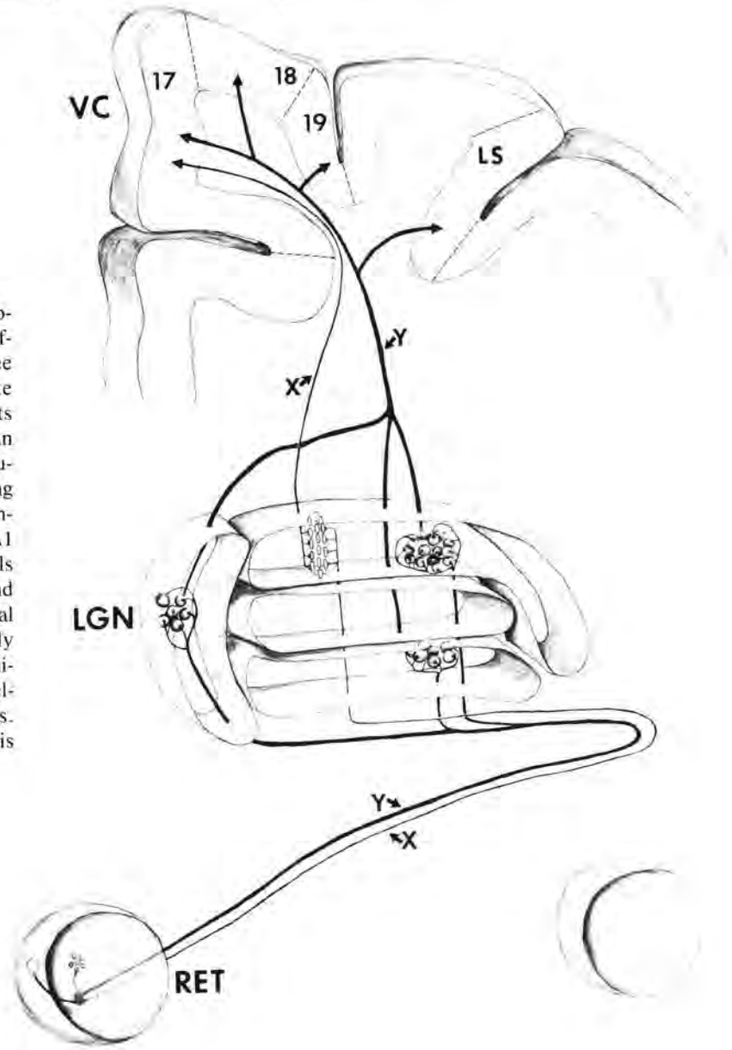


Fig. 15-5 Hypothetical diagram of retino-geniculo-cortical pathways, showing different divergence for X- and Y-cells (see ref. 57 for details). Each retinogeniculate and geniculocortical Y-cell axon contacts many more postsynaptic neurons than does an X-cell axon. The Y-cell geniculocortical pathway is shown as branching from a single axon, but this is an oversimplification. Y-cells from laminae A and A1 project to areas 17 and 18, whereas Y-cells from the medial interlaminar nucleus and lamina C project to area 19 and the lateral suprasylvian cortex. Thus a relatively small proportion of retinal Y-cells dominates much more cortex than does the relatively large proportion of retinal X-cells. The possible functional significance of this is discussed in the text.

less cortex but more peripheral elements (retinal X-cells).

### Conclusions

It must again be emphasized that the foregoing discussion represents speculative material that for the moment serves as little more than a working hypothesis on the role of the various neuron types and pathways in vision. However, since, as we shall see, the W-, X-, and Y-cell pathways seem to be affected quite differently from one another during rearing with visual deprivation, it is important to understand the functional roles of these cell types. In many ways, the notion that Y-cells are particularly important to basic form analysis leads to the clearest interpretation of the significance of data from visually deprived cats. This notion is thus useful to consider. Unfortunately, there is little direct evidence to support it.

## BINOCULAR AND MONOCULAR SEGMENTS

A final organizational feature of the cat's central visual pathways to be considered before discussing visually deprived cats is a division of these pathways into binocular and monocular segments (Fig. 15-6). This division is useful because, as reviewed in the following section on monocularly deprived cats, monocular deprivation affects these segments differently.

The horizontal visual field of a cat extends from 90 degrees left to 90 degrees right.[211, 254] Within this is a central region, from 45 degrees left to 45 degrees right, that is viewed by both eyes; this is the binocular segment. The peripheral segment from 45 to 90 degrees on each side is viewed only by the extreme nasal retina on that side; these are the monocular segments. Because the visual field is retinotopically mapped onto each of the central visual structures considered in this review, the binocular and monocular segments can be defined for each of these structures.

In the lateral geniculate nucleus, for example, the binocular segment is represented by input from the ipsilateral temporal retina and the corresponding contralateral nasal retina (Fig. 15-6). Lamina A1 and the corresponding portion of lamina A are in the binocular segment. The monocular segment includes the region where lamina A extends laterally beyond lamina A1, and the cells in this segment have receptive fields beyond 45 degrees eccentric

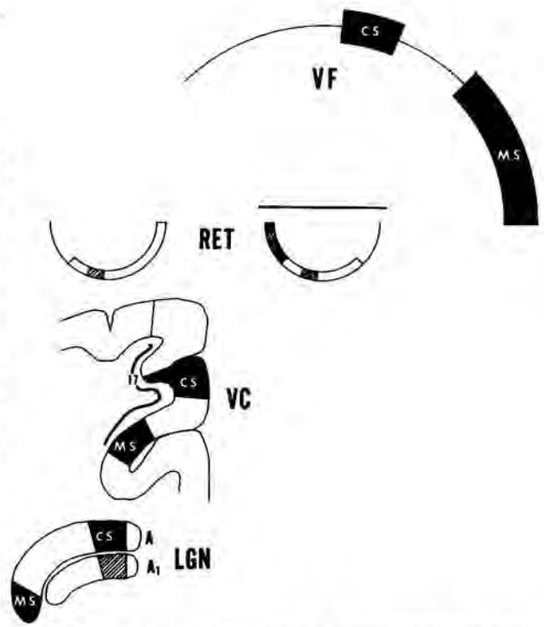


Fig. 15-6 Schematic drawing of the binocular and monocular segments in the cat's visual field and central visual pathways. In this example, the right eye is sutured and its monocular segments are illustrated. Both natural (MS) and artificial (CS) monocular segments are shown. The artificial monocular segment has also been called the critical segment.[77] The natural monocular segment relates to the extreme nasal retina of the right eye, which extends beyond the corresponding portion of the left eye's temporal retina. There is thus a portion of the visual field (VF), lateral geniculate nucleus (LGN), and area 17 of the visual cortex (VC) representing only the right eye. By making a retinal lesion in the left eye (cross-hatching), the corresponding portion of the right retina becomes an artificial monocular segment, with monocular regions of visual field and the central visual pathways as shown. (Modified from Sherman SM: Development of the lateral geniculate nucleus in cats raised with monocular eyelid suture. In Freeman RD, ed: Developmental Neurobiology of Vision. New York, Plenum Press, 1979.)

from the area centralis in the contralateral hemifield (for further details, see refs. 77, 81, 102, 106, 222, 223, 248, 288, 289).

The monocular segment considered above is the naturally occurring one. An artificial monocular (or "critical") segment can also be created by making a lesion in the binocular segment of one retina (see Fig. 15-6). Such a preparation has been most useful in the study of monocularly sutured cats (e.g., refs. 77, 222, 228).



## MONOCULARLY DEPRIVED CATS

The literature abounds with descriptions of the effects of monocular eyelid suture on the development of the central visual pathways. Far more is known about the consequences of this deprivation condition than any other. A particular advantage of this experimental preparation is that it offers an internal control: that is, one can compare neurons or structures related to the deprived eye with those related to the open eye within a single cat, although this does not imply that the open eye has no effect on connections formed by pathways related to the closed eye (or vice-versa).

To the extent that nondeprived cells and pathways are normal, this intrasubject comparison constitutes an important control. Generally, response properties related to the nondeprived eye are normal in monocularly sutured cats, with few reported exceptions (e.g., ref. 289). There is, however, clear hypertrophy noted for certain neurons and pathways related to the nondeprived eye.[95, 155, 207]

Unfortunately, few experiments are actually designed to study cats raised from birth to complete adulthood (i.e., at least 6 to 12 months) with monocular suture. The experiments considered below are lumped together because they seem to involve deprivation during a sufficiently large portion of the critical visual development period[15, 114] to permit a reasonably consistent understanding of the developmental events during this period.

## RETINA

Studies of deprived retinal ganglion cells and optic tract fibers consistently yield data within the normal range. These cells display normal soma sizes,[226] qualitatively normal response properties,[285] and a normal distribution of W-, X-, and Y-cells.[226] Contrast sensitivity and resolution are also normal for deprived retinal X- and Y-cells,[138] and this has been extended to normal spatial acuity for deprived X-cells in the area centralis.[35] Finally, Jones[124] recorded gross potentials in the optic tract evoked by a temporally modulated patch of light, and found no difference in the stimulation of deprived and nondeprived eyes. Therefore, the abnormalities seen in the central visual pathways of monocularly deprived cats probably occur central to the optic tract.

## LATERAL GENICULATE NUCLEUS

The lateral geniculate nucleus represents the most peripheral site for which well-documented effects of early lid suture occur. Both morphological and physiological abnormalities have been described. None of these abnormalities seem to be related to any physical loss of cells, since counts among geniculate neurons innervated by the sutured eye indicate normal cell numbers.[128, 143]

### MORPHOLOGY

#### Soma Sizes

Wiesel and Hubel first observed that somata in deprived geniculate laminae A and A1 (i.e., the A laminae that receive direct retinal afferents from the deprived eye) are smaller than those in the nondeprived A laminae. This has since been confirmed by every published study of soma sizes in monocularly sutured cats (e.g., refs. 77, 81, 93, 95, 128, 152, and many others).

Hickey et al.[95] argued that this soma-size pattern results mainly from deprived somata that are smaller than normal, but that there is also significant hypertrophy of nondeprived somata. Kalil,[128] however, has challenged this conclusion with the claim that no substantive hypertrophy occurs among nondeprived somata. This point must remain somewhat doubtful until future studies explain these discrepant results.

The foregoing descriptions apply to laminae A and A1. Kratz et al.[143] showed that deprived somata of the medial interlaminar nucleus are also smaller than their nondeprived counterparts. Hickey[93] reported that deprived lamina C somata show similar effects of deprivation, but that laminae C1 and C2 do not show significant changes. It may be that W-cells are not substantially affected by lid suture.

Guillery and Stelzner[81] extended these observations in a crucial manner by showing that such soma-size changes in deprived laminae A and A1 are practically limited to the binocular segment. That is, the deprived monocular segment of lamina A contains somata of normal size. However, Hickey et al.,[95] reported that the deprived monocular segment of lamina A exhibits slightly smaller than normal soma sizes. There is still agreement that the soma-size changes are substantially greater in the binocular than in the monocular segment.

This difference in the effects of lid suture on the binocular and monocular segments of the central visual pathways is a recurring theme of this chapter and is considered repeatedly below.

Guillery[77] offered an important control for these observations. He raised kittens with monocular suture and a neonatal lesion made near the central retina of the open eye. This created two monocular segments for the deprived eye: a natural one and an artificial one (called the "critical segment" by Guillery[77]) related to the retinal area corresponding to the lesion in the open eye (see Fig. 15-6). Guillery[77] showed that both deprived monocular segments (i.e., the natural and the artificial) of the A laminae exhibit the same relatively normal soma-size distribution. This establishes that the deprived monocular segment is relatively unaffected in terms of soma growth not because it is found in lamina A or maps the peripheral visual field, but because it maps a monocular segment of the visual field. In other words, the artificial monocular segment typically maps a fairly central portion of the visual field and can be located in deprived lamina A1.

Given the importance attached to these differential effects of lid suture on the binocular and monocular segments, it seems worth noting that these differences have been studied for the lateral geniculate nucleus only in the A laminae. No published account describes a similar analysis for the C laminae or the medial interlaminar nucleus.

### Geniculocortical Projections

The effects of lid suture on the geniculocortical projections have been investigated with both orthograde and retrograde tracing techniques. These studies have been limited to the binocular segment of the A laminae and visual cortex.

Shatz and Stryker[207] employed autoradiography of striate cortex tissue following intraocular injection of tritiated markers and the transneuronal transport of these markers to the cortex. These authors found that ocular dominance columns in layer IV related to the deprived eye become abnormally small, while those related to the nondeprived eye hypertrophy. The shape of the deprived patches is interesting, since they are larger ventrally than dorsally. Thus, the X-cell input to ventral layer IV is less affected by lid suture than is the Y-cell input to dorsal layer IV (e.g., refs. 25, 52, 69).

Both Garey and Blakemore[62] and Lin and Sherman[164] used a retrograde tracing method to study the differential effects of lid suture on the cortical projections from the lateral geniculate nucleus to areas 17 and 18. HRP was injected separately into each area, and the pattern of labelling was noted in the A laminae. Deprived laminae exhibited labeled neurons that were smaller[62] and fewer in number[164] than those in the nondeprived laminae. However, both of these abnormalities were found to be considerably more severe following the injection of HRP into area 18 than after its injection into area 17. Therefore, the Y-cell pathway to area 18 is more affected by lid suture than is the pathway to area 17 that includes X- and Y-cells mixed together (cf. ref. 265).

