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Organization of Visual Pathways in Normal and Visually Deprived Cats

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I. INTRODUCTION

The extent to which development of brain structure and function depends on early experience is of central interest to neuroscientists. This question has been studied most extensively in the visual system, perhaps because of the relative ease with which the visual environment can be manipulated. Many experiments have shown that the postnatal development of mammalian visual pathways is dramatically influenced by the organism's early visual experience. For example, an environment during early visual development that restricts patterns but allows nearly normal levels of diffuse light can alter neural connections and severely reduce visual capacities later in life. Moreover, after a relatively limited developmental period (the critical period), these alterations become very difficult, if not impossible, to reverse; similarly, such deprivation after the critical period does not deleteriously affect visual pathways that have developed normally. The basic observation that early visual experience can alter the structure and function of the brain has been verified in a wide variety of species, including humans. It is thus a general phenomenon.

The importance of studying the effects of experience on neural development is twofold. First, it can provide a phenomenological description of the kinds of experience leading to specific types of neural abnormalities. This is important for understanding how malleable the system is, and it is also of potential clinical importance. Second, studies of the effects of early experience can provide information about the mechanisms of both normal and abnormal neural development. That is, how do the 10^{10}–10^{14} neurons in the (human) brain form their incredibly specific interconnections, and what are the mechanisms by which they are modified by the environment?

Our goal in this review is to consider what is known about the mechanisms of normal and abnormal development of the central visual pathways. Rather than simply provide a phenomenological description of the superficial changes occurring during development in normal and deprived animals, we attempt to evaluate the underlying processes involved. Do the changes during development in an impoverished environment result from atrophy, a failure to develop, or active but abnormal development that leads to altered connectivity? What are the sites of the abnormalities, and which are due to primary alterations as opposed to secondary reflections of changes occurring elsewhere in the system? What synaptic events underlie the changes in normal and abnormal development? What are the mechanisms of these synaptic events? These and related issues are addressed in this review.

Most information about these issues has derived from studies of the visual system of the cat, although many basic observations have been confirmed in other species, including primates. Therefore we confine ourselves almost exclusively to the cat visual system. We begin by considering the organization and function of the normal visual pathways in the cat (sect. II). Then we preview some classes of developmental mechanisms that have

been studied extensively by deprivation experiments and consider the conditions required to test them (sect. III). This is followed by a review of the three visual-deprivation conditions that have been studied in greatest detail and that have provided the most information about the mechanisms of normal and abnormal development: monocular deprivation of pattern vision, binocular deprivation of pattern vision, and total light deprivation (sect. IV and V). In sections IV and V we review the final outcomes of rearing with visual deprivation from birth to adulthood. In section VI the course of abnormal development is compared with the normal development of the visual system. Finally, we attempt to bring together what this literature has and has not revealed about the causes, sequencing, and neural sites of abnormal visual development and the mechanisms of both normal and abnormal development (sect. VII). Section VIII briefly summarizes this review. The individual sections are clearly related to each other. Because of the breadth of the literature covered and the consequent length of the review, however, each section has been written so that the reader interested in only one or two topics can read only the relevant sections.

Some topics are not covered here. Because we are concerned with examples of robust developmental neuroplasticity that are sensitive to the sensory environment, we do not discuss studies dealing with changes caused by adult sensory deprivation (e.g., 49) or describing deprivation-induced changes that disappear after a relatively brief exposure to a normal sensory environment (e.g., 9). In addition we do not consider a number of interesting forms of visual deprivation, such as strabismus, deprivation of specific patterns, etc., because relatively little is known about the sites and mechanisms of the abnormalities produced by these conditions. The abnormalities produced by these conditions have been described in several recent reviews (20, 136, 255). Finally, we attempt to provide a comprehensive review of the literature that is considered, but this area of research continues to be extremely active, and we found ourselves rushing to read and incorporate papers published as we were writing. A line had to be drawn somewhere, and regrettably papers appearing after the spring of 1981 could not be included.