Two conclusions can be drawn from these studies. First, anatomical changes due to lid suture can be found in the geniculocortical projections, and these changes tend to be larger for the Y-cell pathway than for the X-cell pathway. Second, despite these changes, many deprived geniculocortical axons develop in monocularly sutured cats.

### Cytoplasmic Laminated Bodies

LeVay and Ferster[152] divided geniculate neurons in the A laminae into three types on the basis of their soma size and the presence or absence of a "cytoplasmic laminated body." This body is a small aggregated clump of parallel tubules located in the cytoplasm (see ref. 129 for a further discussion of such structures among other neuron populations). According to LeVay and Ferster,[152] the type 1 neuron has a large soma without a cytoplasmic laminated body, the type 2 neuron has an intermediate-sized soma with a cytoplasmic laminated body, and the type 3 neuron has a small soma with no cytoplasmic laminated body. LeVay and Ferster[152] showed that the type 3 cell is unaffected by lid suture, that the type 2 cell is moderately affected, and that the type 1 cell is most severely affected. Slightly fewer normal type 1 cells are found in deprived laminae, and these cells are much smaller than normal. However, since deprived type 2 cells are also somewhat smaller than normal, they are still slightly smaller than type 1 cells in deprived laminae.

Of particular interest with regard to this classification scheme is the suggestion by LeVay and Ferster[152] that, in the normal cat, type 1 cells are Y-cells and type 2 cells are X-cells (see also refs. 129, 202). This has been partially confirmed by Friedlander et al.[57] for normal cats, but it is not clear that the same structure/function correlation applies to deprived neurons.[58]



## Single Neuron Response Properties

Most recent physiological studies of deprivation effects in the lateral geniculate nucleus have focused on X- and Y-cells. No published studies of the effects of visual deprivation on W-cells have yet appeared.

### X-Cells

Sherman et al.[223] pointed out the relatively normal properties of deprived geniculate X-cells. These cells were found in normal numbers and exhibited brisk responses to visual stimuli. However, more detailed receptive-field analyses, based on the generation of contrast sensitivity functions, have revealed a subtle deficit for deprived X-cells in the form of a reduced spatial acuity.[104, 148, 167, 169] This reduced spatial acuity is due to a reduction of sensitivity only to higher spatial frequencies, since normal sensitivity develops to lower frequencies. Furthermore, this X-cell deficit exists to the same extent in the deprived binocular and monocular segments of the A laminae.[148]

Recently, Shapley and So[205] raised doubts that this subtle deficit for deprived X-cells occurs at all. These authors found no difference in the spatial acuity of deprived and nondeprived X-cells, although the overall acuity values they reported were as low as those reported for deprived X-cells in prior studies.[104, 148] The issue of whether there is any effect of deprivation for geniculate X-cells must therefore remain in doubt, although any such effect is clearly small.

### Y-Cells

Sherman et al.[223] first noted that Y-cells are fairly selectively affected by early visual deprivation. After monocular deprivation, few normal Y-cells could be recorded in the binocular segment of deprived laminae A or A1, although a normal complement of Y-cells was found in the deprived monocular segment (see Fig. 15-7). This analysis was extended to monocularly deprived cats raised with an artificial monocular segment (see the section on soma sizes). Here, deprived Y-cells were recorded mainly in the natural and artificial monocular segments, but not in the binocular segment.[228] Furthermore, not only is the loss of recorded Y-cells limited to the binocular segment, but also deprived Y-cells in the monocular segment exhibit normal spatiotemporal contrast sensitivity.[148] The pattern

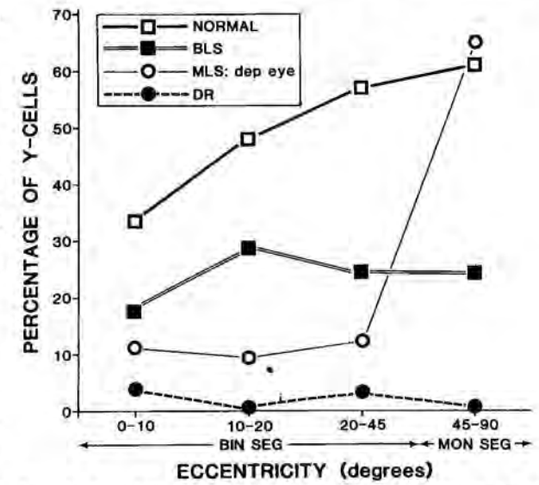


Fig. 15-7 Relative percentage of Y-cells as a function of eccentricity in the geniculate A laminae of normal and visually deprived cats. This represents combined electrophysiological data from the laboratory of one of the authors (S.M.S.) and includes nearly 2,000 neurons. The percentage of Y-cells refers to the number of recorded Y-cells divided by the total number of X- and Y-cells. In the A laminae, X- and Y-cells comprise over 95 percent of the recorded neuronal population. Eccentricity refers to the distance of a neuron's receptive field from the area centralis, and four groupings are indicated (0 to 10 degrees, 10 to 20 degrees, 20 to 45 degrees, and 45 to 90 degrees), as well as the binocular and monocular segments of the visual field. In normal cats, the proportion of recorded Y-cells rises monotonically with increasing eccentricity. In binocularly sutured (BLS) cats, a moderate loss of recorded Y-cells develops for all eccentricities. For the deprived eye of monocularly sutured (MLS) cats, few Y-cells are recorded in the binocular segment, but the monocular segment contains the normal complement of Y-cells. The nondeprived eye of these cats has associated with it an essentially normal distribution of geniculate Y-cells. For dark-reared (DR) cats, the loss of recorded Y-cells is most severe and occurs for all eccentricities. Note the different effects of these forms of visual deprivation in the monocular segment (see text for details). (Modified from Sherman SM: Development of the lateral geniculate nucleus in cats raised with monocular eyelid suture. In Freeman RD, ed: Developmental Neurobiology of Vision. New York, Plenum Press, 1979.)

of Y-cell changes caused by monocular suture is thus quite different from that of X-cell changes: Y-cell abnormalities are limited to the deprived binocular segment, whereas the abnormalities in X-cells are equal in both the binocular and monocular segments.[148]

Kratz et al.[143] reported few normal Y-cells in deprived portions of the medial interlaminar nucleus, although many cells with abnormal receptive fields were recorded there. Since this region represents a nearly exclusive Y-cell domain,[46, 142] many neurons that normally would develop into Y-cells in the medial interlaminar nucleus presumably develop abnormal properties as a result of monocular deprivation.

Although it has been repeatedly observed that deprived Y-cells are difficult to record,[50, 66, 100, 101, 223, 228, 291] (but see ref. 205), and this correlates in a general way with other morphological and physiological data, the interpretation of this loss of recorded Y-cells is far from clear. Two general explanations have been offered. First, that the smaller deprived somata might create unusual electrode sampling characteristics such that Y-cells are actually present and fairly normal, but difficult to record.[50, 205, 223] Second, that these data reflect a genuine and significant functional pathology in the Y-cell pathway.

Given the potential importance of Y-cells to normal vision (see the section on functional roles of W-, X-, and Y-cells), it is important to establish the nature of the Y-cell deficits. No single experiment completely establishes the extent to which the data that have been collected represent electrode sampling artifacts or functional abnormalities, and it is therefore not yet possible to choose unequivocally between the alternatives. However, when all of the relevant data are considered together (see also below), an impressive case can be made that the loss of recorded Y-cells in deprived laminae represents a genuine functional abnormality (for details, see ref. 225).

### Evoked-Potential Studies

Two studies of evoked potentials in the lateral geniculate nucleus have produced further evidence of retinogeniculate deficits in monocularly sutured cats. In one, Jones[124] studied gross potentials evoked by stimulation of each eye with a diffuse light spot flickered at various rates. These potentials were roughly equivalent for each eye at lower flicker rates, but at higher rates the potentials evoked by stimulation of the deprived eye were markedly smaller than those from the nondeprived eye. Since similar evoked potentials recorded in the optic tract revealed no abnormalities, this reduction in potential represents a retinogeniculate deficit. Also, since Y-cells are normally much more sensitive than X-cells to lower spatial and higher temporal frequencies, Jones[124] argues that these evoked-potential data represent a fairly selective loss of transmission in the deprived Y-cell pathway, with little or no deficit in the X-cell pathway.

In the second study, Mitzdorf and Neumann[170] calculated the retinogeniculate synaptic current sources and sinks from the second spatial derivative of geniculate potentials evoked by electrical stimulation of the optic nerves (i.e., a current-source density analysis). From the latency of these potentials, these authors could distinguish X-cell synaptic currents from those of Y-cells. They concluded from this that lid suture significantly, and roughly equally, affects retinogeniculate transmission for the X- and Y-cell pathways.

Both of these evoked-potential studies suggest that monocular deprivation produces a retinogeniculate transmission failure within the Y-cell pathway; however, the two studies disagree over the existence of a similar deficit in the X-cell pathway. Whether this discrepancy reflects differences in methodology (e.g., electrical versus visual stimulation) or other factors is presently unclear. In any case, there is no straightforward relationship between these evoked-potential data and the morphological or single-unit physiological data considered above.

### Structure/Function Correlations for Single Cells

Indirect evidence suggests that, as compared to their nondeprived counterparts, both deprived X- and Y-cells are abnormally small, that this abnormality is more pronounced for Y- than for X-cells, and that deprived Y-cells nonetheless are larger than deprived X-cells.[62, 152] Since the Y-cell abnormalities are limited to the binocular segment of the A laminae while the X-cell abnormalities are not, this might explain why soma sizes seem much more affected by lid suture in the binocular than in the monocular segment.[95]



Recently, Friedlander et al.[58] obtained direct structure/function relationships for A laminae neurons in monocularly deprived cats. Not surprisingly, nondeprived neurons and many deprived X-cells have normal structure/function relationships (see ref. 57). However, two types of unusual structure/function relationships were noted for deprived neurons that might at least partially explain the loss of recorded Y-cells. First, some abnormally or poorly responsive cells thought to be abnormal Y-cells have structural features never seen in normal neurons. These cells possess extremely fine, sinuous, varicose dendrites that comprise a very dense and extensive arbor. Second, some cells physiologically identified as X-cells have morphological features of normal Y-cells, including large somata and thick, cruciate dendrites arranged in a spherically symmetrical arbor. It seems that somehow, as a result of the lid suture, some geniculate neurons that, under normal conditions, accept or maintain optic-tract inputs only from Y-cells, accept or maintain X-cell inputs instead.

## CORTICAL AREA 17

### Single-Neuron Response Properties

#### Receptive Fields

The body of literature devoted to receptive-field studies of the striate cortex in monocularly deprived cats is perhaps the best documented and least controversial of any related to mammalian visual development. Instead of the binocularly activated simple and complex cells seen in normal cortex, the cortex of monocularly deprived cats is dominated by the nondeprived eye. Most of these cells are normal simple or complex cells that can be influenced only by the nondeprived eye; only 5 to 10 percent of the neurons can be influenced by the deprived eye, typically in an abnormal fashion.[38, 100, 140, 207, 222, 233, 239, 247, 286, 289] These observations are common throughout the binocular segment. However, Shatz and Stryker[207] noted that somewhat more activity can be influenced by the deprived eye among neurons in layer IV, and indeed, that some of these neurons display fairly normal simple receptive fields for the deprived eye.

In contrast to the inability of the deprived eye to influence neurons in the binocular segment, this eye can activate many neurons in the natural and artificial monocular segments of the striate cortex.[222, 289] Furthermore, the normal proportion of normal simple cells is observed in this cortex, with the remaining cells being either abnormally unselective for stimulus parameters or unresponsive to visual stimuli. Thus, the deprived eye develops normal pathways to simple cells in the monocular but not in the binocular segment. By contrast, normal complex cells are rare in the deprived monocular segment. Thus, deficits are seen in the deprived monocular segment, particularly with regard to the development of complex cells, but these deficits for the deprived eye seem much less pronounced than those in the binocular segment. In many ways these conclusions resemble those from the analysis of abnormalities in the lateral geniculate nucleus described above.

#### Subthreshold Afferents from Deprived Geniculate Laminae

Although anatomical data provide clear evidence for the presence of many geniculostriate axons arising from deprived laminae, few receptive fields in the binocular segment of the striate cortex can be influenced by the deprived eye. There is now compelling evidence from three sets of experiments of the presence of many subthreshold geniculostriate inputs representing the deprived eye.

First, if the nondeprived eye is removed in adulthood, the percentage of striate cortex cells that can be activated by the deprived eye increases within a few hours from roughly 5 percent to over 30 percent.[38, 100, 140, 239, 247] Receptive fields for the deprived eye, however, continue to be quite abnormal. This rather sudden increase in responsiveness suggests that inputs representing the deprived eye are present in cortex, but are expressed in a suprathreshold fashion only after removal of the nondeprived eye.

Second, intravenous injection of either bicuculline or ammonium acetate similarly increases, to over 50 percent, the proportion of cortical neurons that respond to the deprived eye.[48] This increase in responsiveness occurs within seconds after the drug injection, and has been observed reversibly for single neurons. Duffy et al.[48] suggest that afferents from the deprived geniculate laminae are present in striate cortex but that their influence is tonically inhibited; interference with presumed inhibitory transmitter systems by the injection of bicuculline

or ammonium acetate reveals these afferents. Recently, Burchfiel and Duffy[27] repeated these observations with the "micro-iontophoretic" application of bicuculline into striate cortex.

Third, single-unit studies of area 17 have also employed electrical stimulation of the optic nerves. Just as these cortical neurons in the binocular segment do not respond to visual stimulation of the deprived eye, neither do they respond to electrical stimulation of the deprived optic nerve.[14, 233, 274] However, Tsumoto and Suda[274] showed that, if a neuron's threshold is lowered by visual stimulation of the nondeprived eye, the neuron frequently will respond to electrical stimulation of the deprived optic nerve. The conduction latency of such activation suggests X-cell rather than Y-cell input. It thus appears that many (X-cell) geniculostriate afferents represent the deprived eye, but only as subthreshold inputs.

### Evoked-Potential Studies

Three studies of gross potentials recorded in the striate cortex further indicate the presence of geniculocortical X-cell afferents and the relative absence of those from Y-cells.

First, Jones and Berkley[124] and Jones[125] measured the potentials evoked by stimulating each eye with a flickering field of light. As compared to stimulation of nondeprived pathways and pathways in normal cats, stimulation of the deprived pathways evoked much smaller potentials at higher flicker rates. This was interpreted as a deficit in the Y-cell pathway, since Y-cells are more sensitive than are W- or X-cells to higher temporal frequencies (see above and Fig. 15-2).

Second, Snyder and Shapley[240] and Bonds et al.[19] reported analogous results. Their studies employed sine-wave gratings as the stimulus, and the spatial rather than temporal frequency of the stimulus was varied (see footnote on p. V:389 for a description of this stimulus). Here, deficits in the evoked potential were more pronounced for lower than for higher spatial frequencies. Again, deficits in the Y-cell pathway are implicated, since Y-cells are much more sensitive than are W- or X-cells to lower spatial frequencies.

Third, Mitzdorf and Singer[171] calculated the current source densities evoked in area 17 by electrical stimulation of each optic nerve. The latencies of these evoked potentials were used to identify them as a consequence of X- or Y-cell input (W-cell input proved difficult to identify). These authors concluded that synaptic currents are very much reduced along the deprived pathways, but that this reduction is considerably more marked for the deprived Y-cell than for the deprived X-cell input.

In general, these evoked-potential data tend to support the aforementioned conclusions: first, that input from deprived geniculate laminae remains following monocular suture, even though few cells exhibit receptive fields for the deprived eye; and second, that the deprived X-cell geniculocortical input seems less affected by lid suture than does the deprived Y-cell input.

## CORTICAL AREA 18

Area 18 represents a particularly interesting region in monocularly sutured cats, since it normally receives W- and Y-cell but not X-cell input from the lateral geniculate nucleus (see the above section on projections of W-, X-, and Y-cells). Unfortunately, only two studies have been published on the effects of monocular lid suture on the development of area 18 neurons.

Singer[234] recorded properties of the responses evoked by visual and electrical activation of the visual pathways. Ocular dominance was assessed chiefly on the basis of electrical activation, although in two cats this was correlated with ocular dominance assessed by more traditional visual stimulation. Singer[234] concluded that very few cells in area 18 ipsilateral to the deprived eye can be activated by electrical stimulation of the deprived optic nerve. Curiously, many, but still abnormally few, cells contralateral to the deprived eye can be excited via the deprived pathway. This interhemispheric difference is puzzling.

Mitzdorf and Singer[171] extended their current source density analysis to area 18 in monocularly sutured cats. They concluded that geniculocortical synaptic currents along the deprived Y-cell pathway to area 18 are greatly reduced by roughly the same amount as seen in the deprived Y-cell pathway to area 17. No interhemispheric difference was noted in this reduction. Current sources generated through W-cell geniculocortical connections are not clearly defined by the current source density method as used by Mitzdorf and Singer.[171] It it thus possible that the interhemispheric difference in the effects of monocular suture on area 18 neurons, as described by Singer,[234] might reflect interhemispheric differences in the deprived W-cell input to area 18.



## SUPERIOR COLLICULUS

### General Response Properties

As expected, the receptive fields of collicular neurons are essentially normal for the nondeprived eye of the monocularly sutured cat, but few neurons in the binocular segment can be influenced by the deprived eye.[102, 284] Furthermore, most of the few receptive fields associated with the deprived eye are abnormal, since they lack direction selectivity and respond well to stationary targets. Hoffmann and Sherman[102] reported that these deficits are effectively limited to the binocular segment. Neurons in the deprived monocular segment have normal receptive-field properties for the features studied.

However, although the pattern described above seems to be the general result of monocular suture, exceptions to it have been noted: patches of colliculus contralateral to the deprived eye,[102] and in some cats the entire colliculus contralateral to the deprived eye[9] seem to be dominated by that eye. The reason for this variability is not at all clear.

### Afferents to the Superior Colliculus

Hoffmann[99] analyzed the afferents to the superior colliculus by means of electrical stimulation, and described three pathways: a major, direct retinotectal W-cell pathway; a minor, direct retinotectal Y-cell pathway; and a major, indirect retino-geniculo-cortico-tectal Y-cell pathway. The same analysis has been applied to monocularly sutured cats.[102] The deprived retinotectal pathways, both W- and Y-cell, seem unaffected by the lid suture. However, abnormally few collicular cells can be influenced from the deprived eye along the indirect Y-cell pathway (see Fig. 15-4B). This is consistent with the notion that gesticulate Y-cells, an integral link in the indirect pathway, do not develop normally in deprived laminae.[223]

The conclusions reached by Hoffmann and Sherman[102] confirmed those reached earlier by Wickelgren and Sterling.[284] These latter authors first described the dramatic effect of lesions of the visual cortex (areas 17, 18, and 19) on neuronal ocular dominance in the superior colliculus. Preoperatively, neurons in both the right and left colliculi are dominated by the nondeprived eye, but postoperatively these neurons are dominated by the contralateral eye, whether deprived or nondeprived. In terms of both ocular dominance and other receptive-field properties, normal and monocularly deprived cats exhibit virtually identical response properties for collicular neurons following removal of the visual cortex.

Two conclusions can be drawn from these studies.[102, 284] First, retinotectal inputs develop normally during monocular deprivation, with collicular deficits due to lid suture reflecting an abnormal corticotectal input. Second, subthreshold retinotectal inputs from the deprived eye must exist, since they are revealed by cortical removal; this may be analogous to subthreshold inputs to the striate cortex from the deprived eye that can be revealed after removal of the nondeprived eye.

## LATERAL SUPRASYLVIAN CORTEX

The analysis of deprivation effects on neurons in the lateral suprasylvian cortex is complicated because this cortex is innervated by at least three major visual pathways: the geniculocortical pathway from the C laminae and medial interlaminar nucleus, the corticocortical pathway from the visual cortex (areas 17 and 18), and a retino-tecto-thalamo-cortical pathway (see the section on effects of lesions to areas 17 and 18). In many ways, the effects of monocular suture on the development of the lateral suprasylvian cortex resemble those on collicular development discussed in the previous paragraphs.

### General Response Properties

Spear and Tong[248] recently reported that, following monocular deprivation, few lateral suprasylvian cortex neurons have receptive fields for the deprived eye, and that those that do tend to have abnormal receptive fields for that eye. By contrast, most cells in the deprived monocular segment are clearly responsive, but their fields are abnormal. As is the case with the other visual structures analyzed separately for the monocular and binocular segments, monocular deprivation affects deprived neu-

rons more substantially in the binocular than in the monocular segment, although abnormalities are also present in the monocular segment.

### Afferents to the Lateral Suprasylvian Cortex

Tong and Spear[272] compared deficits in the lateral suprasylvian cortex before and after removal of the visual cortex (areas 17 and 18), in an effort to determine the site of abnormalities. Ipsilateral to the deprived eye, deficits in the lateral suprasylvian cortex are secondary to an abnormal visual cortical input. That is, after similar cortical removal, normally reared and monocularly sutured cats exhibit little difference in their lateral suprasylvian cortical neurons. After such a lesion, most neurons are dominated by the contralateral (nondeprived) eye, with abnormal receptive-field properties.

Contralateral to the deprived eye, the situation is more complex. After visual-cortical lesions, neurons in the lateral suprasylvian cortex exhibit a bimodal ocular-dominance distribution: they are dominated by one or the other eye in roughly equal numbers. Nevertheless, the receptive fields are quite abnormal for either eye, as is the case in normally reared cats with such a visual cortex lesion.

In both hemispheres, one can conclude that inputs from the visual cortex, representing the deprived eye, are abnormal. However, abnormalities in the thalamocortical input are limited to the hemisphere contralateral to the deprived eye, and these abnormalities involve both eyes. There is a decreased input from the contralateral deprived eye and an increased input from the ipsilateral nondeprived eye.[272]

## BINOCULARLY COMPETITIVE AND NONCOMPETITIVE MECHANISMS

At nearly every level of the central visual pathways considered above, there are differences in the abnormalities that develop in the binocular and monocular segments during monocular deprivation. In all cases studied so far, the natural monocular segment and artificial one created by a retinal lesion respond to lid suture in a similar manner.[77, 222, 228] Also, the abnormalities caused by lid suture are generally more severe in the binocular than in the monocular segment, although deficits are consistently found in the monocular segment. These patterns can be used to deduce with reasonable confidence whether a binocularly competitive or noncompetitive mechanism is involved in the development of the central visual pathways (for further details of such analysis, see refs. 77, 81, 222, 223, 225).

### Identification of Binocular Competition

Wiesel and Hubel[287] first suggested a process of binocular competition for development of the central visual pathways on the basis of a comparison of the striate cortex deficits seen following monocular and binocular suture. This comparison is considered in the section on competitive and noncompetitive mechanisms of development. The concept of binocular competition implies that, during development, pathways related to each eye compete with one another for the development, maintenance, and (or) elimination of central connections.

In the years since Wiesel and Hubel[287] proposed the process of binocular competition, we have been able to specify neither the synaptic mechanisms by which binocular competition occurs nor the neural site of its action. Nevertheless, Figure 15-8 illustrates this process by assuming that it occurs among geniculostriate synapses. Perhaps during the first few postnatal weeks there is a dramatic increase in the number and (or) strength of these synapses, and they somehow compete for postsynaptic space on and control of the cortical neuron. With a normal, binocular environment, synapses from neither lamina in the binocular segment gain a competitive advantage, a balanced synaptic development ensues, and the cortical cell becomes binocular (Fig. 15-8 left). However, the closure of one eye somehow confers a competitive advantage on neurons in the nondeprived laminae, perhaps because these cells respond to visual stimuli with greater peak firing rates than do their deprived counterparts. This leads to preferential development of the nondeprived synapses at the expense of the deprived ones, and the cortical cell becomes dominated exclusively by the nondeprived eye (Fig. 15-8 middle). However, deprived geniculate neurons in the monocular segment, by definition, cannot be put at a competitive disadvantage. They may be able to develop or maintain stable geniculocortical synapses, although perhaps not at a normal rate or not to normal levels.



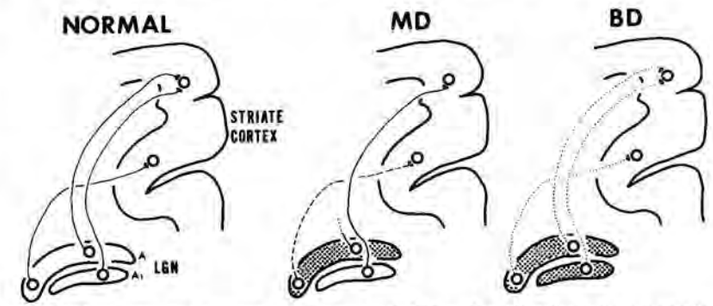


Fig. 15-8 Hypothetical diagram to demonstrate binocular competition. The actual site or sites and synaptic mechanisms of binocular competition are not known, but purely for the sake of illustration, this diagram assumes that the competitive interactions occur among geniculocortical synapses as follows. During normal postnatal development, there is a dramatic increase in the strength and (or) number of these synapses, and they compete with one another for control of cortical neurons. If a normal binocular visual environment is present, synapses related to one eye do not gain a competitive advantage over those of the other; rather, a balance is struck, and cortical neurons develop binocularly. However, during monocular deprivation (MD), neurons in the binocular segment of the deprived lamina (stippled) are somehow put at a competitive disadvantage with respect to nondeprived neurons. This allows the nondeprived neurons to develop dominance of cortical neurons, which thereby become influenced only by the nondeprived eye. Deprived neurons in the monocular segment, by definition, cannot be put at a competitive disadvantage, and can thus develop or maintain more central connections than can their deprived counterparts in the binocular segment. During binocular deprivation (BD), neurons in both laminae are equally deprived and no clear competitive advantage is present for either eye. Curiously, even though the deprived monocular segment seems to experience the same deprivation during monocular and binocular suture, more serious abnormalities are consistently found among these neurons in binocularly deprived cats than in monocularly deprived cats (see text for details). (Left and middle panels from Sherman SM: Development of the lateral geniculate nucleus in cats raised with monocular eyelid suture. In Freeman RD, ed: Developmental Neurobiology of Vision. New York, Plenum Press, 1979.)

By this reasoning, competitive development of a deprived neuron depends upon its interactions with developing neighbors. If abnormal binocular interactions alone control development of a pathway, one would expect geniculocortical synapses in the deprived monocular segment to develop completely normally. Equal deficits for the deprived pathway in the binocular and monocular segments would suggest a binocularly noncompetitive mechanism of development. For instance, the level of activity among a neuron's afferents might control its ability to develop or maintain efferent connections, irrespective of the activity along nondeprived pathways. Finally, a combination of competitive and noncompetitive mechanisms would lead to deficits in both segments, but to more serious deficits in the binocular segment. In such a case, deficits in the deprived monocular segment would establish the binocularly noncompetitive component of the deprivation effects, and further deficits in the binocular segment would establish the competitive component.