II. VISUAL PATHWAYS OF THE NORMAL CAT

The retina has direct projections to many structures in the brain. The largest retinal projection terminates in the dorsal lateral geniculate nucleus. There is also a substantial retinal input to the superior colliculus, plus smaller projections to the suprachiasmatic nucleus of the hypothalamus, to various pretectal nuclei, to the midbrain raphe, to the ventral lateral geniculate nucleus, and to small cell groups in the tegmentum (11, 75, 89, 122, 206, 246, 281). Furthermore recent electrophysiological mapping studies have emphasized the large number of distinct cortical representations of the visual field (271, 383-385). These have complex connections among them-

selves and also among various thalamic nuclei, including the lateral geniculate nucleus.

It is well beyond the scope of this review to describe all these visual pathways in great detail; several recent reviews have appeared on this subject (209, 281, 344, 363). In this section we focus on those features of the normal pathways of the cat that have been most fruitfully studied from the perspective of visual development, including the retina, the dorsal lateral geniculate nucleus, the superior colliculus, and certain visual areas of the cerebral cortex. First we consider the retinogeniculocortical pathways to areas 17 and 18, followed by a discussion of certain extrageniculate pathways and the lateral suprasylvian visual cortex.

A. General Morphological Features of Retinogeniculocortical Pathways

1. Retina

The vertebrate retina is a layered structure consisting of receptors (rods and cones) with somata in the outer nuclear layer, interneurons (bipolar cells, horizontal cells, interplexiform cells, amacrine cells) with somata in the inner nuclear layer, and output neurons (retinal ganglion cells) with somata in the ganglion cell layer. Axons of the retinal ganglion cells enter the optic nerve and form the retinofugal pathways. Further details of retinal organization can be found elsewhere (64, 65, 280).

2. Dorsal lateral geniculate nucleus

a) Laminar arrangements. Six laminae have been recognized in the laminated portion of the cat lateral geniculate nucleus (Fig. 1); these have been named A, A1, C, C1, C2, and C3 by Hickey and Guillery (134). These laminae are stacked in retinotopic register so that a perpendicular line through them represents the same region in visual space (291). Laminae A and A1, the largest and most recognizable, form a reasonably matched pair, with one representing each eye. The C laminae have been analyzed in less detail, and relatively little is known about their reaction to visual deprivation. Medial to the laminated part of the lateral geniculate nucleus is a cell group that also serves as a direct relay from the retina to the visual cortex and carries a separate visual-field representation. This is the medial interlaminar nucleus, which is a division of the dorsal lateral geniculate nucleus (cf. 109, 281). Guillery et al. (109) have recently described another subdivision of the lateral geniculate nucleus[1] (the "geniculate wing") that extends rostrally,

[1] Because this band of retinorecipient cells lies along the lateral edge of the pulvinar, some investigators considered this to be a division of the pulvinar (15, 17, 169, 188, 219). However,

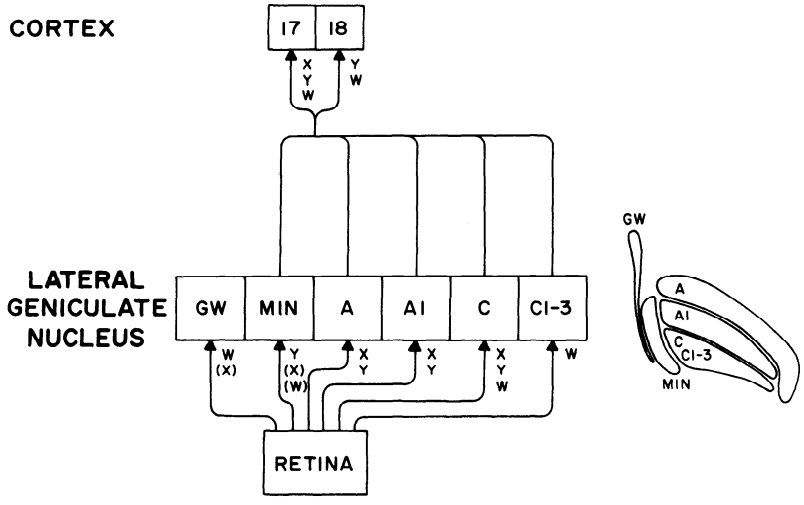

FIG. 1. Schematic diagram of retinogeniculocortical pathways in the cat showing the retina, lateral geniculate nucleus, and cortical areas 17 and 18. W-, X-, and Y-cell pathways are indicated. Geniculate subdivisions include: A, A1, laminae A and A1; C, lamina C; C1-3, laminae C1-C3; MIN, medial interlaminar nucleus; and GW, geniculate wing. Parentheses indicate pathways with little or uncertain W- or X-cell contribution. Not shown are geniculocortical pathways from C laminae, medial interlaminar nucleus, and geniculate wing to area 19. Geniculocortical pathways to the lateral suprasylvian cortex are shown in Fig. 4 (see text for details).