Guillery and Stelzner[81] first recognized this strategy as a means of identifying binocular competition in the neural development of monocularly deprived cats. These authors noted that the abnormally small-sized somata of deprived geniculate neurons are limited to the binocular segment; the deprived monocular segment contains somata of practically normal size. Guillery[77] then developed the artificial monocular or critical-segment preparation described above in order to ascertain that relatively normal development of the deprived monocular segment occurs because that segment represents a monocular visual field, and not because it represents a peripheral visual field. It is this strategy[77, 81] that allows one, in monocularly deprived cats, to identify binocularly competitive and noncompetitive mechanisms of development.

### Distribution of Competitive and Noncompetitive Deficits

A straightforward comparison of deficits in the monocular and binocular segments of each visual structure leads to the following conclusions. For the lateral geniculate nucleus, soma growth is controlled mainly by binocular competition, but a small noncompetitive process is also present.[77, 81, 95] Y-cell development is controlled entirely by binocular competition,[148, 223, 228] while X-cell deficits are determined by a noncompetitive process.[148] In the striate and lateral suprasylvian cortices, both competitive and noncompetitive mechanisms apply.[222, 248, 289] The monocular segment of cortical area 18 has not been studied in monocularly deprived cats.

Finally, binocular competition alone seems adequate to explain the development of the superior colliculus in monocularly deprived cats.[102]

## CONCLUSIONS

Several general conclusions about the effects of monocular lid suture on development of the central visual pathways can be briefly listed. First, the deprived retina and optic tract axons appear to be normal; clear deficits are seen most peripherally in the lateral geniculate nucleus. Second, the Y-cell pathway seems to be the one most seriously affected by early lid suture; relatively minor abnormalities are present among W- and X-cells. Third, deficits in the superior colliculus and lateral suprasylvian cortex are for the most part secondary to abnormalities in the geniculocortical pathways, including those that innervate the lateral suprasylvian cortex. Fourth, many pathways from the deprived eye are present, but their activation of cortical neurons is largely subthreshold, and these pathways are suppressed by others related to or dominated by the nondeprived eye. Fifth, abnormal binocular competition in some as yet unspecified form causes many of the abnormalities seen in monocularly deprived cats, although many of these deficits are also caused by binocularly noncompetitive processes.

## BINOCULARLY DEPRIVED CATS

Two types of binocularly deprived cat have commonly been studied. One is an animal raised with binocular lid suture; the other is a cat raised in total darkness. Considerable diffuse light is available to the retina of a binocularly sutured cat. In kittens, the closed eyelids attentuate only about 2 log units of light,[36, 165] and enlarged pupils can potentially compensate for this light loss.[165] Therefore, while both dark rearing and binocular lid suture effectively remove spatiotemporal patterns from the visual environment, the former condition completely eliminates photic stimulation of the retina, whereas the latter condition may have little effect on this parameter. Indeed, behavioral[165] and receptive-field[250] studies indicate that the visual system can make use of photic stimuli passing through the closed eyelids.

Unfortunately, only rare attempts have been made in the same laboratory to compare the effects of these two deprivation conditions in any systematic manner. In most cases these effects seem at least qualitatively similar. The effects of dark rearing and lid suture will nonetheless be identified separately in this section.

## RETINA

Only one study has been published on the effects of binocular deprivation on the retina, and it is limited to lid suture.[226] As expected, the results are indistinguishable from those seen in the deprived retina of monocularly sutured cats. Normal soma sizes, receptive field properties, and distributions of W-, X-, and Y-cells were noted. However, detailed receptive-field studies were not done, and it seems important to determine the status of the retina after total dark rearing.

## LATERAL GENICULATE NUCLEUS

In the lateral geniculate nucleus, only laminae A and A1 have been studied following binocular deprivation, and these studies have been somewhat limited.

### BINOCULAR SUTURE

#### Soma Size Distribution

Wiesel and Hubel[287] suggested that geniculate somata in binocularly sutured cats are as small as those in the deprived laminae of monocularly sutured cats. However, more recent and detailed measurements[78, 95] demonstrate a very different pattern. During binocular suture, the somata of geniculate neurons grow to essentially normal size, there being a less than 10 percent difference from normal.

Hickey et al.[95] compared the effects of visual deprivation on the binocular and monocular segments of the A laminae and arrived at two rather interesting conclusions. First, the very slight effect of binocular suture on soma growth affects both segments equally. Second, soma growth in the deprived monocular segment is more affected by binocular than by monocular suture. These general conclusions were first reached by Sherman et al., on the basis of physiological data,[223] and seem to be generally valid for other visual structures. These points will thus be repeatedly stressed in the rest of this section.



#### X- and Y-Cells

Sherman et al.[223] found that binocular suture reduces the proportion of recorded Y-cells and has rather little effect upon X-cell development; contrast sensitivity functions, however, have not yet been obtained for these deprived geniculate neurons. The loss of recorded Y-cells is most interesting in the context of the lack of dramatic abnormalities in the soma-size distribution for these neurons.[78, 95] In the binocular segment, there is a smaller loss of recorded Y-cells than that observed in deprived laminae following monocular suture, but the reverse is true in the monocular segment.[223] Figure 15-7 illustrates these relationships.

### DARK REARING

To date, only three studies have been published on the effects of total dark rearing on the development of geniculate neurons. First, Kalil[127] observed that the final soma size is unaffected by dark rearing (see also ref. 139). Second, despite normal soma sizes, Kratz et al.[139] found few normal Y-cells in deprived laminae (see Fig. 15-7). These authors established a normal soma-size distribution for the same cats from which receptive-field data were obtained. The X-cells in deprived laminae seemed grossly normal, but no detailed receptive-field analysis was done. Again, the loss of recorded Y-cells was equally severe in the binocular and monocular segments (see Fig. 15-7). Third, Kalil and Worden[129] found roughly twice as many geniculate neurons with cytoplasmic laminated bodies in dark reared cats than are found in normal cats. Given the prior suggestion[152] that these cytoplasmic structures mark X-cells, Kalil and Worden[129] suggested that many geniculate neurons that might normally develop as Y-cells become X-cells instead.

## CORTICAL AREA 17

### RECEPTIVE-FIELD PROPERTIES

#### Binocular Segment

Since binocular suture and dark rearing seem to produce essentially equivalent receptive-field abnormalities in the striate cortex, these deprivation conditions are treated together here. As indicated below, a considerable number of studies have been directed at the receptive-field properties of area 17 in binocularly deprived cats.

Many deficits have been noted for neurons in the binocular segment. Although most of these cortical neurons still respond to visual stimuli, roughly one-third do not.[16, 22, 55, 159, 236, 281, 287] These estimates vary from report to report, probably because of different criteria used to determine responsiveness (see discussion in ref. 281), although other factors could also be involved. Even responsive cells tend to have abnormally low firing rates and a high response variability.[159, 281]

Furthermore, the receptive fields tend to be abnormal among the responsive cells. Very few of these neurons exhibit normal direction or orientation selectivity, and thus few normal simple or complex cells develop.[16, 17, 22, 55, 140, 159, 187, 281, 287] Again, the precise estimate of normal neurons varies from report to report.

Binocular deprivation also affects the development of binocular integration. Precise disparity tuning fails to develop during such deprivation.[186] Also, most studies report that fewer than the normal proportion of cells have binocular receptive fields.[16, 39, 140, 159, 281, 287] Considerable disagreement exists over the degree of this effect, and some studies of dark-reared cats even report a normal ocular-dominance distribution.[22, 55, 123] Studies that have uncovered abnormal ocular-dominance patterns also report an interaction of this parameter with other receptive-field abnormalities: more specific fields tend to be monocular, and binocular fields tend to be nonspecific.[16, 140, 159, 281]

#### Monocular Segment

Watkins et al.[281] further compared the effects of binocular suture on the binocular and monocular segments of the striate cortex. They found that abnormalities appeared to be precisely equivalent in the two segments. Fewer responsive cells, many cells with diffuse fields, and only rare normal simple and complex cells were found in either segment. Curiously, Watkins et al.[281] also reported that binocular lid suture affects development in the deprived monocular segment of area 17 more seriously than does monocular suture. After the latter deprivation, few unresponsive neurons and many normal simple cells can be found.[289]

### Electrical Activation of Afferents

Singer and colleagues[236, 237] have compared the responsiveness of area 17 neurons in normal and binocularly sutured cats to electrical activation of the optic chiasm and radiations. Compared to normal cats, binocularly deprived cats exhibit roughly only a 20 percent loss of neurons responsive to optic radiation stimulation; however, the loss to optic chiasm stimulation is twice as large. This indicates a retinogeniculate transmission failure in binocularly sutured cats.[236] Unfortunately, even in normal cats only 36 percent of these cortical neurons respond to optic chiasm stimulation,[237] thus limiting the analysis to a minority of available neurons. Singer and Tretter[236] further noted that in binocularly deprived cats, there is no loss of polysynaptic responses of cortical neurons to afferent stimulation beyond the loss that is seen for monosynaptic responses. These authors thus found no evidence for abnormalities of intracortical circuitry in binocularly deprived cats.

## CORTICAL AREA 18

There has been only one published study of area 18 neurons in binocularly deprived cats, and these cats were lid sutured.[236] The abnormalities of these neurons were rather similar to those reported for area 17 cells, although relatively few specific parameters were investigated. After binocular deprivation, many area 18 neurons were unresponsive, and the responsive cells tended to exhibit diffuse and nonspecific receptive fields. Unfortunately, Singer and Tretter[236] did not present data regarding ocular dominance of these neurons. Electrical stimulation revealed deficits similar to those reported for area 17. There was a 19 percent reduction in area 18 neurons responsive to optic radiation stimulation, but a 40 to 44 percent reduction in neurons responsive to optic chiasm stimulation. Many of the cells responsive to optic radiation stimulation were unresponsive to both optic chiasm and visual stimulation. Again, these data indicate a retinogeniculate deficit. Polysynaptic responses in the cortex exhibited no further reduction from that seen among neurons receiving geniculocortical input, and thus Singer and Tretter[236] found no evidence for deficits in intracortical transmission after binocular deprivation.

## SUPERIOR COLLICULUS

### General Response Properties

Binocular lid suture and dark rearing appear to affect the development of collicular neurons in the upper three layers in practically the same fashion.[53, 103, 260] Although virtually every collicular neuron in normal cats responds to visual stimulation, roughly one-fourth of the cells are unresponsive after binocular deprivation. Additionally, responsive cells have abnormal receptive-field properties, including dominance by the contralateral eye, lack of direction selectivity, and better responses to slowly moving or stationary stimuli.

Hoffmann and Sherman[103] reported on a sample limited to 10 neurons in the monocular segment of the superior colliculus, and found deficits similar to those in the binocular segment. Clearly, more data on the superior colliculus are needed, but the available data are consistent with the pattern seen in other visual structures. That is, binocularly deprived cats exhibit no substantive differences in abnormalities between the binocular and monocular segments of the superior colliculus, yet the deprived monocular segment exhibits greater deficits after binocular than after monocular suture.

### Afferents to the Superior Colliculus

The receptive-field properties described above for collicular cells in binocularly deprived cats are virtually indistinguishable from those seen in normally reared cats following removal of the visual cortex (see the section above on the superior colliculus). This suggests that retinotectal pathways develop normally during binocular deprivation, but that corticotectal pathways do not. Hoffmann and Sherman[103] confirmed this by analyzing afferents to collicular neurons, using electrical stimulation. Hoffmann[99] established this approach in normal cats to identify a large W-cell retinotectal pathway, a small Y-cell retinotectal pathway, and a large Y-cell retino-geniculo-cortico-tectal pathway. When the optic chiasm is stimulated in a binocularly sutured cat, collicular neurons respond normally via the W-cell retinotectal pathway, there is some reduction in the number of neurons activated by the Y-cell retinotectal pathway, and no collicular cell can be activated via the Y-cell corticotectal pathway.[103] Therefore, during binocular suture, the superior colliculus develops no effective corticotectal input accessible from either eye. Yet when the corticotectal pathway is activated directly by electrical stimulation of the cortex, collicular neurons in binocularly deprived cats are quite responsive.[103] Presumably, the Y-cell corticotectal input is nonfunctional because of a failure of geniculocortical Y-cells to develop normally. These results are summarized in Figure 15-4 right.

One puzzling difference between the effects of monocular and binocular suture on collicular development remains to be explained. In both cases, the deprived retinotectal pathways develop fairly normally. But while this pathway is clearly active after binocular deprivation, it is subthreshold after monocular suture, and only becomes evident after cortical lesioning.

## LATERAL SUPRASYLVIAN CORTEX

### General Response Properties

Only one study of the lateral suprasylvian cortex in binocularly sutured cats has been reported.[273] Dark-reared cats have not yet been used for the investigation of this cortical area; however, there is a severe loss of responsive cells in the lateral suprasylvian cortex as a result of binocular suture. Nearly 90 percent of these cortical neurons are responsive in normal cats, compared to roughly 25 percent in the binocularly deprived cats. Nearly all of the remaining responsive cells have abnormal receptive fields, and most respond best to changes in diffuse illumination. Also, the ipsilateral eye influences only about half of these responsive cells. The foregoing deficits appear to exist equally in the binocular and monocular segments. Furthermore, after binocular suture, the deprived monocular segment contains more abnormalities than it contains following monocular suture.[248, 273]

### Afferents to the Lateral Suprasylvian Cortex

As was done in normal and monocularly deprived cats, deficits in pathways to the lateral suprasylvian cortex following binocular suture were analyzed before and after removal of the visual cortex.[273] Cortical removal further reduced the fraction of responsive cells that could be activated by the ipsilateral eye. No other receptive-field changes were seen. Overall, a normally reared cat exhibited more responsive cells in the lateral suprasylvian cortex than did a binocularly deprived cat after each was subjected to visual cortex removal. This suggests that some of the deficits in the visually deprived cats existed in the thalamocortical pathways. It is not yet clear whether this represents an abnormal geniculocortical or tecto-thalamo-cortical pathway, or both.

## CONCLUSIONS

In general, much less is known about the effects of binocular deprivation than about those of monocular deprivation. Deficits have not yet been reported for the retina after binocular deprivation, but every central structure so far investigated develops abnormally in binocularly deprived cats. In each structure, equivalent deficits are seen in the binocular and monocular segments. Curiously, the deprived monocular segments of these structures develop more normally during monocular suture than during binocular suture. Deficits common to the two rearing conditions include poor Y-cell development, poor cortical development, and lack of a functional corticotectal pathway.

# POSTNATAL DEVELOPMENT

The second, third, and fourth sections of this chapter consider the effects of visual deprivation on visual system development by comparisons among cats raised normally, cats raised with monocular suture, and cats raised with binocular deprivation. A key issue concerns the developmental dynamics during the early postnatal months that lead to the adult patterns that are observed. In this section, the limited data relevant to this issue are considered. Unfortunately, the physiological data often seem inconsistent or unreliable, probably because of the frailty and instability of physiological preparations in neonatal kittens.

## OPTICAL DEVELOPMENT

Since many receptive-field properties are abnormal or "immature" in neonatal kittens, one must consider to what extent poor optics contribute to

this. Bonds and Freeman[18] measured optical modulation transfer functions of kitten eyes at various ages. Between the first and fifth postnatal weeks, there was roughly a twofold improvement in optics, with a gradual and slight improvement thereafter. The early improvement generally coincides with the clearing of the optic media, particularly the vascular network covering the lens.[270] When one compares the kitten's optics with receptive-field data at various ages (see below), it usually seems obvious that optics are not responsible for many of the "immature" response properties described.

Another important factor in the kitten's optical development relates to the eye's physical growth.[183, 270] From birth to adulthood, most ocular dimensions, including axial length, approximately double in size. One implication of this doubling of axial length is that a given visual object subtends twice as much retinal area in the adult as in the neonate. Thus, an improvement seen in spatial acuity during development could at least partially result from this aspect of optical development.[183]

## RETINA

### ANATOMY

Much of the anatomical development of retinal ganglion cells in the kitten is completed by 3 weeks of age[43, 279] (but see ref. 275). Rusoff and Dubin[200] made the interesting observation that beta cells near the area centralis already appear adult-like by 3 weeks of age. Given the continued growth of the eye beyond 3 weeks of age, this suggests that on the average, each dendritic field of a beta cell in young kittens subtends twice the visual angle across the retina as does the dendritic field of an adult beta cell.

### PHYSIOLOGY

Rusoff and Dubin[198] made recordings from retinal ganglion cell somata in normal kittens 3 to 7 weeks of age. At 3 weeks, most of the cells are poorly responsive, with large, diffuse fields. At 4 weeks, some adult-like responsive cells begin to appear, which can often be identified as W-, X-, or Y-cells. Since adult-like cells are often recorded next to immature ones, poor optics do not seem to cause the immature responses. Most adult-like cells gradually appear during the next 3 weeks. Receptive-field centers mature before surrounds, so that even at 7 weeks, surround antagonism of the center response is poor or absent. Finally, the adult-like cells in these young kittens have center sizes roughly twice those in the adult, which can be explained by growth in the eye and its effect on optics, with no need to incorporate neural changes.

Recordings from the optic tract provide rather different conclusions.[82, 83] In these studies, Y-cells were found earlier than were W- or X-cells, and the basic center/surround organization was already present at 3 weeks. Subtle abnormalities were noted that gradually disappeared by 12 weeks of age. It should be noted that electrode sampling among fibers (i.e., the optic tract) is probably different from that among somata (i.e., retinal ganglion cell somata), and that optic tract recordings might therefore reflect an unrepresentative sample limited to the most mature retinal ganglion cells with the largest or most heavily myelinated axons.

## LATERAL GENICULATE NUCLEUS

### ANATOMY

Kalil[127, 128] and Hickey[93] described the growth of geniculate somata in the A laminae of normal and monocularly sutured cats. In normal cats, the somata grow rapidly until 4 weeks of age, with less rapid growth occurring until 8 weeks, at which time a nearly normal adult pattern is obtained. In nondeprived laminae of monocularly deprived cats, the growth pattern is normal. Deprived somata nearly match nondeprived somata until 4 weeks of age, after which soma growth in deprived laminae ceases. Some atrophy may occur. By 8 weeks of age, these geniculate soma sizes closely resemble those of cats raised to adulthood with monocular suture, although very slight atrophy of deprived somata may continue until 16 weeks of age.

### PHYSIOLOGY

Norman et al.[180] and Daniels et al.[40] studied the development of normal geniculate neurons in cats between 1 and 6 weeks of age. They reached four main conclusions. First, the development of geniculate neurons lags behind that of their optic-tract input. In some cases, pairs of units that included an optic-tract fiber and its postsynaptic geniculate neuron were recorded, and the optic-tract fiber was adult-like while the geniculate neuron was immature. Second, by 6 weeks of age, geniculate neurons are not yet completely mature, and the surround responses in particular are still poorly developed at this age. Third, X-cells mature earlier than do Y-cells; many fairly responsive X-cells are seen at 3 to 5 weeks of age, but only after this age are neurons identified as Y-cells seen. However, given the difficulty of cell classification in such young kittens, this conclusion should be qualified. Fourth, since cells with very immature receptive fields (large diffuse borders, sluggish responses) are often located next to cells with fairly mature responses, poor optics are not responsible for the very immature responses.

Although fairly responsive geniculate X- and Y-cells can be found at 6 weeks of age, there is continued gradual maturation for the next month or two. For instance, Ikeda and Tremain[121] reported that geniculate X-cells do not attain normal spatial acuity until 12 weeks of age, although some of this might be attributed to optical development. Mangel[169] found that many geniculate Y-cells have poorly developed or unstable nonlinear responses (i.e., the "nonlinear subunits" described in ref. 98) until 12 to 16 weeks of age.

## CORTICAL AREA 17

Many experiments have focused on the development of receptive-field properties among striate cortex cells in normal and visually deprived kittens. Unfortunately, the reports of these experiments represent a most confused and conflicting body of evidence.

### NORMAL KITTENS

Visually responsive cells can be recorded in area 17 as early as 4 to 6 days of age,[120] but estimates of the proportion of such cells at 8 to 9 days of age vary from 10 percent[55] to more than 80 percent.[16] Regardless of their proportion, the responsive cells in these young kittens are quite sluggish and fatigue rapidly.

At 2 weeks of age, cells in the striate cortex begin to display stimulus specificity, but the claims for this vary from nearly adult-like properties[111, 209] to very immature responses, with possible direction, but not orientation selectivity.[16, 17, 22, 55, 187] Most investigators agree that by 6 weeks of age, striate cortex cells seem to have fairly mature receptive-field properties.

A similar disagreement applies to descriptions of the development of ocular dominance. Many investigators report an adult-like ocular dominance pattern by 2 weeks of age.[16, 111, 155] Yet Fregnac and Imbert[55] claim that these cells are mainly monocularly activated until 4 weeks of age and that these monocular cells tend to be selective for vertical or horizontal stimulus orientations.

### BINOCULARLY DEPRIVED KITTENS

#### Dark Rearing

A number of studies have compared striate cortex development in normal and dark-reared kittens. Fregnac and Imbert [55] found no difference in the development of ocular dominance in normal and dark-reared kittens, although, as noted above, their normal data are inconsistent with those reported by other laboratories. Fregnac and Imbert[55] also found little difference in the development of receptive-field specificity until 3 to 4 weeks of age, after which time normal cats continue to develop more specific neurons, while dark-rearing causes a loss of neurons with specific receptive fields. By 6 weeks of age, 90 percent of responsive neurons demonstrate stimulus specificity in normal cats, while less than 5 percent do so in dark-reared cats.

Bonds[17] has challenged these observations. He reports no development of receptive-field specificity of area 17 neurons in dark-reared cats from 2 to 6 weeks of age, with considerable such development in a normal environment. Likewise, Derrington[41] found that spatial-frequency sensitivity improves markedly in normal kittens between 3 and 6 weeks postnatally, but does not change during dark-rearing. These reports thus contend that neither maturation nor deterioration of the striate cortex occurs in the dark.

Leventhal and Hirsch[159] offer yet another scenario for dark rearing. These authors find that dark rearing produces a striate cortex with a high proportion of monocular neurons that tend to prefer horizontal or vertical stimulus orientations, and that the remaining binocular neurons tend to have large, diffuse, nonselective receptive fields. This is much

like the observation of Fregnac and Imbert[55] for neonatal area 17, which in turn suggests a failure of area 17 neurons to develop during dark rearing. However, a comparison between the data of Leventhal and Hirsch[159] and reports of normal ocular dominance for area 17 in neonatal kittens[16, 111, 155] suggests a deterioration of binocular neurons during dark-rearing.

### Binocular Suture

Only two published studies describe the effects of binocular suture on area 17 neurons in young kittens. In one, Pettigrew[187] compared normal and binocularly sutured kittens between 1 and 6 weeks of age. At 1 to 2 weeks of age, both groups of kittens exhibited similar development in that the cortical cells showed no direction or orientation sensitivity. Development seemed to be arrested during the subsequent weeks of lid suture, but normal kittens at 6 weeks of age had many cortical cells with mature response properties. In the second study, Derrington[41] reported similar effects for the development of spatial-frequency selectivity between 3 and 6 weeks postnatally: little development during binocular suture, while considerable development occurred in a normal environment. Thus, both Pettigrew[187] and Derrington[41] offer support for the notion that binocular lid suture arrests development, while neither study suggests significant deterioration or other changes from the neonatal condition during binocular suture.

However, a comparison with other studies appears to qualify this conclusion. Most studies of binocularly sutured cats reveal an abnormally large representation of monocular cells in area 17, with a tendency of monocular cells to have more normal or mature response properties than do binocular cells.[16, 140, 281] Confusion over the starting point (i.e., neuronal properties in the neonatal kitten at the time of eyelid suture) makes it difficult to be certain whether the pattern observed in adult cats visually deprived from birth represents a selective development of monocular cells, a degradation of binocular cells, or a general lack of development.

### Conclusions

The data that different laboratories have derived from normal and binocularly deprived kittens and cats are so variable and contradictory that virtually any hypothesis can be sustained by a careful selection of supporting evidence. One can view development during binocular deprivation as a general failure to develop, a partial normal development of some neurons or properties followed by some deterioration of others, a normal development of some neurons or properties with a failure of others to develop, and a normal development of some neurons or properties with deterioration of others. The reason for such an inconsistent body of data is not clear, but one must remember the technical difficulties and frailty of the neonatal preparation.

## SUPERIOR COLLICULUS

Retinotectal and corticotectal afferents grow into the superior colliculus prenatally.[5, 6, 256] Despite this, collicular neurons cannot be influenced by visual stimuli before roughly 7 days of age.[181, 257] Furthermore, the responses that are seen are quite sluggish and fatigue rapidly until about 4 weeks of age. Other receptive-field features are also abnormal, including dominance by the contralateral eye, preference for stationary or slowly moving targets, and lack of direction selectivity. By roughly 6 weeks of age, collicular neurons display most of the response properties seen in normal adult cats.[181, 257]

In many ways, collicular neurons in cats between 1 and 16 weeks of age closely resemble those in adult cats following visual-cortex lesions.[196, 283] This suggests that the retinotectal pathways mature earlier than do the corticotectal pathways. Later development of the corticotectal pathways could, in turn, result from the relatively late development of geniculate Y-cells[40, 180] that innervate the corticotectal neurons.[99] Finally, it is also noteworthy that collicular neurons in a kitten prior to 6 weeks of age closely resemble those in a cat reared with binocular deprivation,[53, 103, 260] suggesting that such deprivation simply retards development of the superior colliculus by preventing the development of the corticotectal pathway.

## CONCLUSIONS

The literature dealing with the receptive-field properties of neonatal kittens is characterized by contradictory claims. This is especially true for cortical area 17, upon which most studies have focused. The results of studies of the lateral geniculate nucleus and superior colliculus are less controversial, possibly because of the few studies involved. Thus, the conclusions listed below should be considered as qualified and tentative.

Retinal ganglion cells gradually mature during the kitten's first 2 months of life. The few studies done on these cells do not clearly suggest that any particular cell type matures first. However, geniculate X-cells seem to mature substantially earlier than do Y-cells. It is conceivable that the neonatal response properties of striate cortex neurons reflect geniculate X-cell input, and that the later maturation of cortical response properties coincides with Y-cell development, although intrinsic changes in area 17 also occur during development. Certainly this suggestion is consistent with development of the superior colliculus. The observed early retinotectal development followed by later corticotectal maturation in cats might simply reflect the later maturation of the Y-cells that innervate corticotectal neurons. It is interesting to note that the Y-cell pathway, which is one of the last to mature and which undergoes such rapid development during the critical period, is also the most sensitive to the effects of pattern deprivation.