medially, and dorsally from the medial interlaminar nucleus to the pulvinar (see also 15, 17, 188, 219).

b) Interneurons. Classifications of geniculate cells originated with von Monakow (243), who believed he had discovered geniculate interneurons (*Schaltzellen*) in the posterodorsal tail of the cat's lateral geniculate nucleus. Geniculate cells in this region received a retinal input but failed to undergo retrograde degeneration after cortical lesions that von Monakow thought had included all of the visual cortex. We now know that in cats this part of the nucleus projects to the most inaccessible part of the visual cortex, which presumably must have been spared by von Monakow's lesions. These experiments can now be reinterpreted, but the interneurons remain, as has the difficulty of identifying such neurons on the basis of negative evidence. The best morphological evidence for the identification of interneurons now comes from experiments in which horseradish peroxidase (HRP) is injected into the visual cortex, and the subsequent retrograde labeling of geniculate so-

Guillery et al. (109) argued that these retinorecipient cells are an extension of the lateral geniculate nucleus and called them the "geniculate wing." Since these cells receive inputs from the retina (15, 17, 169, 188, 219) and project to the cortex (17, 161, 169, 179), it seems proper to consider them part of the lateral geniculate nucleus. We therefore adopt the terminology of Guillery et al. (109) and refer to them as the geniculate wing in this review.

mata is studied. The somata remaining unlabeled after extensive cortical injection probably are interneurons. Estimates of the proportion of interneurons depend largely on the HRP method and vary considerably, from less than 10% (223) to 20% (91) or 25% (212). Because the higher values depend on negative evidence, they are necessarily somewhat suspect until it has been demonstrated that all cells having axons at an injection site are labeled by retrograde transport. The lower values have been obtained from rather thick frozen sections, so it has been argued (212; but see 261) that unlabeled cells may have been missed because this material is optically less than ideal. The issue remains unresolved and is reconsidered below.

c) Relay cells. Geniculate cells that project to the cortex (i.e., relay cells) were first studied by means of the retrograde reaction produced by lesions of the visual cortex and were later studied by HRP injections into cortex. For laminae A and A1, damage to cortical area 17 alone produced relatively mild changes that tended to spare the largest cells, whereas lesions in area 18 alone produced little or no change (88). Damage to both areas 17 and 18 produced extensive retrograde degeneration of most geniculate cells, including the largest. It was concluded that the largest cells in the A laminae project to areas 17 and 18, that the smaller cells project to area 17 alone, and that few if any cells project solely to area 18.

Injections of HRP have been made into cortical area 17, 18, or 19 by several investigators (17, 85, 91, 94, 150, 169, 205, 216, 219, 224, 229). The results have revealed some discrepancies, and this emphasizes the difficulty in relying on the HRP method for quantitative sampling procedures. However, there is evidence that injections in area 17 produce labeling in laminae A and A1 and to a lesser extent in the C laminae and medial interlaminar nucleus; that area 18 injections produce labeling in all the geniculate laminae plus the medial interlaminar nucleus; and that area 19 injections produce labeling primarily in the C laminae, medial interlaminar nucleus, and geniculate wing. Injections of visual areas in the suprasylvian cortex also label cells in the C laminae and medial interlaminar nucleus (see sect. II*E2a*). These results are in general agreement with those of other recent studies of geniculocortical projections based on orthograde tracing methods (213, 284). The projections from the lateral geniculate nucleus to cortical areas 17 and 18 are shown in Figure 1.

After an area 17 injection, most medium and large cells of laminae A and A1 are labeled, but a number of cells are unlabeled (85, 211, 224). Area 18 injections label the largest cells in laminae A and A1, but the extent of this labeling varies significantly among experiments. LeVay and Ferster (211) found that area 18 injections labeled very few cells in lamina A1 (2–4%) and even fewer cells in lamina A (about 1%), whereas other investigators (91, 94, 150, 224) described many more cells labeled after an area 18 injection (~15%). Hollander and Vanegas (150) also found more cells labeled in lamina A1 than in lamina A after area 18 injections, but this appears to be an inconsistent result (cf. 91, 224).