## BEHAVIORAL CORRELATES

It has been known for many years that cats raised with visual deprivation develop poor vision (see refs. 29, 61), and it is naturally quite interesting to consider the extent to which visual deficits can be ascribed to the anatomical and physiological abnormalities considered in the sections on monocularly and binocularly deprived cats. There are, however, at least two problems with any effort to deduce such relationships. First, many of the earlier behavioral experiments with visually deprived cats concentrated on their ability to discriminate between two geometrical objects (i.e., crosses versus circles, triangles of various orientations, etc.) that bear little relationship to the visual stimuli typically used to study receptive-field properties. Second, most studies of the central visual pathways of visually deprived cats have concentrated on the geniculostriate portion of these pathways, yet normally reared cats suffer only a slight visual disability after removal of the striate cortex.[7, 149, 253] In fact, such normally reared cats actually display better visual capacity after striate cortex removal than do monocularly or binocularly deprived cats with an intact cortex, making it unlikely that the striate cortex abnormalities that have been observed can, by themselves, account for the poor vision that develops during visual deprivation.[149, 150]

This section consequently focuses on two lines of behavioral studies, using normal and visually deprived cats, that can be relatively more easily related to the neurological abnormalities observed in these cats. One line of research involves the role played by various visual structures in the cat's ability to locate visual objects in space (i.e., visual perimetry). The other involves the behavioral study of spatial and temporal contrast sensitivity, making use of the same sine-wave grating stimuli used in many receptive-field studies.

### VISUAL PERIMETRY STUDIES

The visual perimetry studies discussed below are based on a technique described by Sprague and Meikle.[254] This technique makes use of the cat's tendency to fixate steadily on a target of interest (i.e., for a hungry animal, a small piece of food) and to orient rapidly and vigorously with both the head and eyes to a novel stimulus introduced into the visual field. This permits the extent of the functional visual field to be mapped with considerable accuracy (within 5 to 10 degrees) while the cat has either eye occluded or both eyes open.

#### NORMALLY REARED CATS

**Before Neural Lesions**

A normal cat has a visual field with both eyes that extends from 90 degrees on one side of the fixation point to 90 degrees on the other side. With each eye alone, the field extends from 90 degrees ipsilateral to 45 degrees contralateral to the open eye.[211, 254] There is practically no variability among cats regarding these measurements. Thus the nasal retina has a field of view from 0 degrees (i.e., the midline or area centralis representation) to 90 degrees in the ipsilateral hemifield; and the temporal retina has a field of view from 0 degrees to 45 degrees in the contralateral hemifield. These estimates are in close agreement with the optics of the cat's eye and the extent of its nasal and temporal retina.[116] Finally, these data delineate the binocular and monocular segments of the visual field.[211] The binocular segment, which can be seen by each eye, extends to 45 degrees on either side of the midline; the monocular segments, which can be seen by only

one eye, extend from 45 degrees to 90 degrees ipsilateral to the eye in question.

### After Cortical or Collicular Lesions

Sprague[251] first showed that cats can locate visual targets by either collicular or cortical pathways. That is, a cat with either a visual cortex or superior collicular ablation can still orient to visual stimuli, but cannot do so if both structures are removed (see also refs. 212, 215). A curious detail to these observations is that if small cortical lesions (to areas 17, 18, and 19) are made, the cat can still orient visually, whereas cortical lesions involving most of the occipitotemporal cortex render the animal blind until the two superior colliculi are disconnected either by removal of one of the colliculi or a transection of their commissure.[212, 215, 251] The reason why such disconnection is needed for tectal vision is unclear.

Additionally, the superior colliculus seems to subserve visual orienting only for stimuli falling on the nasal retina, whereas the visual cortex subserves visual orienting for both the nasal and temporal retina.[212, 215] Presumably this is because ganglion cell axons from the nasal retina dominate the retinotectal pathways, while the geniculocortical pathways represent a better balance between the nasal and temporal retina.

## Monocularly Sutured Cats

### Before Neural Lesions

As expected, the nondeprived eye of a monocularly deprived cat exhibits a normal field of view, while the field of view of the deprived eye is quite restricted.[211, 213, 224] When using its deprived eye, such a cat orients reasonably well to stimuli in the monocular segment (i.e., from 45 to 90 degrees ipsilateral to the deprived eye), but barely if at all to stimuli in the binocular segment. With binocular viewing, on the other hand, a monocularly deprived cat maintains a full 180-degree field of view.

The extent of the deficits for the deprived eye in monocularly deprived cats have been challenged by van Hof-van Duin[278] and Heitlander and Hoffmann.[88] These investigators report that responses for the deprived eye occur for stimuli falling anywhere on the nasal retina, although in most cases orienting responses are more consistently evoked by stimuli in the monocular segment. Sherman and Sprague[224] discuss in detail possible reasons for these discrepancies, but in any case, these cats when using their deprived eye can locate targets better when the targets are placed in the monocular segment than when they are placed in the binocular segment.

This provides a behavioral analog to the anatomical and physiological studies on monocularly deprived cats. That is, the most severe deficits related to the deprived eye occur in the binocular segment, while less severe deficits exist in the monocular segment. This behavioral analysis was extended to monocularly deprived cats for which an artificial monocular segment was surgically created by placing a lesion neonatally in the nondeprived eye's retina (see above).[222] Two separate functional fields were plotted for the deprived eye of these cats, one for the natural and one for the artificially created monocular segment; it was found that the cats ignored targets in the rest of the visual field. Overall, these data suggest that binocular competition plays a key role in the development of visual orienting behavior during monocular suture.

### After Cortical or Tectal Lesions

On the basis of the studies of normal cats reviewed above, it is clear that cortical pathways are not needed for at least some visual orienting behavior, and that when collicular pathways are used, vision is generally restricted to the nasal retina. Physiological experiments also indicate that the retinotectal pathways from the deprived eye develop reasonably normally during monocular suture, but that they are expressed only after visual cortical ablations.[102, 284] Therefore, appropriate visual cortical ablations in monocularly sutured cats might be expected to reveal (e.g., disinhibit) the normal retinotectal pathways from the deprived eye, thus increasing the useful visual field of the deprived eye from the monocular segment to the entire ipsilateral hemifield.

Indeed, visual cortical lesions do dramatically increase the visual field of the deprived eye as expected.[214, 224] Sufficiently large, bilateral cortical ablations improve the deprived eye's visual behavior and degrade that of the nondeprived eye in visual orienting tasks, such that postoperatively there is little difference between the eyes. This supports the notion that the retinotectal pathways in monocularly deprived cats are fairly normal, and that deficits in the visual system, at least for orienting behavior, are limited mainly to cortical pathways.



## Binocularly Sutured Cats

### Before Neural Lesions

Binocularly sutured cats display a normal 180-degree visual field with binocular viewing, whereas each eye alone responds to targets limited to the ipsilateral hemifield.[208, 210] Apparently, only the nasal retina is useful for target localization in these cats. The visual-orienting behavior of binocularly deprived cats closely resembles that of normally reared cats with bilateral cortical lesions. Given the relatively normal properties of the retinotectal pathways and lack of functional corticotectal input in binocularly sutured cats,[103] these behavioral results are not surprising.

### After Cortical or Tectal Lesions

This explanation regarding the status of the retinotectal and corticotectal pathways has been confirmed by cortical and tectal ablations.[216] Large bilateral or unilateral lesions of the occipitotemporal cortex have no observable effect on the visual-orienting behavior of binocularly sutured cats, and the unilateral lesions produce no asymmetry in the two hemifields. Curiously, collicular disconnection is not required for the re-establishment of visual orienting following such large cortical lesions, as it is in normally reared cats.[212, 215, 251] In contrast to the effect of cortical lesions in binocularly deprived cats, a tectal lesion in such cats produces a permanent hemianopia in the contralateral hemifield.[216] whereas in normally reared cats such a lesion does not have this effect as long as the visual cortex remains intact.[215] It appears that during binocular suture, cortical pathways simply do not develop for orienting behavior, and that such behavior depends instead upon the fairly normal development of retinotectal pathways.

## BEHAVIORAL MEASUREMENTS OF CONTRAST SENSITIVITY

Another behavioral approach useful for correlation with receptive-field properties in the cat involves the measurement of temporal and spatial contrast sensitivity to sine-wave gratings (see footnote on p. V:389 for a description of this stimulus). These functions can then be compared to analogous data for X- and Y-cells (see Fig. 15-2). The poor sensitivity of W-cells suggests that they play little role in psychophysically determined contrast sensitivity. Fortunately, cats are good psychophysical observers and can be trained to indicate their threshold values for various spatiotemporal patterns, including sine-wave gratings.

## Normal Cats

The most extensive study of contrast sensitivity in normal cats was done by Blake and Camisa.[11] They measured spatial functions at several temporal frequencies. At low temporal frequencies (1.5 Hertz), the spatial function shows attenuation (poor sensitivity) for both high and low spatial frequencies. Sensitivity peaks at roughly 0.5 to 1 cycles/degree, and acuity is roughly 5 cycles/degree (the absolute values depend upon the degree of illumination and contrast, but the relative values serve to illustrate the major points). At higher temporal rates (10 Hertz), sensitivity drops somewhat, and the function loses its low-frequency attenuation. At this point a monotonic decrease in sensitivity with increasing spatial frequency becomes evident, and the acuity is reduced to roughly 3 cycles/degree.

The interpretation offered for the foregoing observations is as follows.[11, 149] At low temporal frequencies, both X- and Y-cells are active, and low spatial frequency attentuation with good spatial resolution is evident because of the X-cell activity. That is, contrast sensitivity presumably reflects summed X- and Y-cell activity. At higher temporal rates, the contrast sensitivity is dominated by Y-cell activity. Spatial acuity is lower, but no loss of sensitivity to low spatial frequencies can be seen.

Although quite speculative, this explanation is partially supported by the effects observed after ablations of cortical area 17. Such bilateral lesions have rather little effect on the cat's visual capacity,[7, 149, 253] while greatly reducing or eliminating the X-cell pathway by destroying all or most of its cortical target zone. Sensitivity deficits caused by such area 17 lesions are limited to the high spatial and low temporal frequencies (see Fig. 15-9). At low temporal frequencies, the sensitivity deficits that are observed are limited to the middle and high spatial frequencies, with a spatial acuity loss of roughly 20 percent.[7] No significant low spatial frequency attenuation is evident. Presumably, these

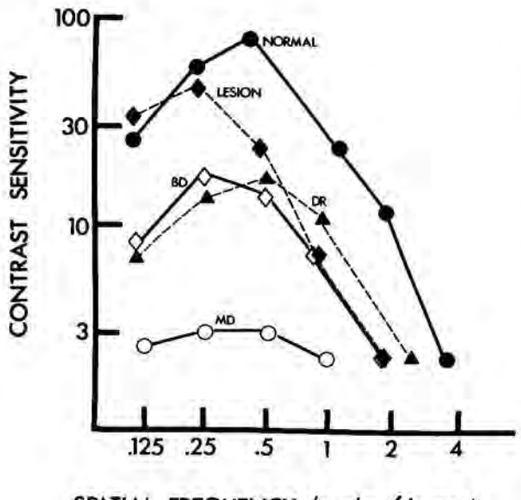


Fig. 15-9 Spatial contrast sensitivity functions for cats obtained from psychophysical measurements.[149] These functions represent sensitivity to sine-wave gratings counterphased at 1 Hertz. Average values for two normally reared cats are shown before (NORMAL) and after (LESION) bilateral removal of area 17 and some of area 18. The sensitivity loss due to the lesion is limited to higher spatial frequencies, and the general postoperative visual behavior is otherwise excellent (see also refs. 7, 253). Also shown are functions for one dark-reared cat (DR), the average of two binocularly sutured cats (BD), and the average of two monocularly sutured cats (MD). The functions from the monocularly sutured cats represent sensitivity for the deprived eye. Visual deprivation causes sensitivity losses for all spatial frequencies, and does not result in a simple acuity or high spatial frequency deficit. Note also that the acuity of binocularly deprived (BD and DR) cats is generally comparable to that of normally reared, de-striate cats (LESION). The visually deprived cats exhibit qualitatively much worse vision than do the normally reared, de-striate cats. This illustrates the importance of the low spatial frequencies to visual performance (see text for details). (Lehmkuhle S, Kratz KE, Sherman SM: Spatial and temporal sensitivity of normal and amblyopic cats. J Neurophysiol 48:372, 1982.)

postoperative contrast sensitivity functions represent Y-cell activity, since the X-cell pathway is interrupted and W-cells are not sensitive at these contrast levels.

### Monocularly Sutured Cats

When using its deprived eye, a monocularly sutured cat exhibits such poor contrast sensitivity that the function tells us little about specific neurological correlates.[149] Nonetheless, sensitivity deficits are seen at all spatial frequencies (see Fig. 15-9). The deficit in contrast sensitivity thus cannot be characterized simply by a loss of spatial resolution, because this should be reflected by a relatively normal sensitivity to lower spatial frequencies and a poor sensitivity for higher ones.

### Binocularly Deprived Cats

Binocularly deprived cats exhibit much better contrast sensitivity than do monocularly deprived cats with their deprived eye (see Fig. 15-9). Blake and DiGianfilippo[12] showed that dark-reared cats exhibit reduced sensitivity for all spatial frequencies. However, the spatial function in dark-reared cats showed marked sensitivity attenuation to low spatial frequencies at both low and high temporal frequencies (1 and 10 Hertz). But while these cats' overall spatial frequency sensitivity was considerably reduced at the higher rate, they did not show the normal disappearance of the low spatial frequency attenuation at the higher temporal frequency. This is consistent with the notion that X-cells and not Y-cells are responsible for these contrast sensitivity functions, an observation consistent with the loss of recorded geniculate Y-cells in these cats.[139] Figure 15-9 shows that binocularly sutured and dark-reared cats exhibit similar contrast sensitivity.[149, 150]

An interesting comparison can be made between a normally reared cat with a bilateral cortical lesion in area 17 and a binocularly deprived cat (see Fig. 15-9). Each has comparable spatial acuity, as estimated from the highest spatial frequency to which the cat responds, but the binocularly deprived cat has much poorer sensitivity to lower spatial frequencies. This is consistent with the qualitative observation that the visual behavior of normally reared cats without a striate cortex seems fairly normal, while that of binocularly deprived cats is clearly deficient. This underscores the importance to visual capacity of sensitivity to low spatial frequencies.

## CONCLUSIONS

The visual perimetry data described above emphasize the importance to visual function of the extrageniculate pathways, and these data can be correlated to neurological deficits in visually deprived cats in several ways. In monocularly deprived cats, the pattern of visual orienting provides additional evidence for binocular competition during development, since with the deprived eye, these cats orient better to stimuli in the monocular than in the binocular segment. Furthermore, visual cortical lesions in these cats reduce differences in the visual capacity of the eyes, as predicted by neurophysiological studies of the superior colliculus before and after such lesions. Finally, the results of studies of binocularly deprived cats are consistent with the fairly normal retinotectal pathway development and lack of normal corticotectal pathway development in these animals.

Psychophysical contrast-sensitivity measurements can also be correlated to the neurological deficits observed in visually deprived cats, but only to a limited and superficial extent. The deprived eye of monocularly sutured cats exhibits such poor sensitivity that it is difficult to be certain of the shape of the spatial function. However, the spatial-contrast sensitivity exhibited by binocularly deprived cats suggests greater Y-cell deficits than X-cell deficits, and this does correlate in a general way with the physiological deficits.

## SPECULATIVE CONCLUSIONS

As can be seen from the preceding sections, data on the development of the central visual pathways during monocular and binocular deprivation are seriously flawed by many gaps, uncertain interpretations, and contradictory claims. The data do not yet permit the formulation of confident conclusions. Nonetheless, this section will attempt to establish a unified, theoretical framework for these data. Although necessarily quite speculative, such a framework can serve as a useful hypothesis for further work.

The main conclusion to be drawn from the data so far collected is that one of the major primary abnormalities in the visual system develops among geniculate Y-cells during visual deprivation, and that this occurs in monocularly deprived cats because of abnormal binocular competition. Since many other (but not all) abnormalities described in other structures are secondary to these Y-cell deficits, this concept also has some implications for clinical disorders of vision. Details can be found elsewhere for many of these conclusions concerning the effects of visual deprivation upon development of the Y-cell pathway and the consequences of these effects for vision.[210, 217, 220, 225]

## COMPETITIVE AND NONCOMPETITIVE MECHANISMS OF DEVELOPMENT

Although it has been years since Wiesel and Hubel[287] proposed a mechanism of binocular competition among developing neurons in the central visual pathways, and considerable research has been directed at this topic in the intervening time, we still know precious little about this mechanism in detail. We do not know precisely where it occurs, what cell populations are involved, precisely how the normal competitive balance can be disrupted, nor what synaptic events subserve this process. Despite this, we probably know more about binocular competition than about any other developmental mechanism responsible for abnormalities in visually deprived cats.

Binocular competition is only one of many possible competitive mechanisms that could exist in the developing visual system. In the sense that binocular competition implies competitive interactions for synaptic development between central pathways related to each eye, one can also imagine analogous competitive interactions during development for X-versus Y-cells, ON versus OFF center cells, retinotectal versus corticotectal pathways, geniculate A laminae versus C laminae, and many other elements of the visual system. However, while the demonstration of binocular competition is reasonably straightforward, it is most difficult to demonstrate other competitive interactions. For instance, one can compare, in a monocularly sutured cat, regions where binocular competition is possible (i.e., the binocular segment) with regions in which such competition cannot occur (i.e., the monocular segment). Such a comparison has not yet been done for any other plausible competitive interaction. Nonetheless, limited and indirect data can be used to examine the possibility of competitive interactions between X- and Y-cell pathways and retinotectal and corticotectal pathways, in addition to binocular competition.

### Binocularly Competitive and Noncompetitive Processes

Two general approaches have been used to distinguish deficits resulting from abnormal binocular competition from those that do not. The first is the comparison of deficits in the binocular and monocular segments in monocularly sutured cats. This

has already been described in detail above in the section on binocularly competitive and noncompetitive mechanisms. The second is the comparison of deficits in monocularly and binocularly sutured cats. Wiesel and Hubel[287] first suggested the process of binocular competition on the basis of such a comparison. They reasoned that, since binocular deprivation is balanced for the two eyes, the deficits that develop in binocularly deprived cats do not result from abnormal binocular competition. Thus, deficits in the binocularly sutured cat established the binocularly noncompetitive component of deprivation, and additional deficits seen for the deprived eye of monocularly sutured cats indicate the competitive component.

The monocular/binocular segment comparison has the virtue of being an intrasubject comparison, whereas the monocular/binocular suture comparison is made between different cats. As shown below, these comparisons often yield different conclusions.

### Monocular/Binocular Segment Comparison

The conclusions drawn in the section on binocularly competitive and noncompetitive mechanisms can be briefly reiterated here for monocularly sutured cats. Deficits in the deprived monocular segment establish a binocularly noncompetitive component of the deprivation-induced abnormalities, while additional deficits in the binocular segment indicate the competitive component.

In the lateral geniculate nucleus, such an analysis indicates that soma growth is dominated by binocular competition, but a small noncompetitive effect is also present. The response properties of X-cells develop entirely by a noncompetitive process, whereas binocular competition completely controls these properties for Y-cell development. It is possible that Y-cell soma growth is entirely controlled by binocular competition, whereas X-cell soma growth is controlled by a noncompetitive process.

In the striate and lateral suprasylvian cortices, both competitive and noncompetitive processes are evident. However, since the deprived eye can influence most of these cortical cells in the monocular segment and very few in the binocular segment, binocular competition seems to be the major process. Also, simple-cell development in area 17 can be entirely accounted for by a competitive process.

Finally, the development of superior colliculus neurons seems entirely under the control of binocular competition. This is not surprising, since normal corticotectal input seems to depend upon geniculate Y-cell development which, in turn, is completely controlled by binocular competition.

### Monocular/Binocular Suture Comparison

The between-animal comparison leads to a rather different picture of the importance of binocular competition than that provided by the monocular/binocular segment comparison within monocularly sutured cats.

Soma size in the lateral geniculate nucleus is smaller than normal after binocular suture, but not as small as that seen in the deprived laminae of monocularly sutured cats. This suggests that binocularly competitive and noncompetitive mechanisms control soma growth, and represents the only parameter for which both comparisons (between-segment and between-deprivation conditions) yield approximately the same conclusion. Since abnormally few geniculate Y-cells are recorded in binocularly sutured cats, but more are recorded in these cats than in deprived laminae after monocular suture, both competitive and noncompetitive processes are implicated for Y-cell development. No detailed data are available on the effects of binocular suture on X-cell spatiotemporal sensitivity.

The deficits in the striate cortex following binocular suture suggest a noncompetitive component of development for both simple and complex cells. Yet the observation that many striate cortex cells respond to visual stimulation in binocularly sutured cats, but are unresponsive to the deprived eye of monocularly sutured cats, suggests that binocular competition also occurs in this location. In the lateral suprasylvian cortex, a strong noncompetitive component is indicated by the development of only few visually responsive cells during binocular suture. The slightly smaller neuronal population influenced by the deprived eye of monocularly sutured cats suggests that binocular competition, if it occurs at all for development of these neurons, plays a decidedly minor role.

The obvious deficits among collicular neurons in binocularly deprived cats implicate a binocularly noncompetitive process as a major developmental mechanism. However, because more collicular neurons respond to visual stimuli in binocularly sutured cats than respond to the deprived eye in monocularly sutured cats, a mechanism of binocular competition is also implicated.

These conclusions are often incompatible with those reached on the basis of the monocular/binocular segment comparison. This latter comparison leads to the conclusion that development of geniculate Y-cells, simple cells in cortical area 17, and collicular neurons is completely controlled by binocular competition, whereas the between-animal comparison suggests an important noncompetitive component of the development of each of these neurons. Furthermore, the between-segment comparison suggests a key role for binocular competition during development of the lateral suprasylvian cortex, whereas the between-animal comparison does not. Some insight into the reasons for these different conclusions can be gained from a consideration of the deprived monocular segments that develop during monocular and binocular suture.

### Comparison of Monocular Segments

The monocular segment of a central visual structure in a visually deprived cat is a key area for study because, by definition, it is the only area in which binocular interactions cannot occur. Any deficits seen here can thus be operationally defined as the result of a noncompetitive developmental process. Also, as is illustrated in Figure 15-8B and C, neurons in deprived monocular segments suffer from precisely the same type of environmental deprivation during both monocular and binocular suture.

Despite this, the deprived monocular segment consistently develops less normally during binocular than during monocular suture. That this has been observed each time a specific comparison has been made for the lateral geniculate nucleus, the striate and lateral suprasylvian cortices, and the superior colliculus establishes its validity. For example, when these segments are compared in the lateral geniculate nucleus, fewer Y-cells are recorded, and the somata are smaller, after binocular than after monocular suture. In the striate cortex, fewer normal simple cells and more unresponsive cells are found after binocular than after monocular suture. Fewer responsive neurons are found in the monocular segment of the lateral suprasylvian cortex after binocular suture than after monocular suture. Finally, fewer normal neurons are found in the monocular segment of the superior colliculus after binocular than after monocular suture, although the relevant data-base following binocular suture is limited to 10 neurons.

### Conclusions

It follows logically from comparisons described above that the degree of abnormal development due to a binocularly noncompetitive process is greater in a completely (binocularly) deprived visual system than in a partially (monocularly) deprived one. There are two general possibilities that could be invoked to explain this. First, complete deprivation might lead to a much more serious and qualitatively different form of the noncompetitive process than does partial deprivation. Second, complete deprivation might lead to an additional noncompetitive process to that seen in partial deprivation. Two speculative examples are offered below, merely to illustrate these possibilities.

First, it is clear that the central visual pathways of monocularly deprived cats develop considerably from the neonatal state. Perhaps at least some normal vision (e.g., through the nondeprived eye) is needed to trigger this development. As shown in the section on binocularly deprived cats, the central visual pathways of such cats in many ways resemble those of neonates, as if complete deprivation precludes much specific development. Kasamatsu and Pettigrew[132, 188] have even proposed a candidate system through which some useful vision could trigger specific development, but through which complete deprivation might not. This system is the diffuse projection from the locus coeruleus, a nucleus in the brainstem, to many other neural areas, including the central visual pathways (for a recent review, see ref. 173). In any case, it is clearly possible that complete (binocular) deprivation causes a qualitatively different developmental process than does partial (monocular) deprivation.

Second, there may be some global neural interactions in the visual system across the retinotopic map that link together large areas of a given structure. Connections that seem retinotopically inappropriate have been described in morphological material (e.g., refs. 37, 69, 162). If such interactions were important during development, they could explain why a deprived monocular segment develops more poorly when situated next to a completely

deprived binocular segment (i.e., during binocular suture) than when situated next to a binocular segment with many normal connections (i.e., during monocular suture). The abnormalities caused by deficient lateral interactions during binocular suture can be viewed as due to a noncompetitive process that is separate from and can be added to the binocularly competitive and noncompetitive processes that occur during monocular suture. Such a process involving lateral interactions has already been proposed for visually deprived animals (e.g., refs. 80, 221).

It must be emphasized that the above examples are purely speculative and are provided merely to illustrate possible ways by which deprived monocular segments could develop differently during the different deprivation conditions. It is not clear whether additional or a qualitatively different set of mechanisms operate during binocular suture than during monocular suture. If different mechanisms do operate, then a comparison between binocular and monocular suture cannot provide insights into common mechanisms of development (see refs. 210, 221).

### Competition Between X- and Y-Cells

Although there is little evidence concerning possible competition between X- and Y-cells, it seems useful to consider what is available. Kalil and Worden[129] speculated that the increased number of geniculate neurons with cytoplasmic laminated bodies in dark-reared cats could reflect an abnormally large population of X-cells that develops at the expense of Y-cells. Also, the morphological data of Friedlander et al.[58] suggest that in deprived laminae, some geniculate neurons that normally accept only Y-cell input from the retina accept X-cell input instead. In this context, it is interesting that deprived Y-cells seem to be less affected in the medial interlaminar nucleus, where few X-cells exist, than in the A laminae, where many X-cells are found.[143]

Perhaps because Y-cells mature later than X-cells, they require normal activity during their development in order to compete successfully with the already fairly mature X-cells for some synaptic sites. Many pathways seem to undergo retraction or a "pruning" of extraneous connections during the course of normal development (e.g., ref. 189), and X-cell input to geniculate neurons may normally undergo such pruning as Y-cell input develops. Deprivation might limit the ability of this later Y-cell development to compete successfully with and thus eliminate excessive X-cell synapses. This speculation should be regarded as nothing more than a working hypothesis, but it does serve to illustrate the possibility that competitive interactions other than that based on ocularity can occur and be important for development.

### Competition Between Corticotectal and Retinotectal Pathways

A similarly speculative case can be made for competition during development between the retinotectal and corticotectal pathways. Collicular cells seem to be dominated by the corticotectal input in both normal and monocularly sutured cats (see Figure 15-4A and B). Many receptive-field features of collicular neurons in these cats reflect features of the corticotectal neurons. However, cortical lesions in these cats dramatically alter the response properties of the collicular neurons, which come to reflect the previously subthreshold retinotectal input. After binocular deprivation, by contrast, the retinotectal pathway predominates and there seems to be no effective corticotectal input (see Fig. 15-4C).

Perhaps the retinotectal pathway develops first, but under normal conditions corticotectal neurons develop dominance over collicular neurons at the expense of the retinotectal input. The necessary condition for this is the development of a normal geniculate Y-cell input to the corticotectal neurons. This occurs in normal cats and via the nondeprived eye in monocularly sutured cats, but does not occur sufficiently in binocularly deprived cats. With Y-cell inputs, the corticotectal pathway then successfully competes with the retinotectal pathway, whereas without these inputs, the corticotectal pathway fails to compete successfully.

### Conclusions

Although much can be written about competitive and noncompetitive mechanisms of development (witness the above paragraphs), little in the way of any specific in-depth appreciation exists of the actual cellular mechanisms involved. We know most about the presence and results of binocularly competitive and noncompetitive mechanisms. Unfortunately, binocular competition is only one of a multitude of competitive interactions that could occur during development. At present, one can do little more than speculate about these possible interactions. Two that have been considered for illustration are competition between X- and Y-cell pathways and between retinotectal and corticotectal pathways, respectively. In sum, despite the large quantity and generally high quality of experiments aimed at investigating normal and abnormal visual development, the mechanisms by which the sensory environment interacts with the developing brain are still largely unknown.



## DEFICITS IN W-, X-, AND Y-CELL PATHWAYS

An issue of obvious importance in the consideration of visually deprived cats is the extent to which the W-, X-, and Y-cell pathways are differentially affected by visual deprivation. Although the available evidence does not yet permit an unambiguous answer to this question, a qualified description of W-, X-, and Y-cell deficits can be offered.

Although it is possible to consider differential effects of deprivation on retinal and geniculate W-, X-, or Y-cells, it is not yet possible to analyze data from other visual structures in this context. The reason for this is that the current understanding of the precise manner in which the W-, X-, and Y-cell pathways normally innervate other structures is so rudimentary that one usually cannot confidently interpret data from these structures in the context of W-, X-, or Y-cell deficits. This seriously limits the ability to describe in a general manner all of the differential abnormalities in the W-, X-, and Y-cell pathways caused by visual deprivation.

### The W-Cell Pathway

Practically no W-cell data are available from visually deprived cats. The only evidence is indirect: Hickey[93] reported that, in monocularly sutured cats, deprived geniculate laminae C1 and C2 develop essentially normal soma sizes, and that these laminae contain a practically exclusive population of W-cells. No physiological data from deprived W-cells central to the retina have yet been published.

### The X-Cell Pathway

Some deficits have been reported in the X-cell pathway of monocularly sutured cats. Detailed receptive-field studies of X-cells in binocularly deprived cats have not yet been reported. Retinal and optic tract recordings indicate normal X-cells from the deprived eye. Geniculate X-cells, however, appear to develop a subtle spatial acuity deficit. Even this slight deficit has been challenged, and thus the conclusion that a specific X-cell deficit occurs at all in monocularly sutured cats must be qualified. With this qualification in mind, any X-cell deficits appear to be controlled by a binocularly noncompetitive mechanism. It is interesting in this context that in normal cats, geniculostriate X-cell axons have a terminal field sufficiently small to be limited to a single ocular dominance column, and that geniculate X-cells always have their dendritic arbor limited to a single lamina and thus a single ocular domain in the lateral geniculate nucleus.

### The Y-Cell Pathway

Many anatomical and physiological studies clearly indicate a relatively selective and severe effect of visual deprivation on geniculate Y-cell development (see the sections on monocularly and binocularly deprived cats; see also ref. 225 for a more complete discussion of this literature). In monocularly sutured cats, geniculate Y-cell development can be entirely explained by a process of binocular competition, since the Y-cell abnormalities seem completely limited to the binocular segment of deprived laminae. This may, in turn, relate to the observations in normal cats that geniculocortical Y-cell axons have a distribution sufficiently wide to have spanned several ocular dominance columns during development, or that geniculate Y-cell dendritic arbors always extend into the next lamina, or to both observations. Thus Y-cells seem to have the opportunity to engage in binocular interactions at several levels.

Another factor in geniculate Y-cell development is its relative delay compared to that of X-cell development. It may not be surprising that Y-cells are more seriously affected by deprivation than are X-cells, since relatively much more X-cell development seems to occur prior to the critical period. Perhaps the combination of being put at a binocularly competitive disadvantage, as well as late de-

velopment (which could result in a competitive disadvantage with respect to earlier developing neurons), results in the rather poor development of deprived Y-cells.

## SITES OF DEPRIVATION-INDUCED ABNORMALITIES

As noted in the sections on monocularly and binocularly deprived cats, every central visual structure so far studied develops abnormally during visual deprivation. However, it is not at all clear how these effects relate to one another. In order to understand completely how the visual environment interacts with the developing brain, it is necessary to determine which deprivation-induced abnormalities are primary results of the deprivation and which are nonprimary (secondary, tertiary, etc.) consequences of the primary changes. For one example, although binocular deprivation seems to prevent normal development of the corticotectal pathway, this appears to be a secondary consequence of failure of a normal Y-cell geniculocortical pathway to develop.

Given the complex interactions of the visual structures considered in this review, establishing the primary abnormalities caused by deprivation is far from a trivial matter. What is needed for this analysis is both a detailed description of the pattern of deprivation-induced abnormalities in cats raised to adulthood and a description of the dynamics of these abnormalities as they develop during the critical period. Unfortunately, such information is not yet available.

It is nonetheless possible to draw two major conclusions from the work that has been done. First, primary deficits are unlikely at the retinal level, since retinal ganglion cells develop normally in deprived eyes. Even this is uncertain, however, because abnormally slow (but ultimately complete) development of retinal ganglion cells could be the primary cause of secondary geniculate deficits. This emphasizes the need for data from the critical period. Second, most (but not all) of the deficits in the superior colliculus and lateral suprasylvian cortex are probably secondary to those in the geniculocortical pathways. Therefore, many of the primary effects of visual deprivation can be attributed to the geniculocortical pathways.

A large number of geniculate and cortical deficits have been described in the sections on monocularly and binocularly deprived cats, but their interrelationships are unclear. On the one hand, it is conceivable that many cortical abnormalities are secondary to abnormal geniculate input. On the other hand, it is equally possible that geniculate deficits are secondary to those in the cortex, for at least two reasons. First, a large corticogeniculate pathway exists (e.g., ref. 277) that, if abnormal, could cause secondary changes among geniculate neurons. Second, abnormalities in geniculocortical synapses (at a cortical locus) could be retrogradely and secondarily reflected among geniculate neurons. For example, failure of a geniculate neuron to develop or maintain synapses in the cortex could cause that cell to develop abnormally. Also, cortical lesions are known to cause transynaptic retrograde degenerative changes that can be detected even in the retina.[249, 282] Thus, even retinogeniculate synaptic deficits might be secondary to cortical ones.

## CLINICAL CORRELATIONS

### Behavior of Amblyopic Cats

As noted in the section on behavioral correlates, behavioral studies of visually deprived cats can be specifically correlated with some of the deficits noted for the central visual pathways of these cats. The results of perimetry studies are consistent with both the emphasis on binocular competition as a developmental mechanism and on the conclusion that structures outside the geniculocortical pathways develop relatively few abnormalities independent of these pathways. Psychophysical studies of contrast sensitivity yield results that are consistent, at a very superficial level, with a relatively large deficit in the Y-cell pathway.

### Comparisons Between Cat and Human

Any attempt to attribute clinical significance to the studies reviewed in this chapter is hampered by two major obstacles. First, differences between the cat and human central visual pathways could alone subvert any such attempt. Second, the etiology of deprivation or strabismic amblyopia in humans is typically so different from the effects of lid suture or dark-rearing in cats that attempts to correlate them are premature. It thus seems pointless to draw any specific homologies between the visually deprived cats described here and amblyopic humans; however, three general points can be briefly and selectively made.



#### Acuity Versus Contrast Sensitivity

First, it is common to assess amblyopia by measuring the patient's visual acuity. Visual acuity represents a single point on the spatial contrast-sensitivity function—namely, the highest spatial frequency that can be detected. Acuity thus does not take into account performance at the important low spatial frequencies.[70, 71, 91, 92, 126] In cats, for instance, it is possible to have two animals (e.g., a normally reared cat with its striate cortex removed and a binocularly deprived cat; see Fig. 15-9) with equivalent acuity but very different low-spatial-frequency sensitivity; the animal with better low-frequency sensitivity has dramatically superior vision (see Fig. 15-9). Hess and Howell[91] have previously described an analogous division for human strabismic amblyopes, with the same consequences. In the assessment of clinical amblyopia, therefore, acuity measurements alone might overlook important information, such as vision at low spatial frequencies.

#### Sensitivity Loss to High and/or Low Spatial Frequencies

Second, it seems tempting to postulate that amblyopia involving a loss of low-spatial-frequency sensitivity might involve Y-cells, among others, whereas amblyopia only at higher frequencies might be limited to an X-cell effect. Ikeda and Tremain[121] report that cats raised with strabismus or ametropia develop abnormalities limited to the X-cell pathway, while behaviorally these animals display good visual capacity with deficits limited to high spatial frequencies. Unfortunately, it is not at all clear that human X-and Y-cells, if they exist at all, have properties at all simiar to those of X- and Y-cells in the cat. However, monkeys have X- and Y-cells with properties in many ways similar to those of X- and Y-cells in cats.[45, 229]

#### Defocus Versus Diffusion

Third and finally, it is possible to describe at least two different types of optical aberrations and their expected effects as forms of visual deprivation. One is defocus or blur, the optical consequence of which is to reduce contrast more in the higher than in the lower spatial frequencies. Among the clinical examples of defocus are myopia, anisometropia, and astigmatism. The second aberration is optical diffusion, which reduces contrast approximately equally for all spatial frequencies. An example of a diffused image is one viewed through fogged or dirty glasses, and complete diffusion (obtained by covering an eye with something like half of a ping-pong ball) leads to the viewing of light without spatial patterns. Among clinical examples of conditions marked by diffusion are cataracts, corneal scarring, and ptosis.

Moderate blur provides a reasonable environment for Y-cells, because of the low spatial frequencies it permits; if great enough, however, blur might deprive X-cells of effective stimuli. Diffusion, on the other hand, would severely deprive both X- and Y-cells. This view is consistent with data from cats, since lid suture, which provides a diffused visual environment, affects development of both X- and Y-cells (see the section on monocularly and binocularly deprived cats); blur, however, affects the development only of X-cells.[121]

#### Conclusions

Some of the variability in clinical deprivation or strabismic amblyopia might be usefully analyzed in this context. Some forms of amblyopia are characterized by fairly good vision despite reduced acuity, while others demonstrate poor vision despite equivalent acuity (e.g., refs. 91, 149). Perhaps this can be related to the specific form of deprivation, particularly with regard to the spatial and temporal frequency content in the visual environment during childhood. For instance, congenital cataracts, which diffuse the visual image, produce severe amblyopia if not removed early,[280] whereas uncorrected astigmatism produces a much more subtle and mild amblyopia.[54] Perhaps when Y-cells develop fairly normally, as with moderate astigmatism or blur, fairly good vision develops, but when they do not, as with cataracts or diffusion, severe amblyopia occurs.[218, 219]

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# 16 Muscle Afferent Contributions to the Regulation of Muscle Length and Tension

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**CONTROL THEORY AND MUSCLE REGULATION**
- Basic Features of Servomechanisms
- Distinction Between Regulation and Control
- Evaluation of Servo Performance
- Definition of the Motor Servo
- Nature of the Variable Regulated by Motor Servo Action
- Separation of Servo from Non-Servo Action: Evaluation of Responses in Intact Preparations

**THE PHYSICAL PLANT**
- Mechanical Properties of Muscle
  - *Length–Tension*
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  - *Nonlinear Muscle Properties*
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- Mechanical Properties of Limbs

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  - *A Nonlinear Model of Spindle-Receptor Response to Stretch*
  - *Asymmetrical Primary Responses to Symmetrical Muscle Stretch and Release*
- Efferent Innervation of the Mammalian Muscle Spindle
  - *Functional Classification of Efferent Innervation of Muscle Spindle*
  - *Efferent Innervation: Effects on Dynamic Response*
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- Mechanisms of Fusimotor Action
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- Muscle Receptors Studied in Intact Preparations
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- Relative Contributions of Gamma and Beta Innervation

**CENTRAL CONNECTIONS OF MUSCLE AFFERENTS**
- Ia Afferent Pathways
  - *Monosynaptic Connections*
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  - *Inhibitory Connections*
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- Force-Feedback Measurements
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- Regulation of Motor Output
- Alternative Hypotheses
- Pathological States: The Clasp-Knife Reflex
- Contributions of Efferent Innervation of the Muscle Spindle to Performance of the Closed-Loop System
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**RELATIONSHIP OF POSTURE AND MOVEMENT**