These experiments confirm the interpretation of the retrograde degeneration experiments that some of the largest geniculate cells project to areas 17 and 18 and that most medium-sized cells project to area 17 alone. Geisert (91) defined these relationships in more detail by injecting two distinguishable markers into the visual cortex, one in area 17 and the other in area 18. He found that 10% of the cells in laminae A and A1 were labeled by both markers. These cells, which must send axons to both cortical areas, were among the largest in the nucleus. About 70% of the cells were labeled only by the marker injected in area 17; these were medium and small cells. About 1% were labeled only by an area 18 injection; these were large cells. In the C laminae more cells were labeled by both markers (50%), including small cells as well as some of the largest. A considerable number of large cells in the C laminae were labeled only by the area 18 marker (10% of total cell population). Geisert's experiments also provide evidence that many lamina C cells have axons that send branches to each of the three visual cortical areas studied (areas 17, 18, 19), although the size distribution of these cells was not determined.

3. Organization of visual cortex

a) Laminar arrangements. The neocortex is usually divided into six layers numbered sequentially, commonly with roman numerals, from the pial surface to the white matter. Studies of the geniculocortical projections demonstrate that these pathways tend to have a distinct laminar pattern of termination (213, 216, 284).

Cells of the A laminae project to cortical areas 17 and 18, and the pattern of terminals is qualitatively similar in both areas. The projection zone fills layer IV most heavily and extends into the most ventral portion of layer III. A less dense but nonetheless significant terminal zone also extends throughout layer VI. The C laminae project to a wide range of cortical areas, including areas 17, 18, and 19, plus suprasylvian cortical areas. Although the terminal pattern has been most extensively studied in area 17, no obvious differences in this pattern were noted among the different cortical areas (213). These terminals are found in layer I plus two tiers along the dorsal and ventral borders of layer IV; these latter probably extend into lower layer III and upper layer V.

The terminal pattern of the medial interlaminar nucleus has not been described in any detail except in area 17. Based on retrograde transport after small cortical injections of HRP, Leventhal (216) concluded that this geniculate subdivision projects to cortical layers I and IV and probably to lower layer III.

Therefore in striate cortex, where this has been studied in greatest detail (213, 216), different geniculate regions project to different cortical layers, although some overlap is evident in these projections. Layer I receives input

from the C laminae and medial interlaminar nucleus, layers II and the upper portion of III receive no geniculate afferents, lower layer III and layer IV receive input from all geniculate subdivisions except the geniculate wing, the uppermost tier of layer V receives input from the C laminae, and layer VI receives terminals from the A laminae. Recently Ferster and LeVay (72) successfully filled with HRP many of the axons projecting to layer IV. They reported that the thicker axons terminate dorsally within the layer, and each has a relatively extensive arborization parallel to the layers; the thinner axons terminate ventrally within the layer, and each has a relatively small arborization. Furthermore even though most of layer V appears to receive no geniculate afferents, a certain class of layer V corticotectal cells may be monosynaptically driven by geniculate input (32, 139; but see 119), presumably via dendrites extending into other cortical layers. Thus one cannot conclude that cortical cells in layers III and V do not receive direct geniculate input from the pattern of geniculocortical terminals.

b) Columnar arrangements. Lorente de No (226) first suggested the columnar organization of cortex in addition to the more obvious layering pattern (see also 251, 277). He pointed out that cortical neurons seem to be stacked above one another across layers and suggested that these form functional columns of cortical circuitry. The layering pattern thus results from the phenomenon of different morphological (and functional) cell types being stacked up in register in neighboring columns.

Hubel and Wiesel (152) provided the first physiological evidence of a columnar organization in the cat's striate cortex (described in sect. II*B2a*). An anatomical demonstration of columnar arrangements in cortical area 17 of the cat was done by Shaltz et al. (299, 300). They injected one eye of a cat with a radioactive tracer, which was carried transneuronally to geniculate neurons and up the optic radiations to layer IV of area 17. Autoradiography thus could elucidate inputs related to that eye. The subsequent picture shows alternate ocular-dominance patches from each eye distributed throughout the binocular segment of layer IV. These patches have a period of roughly 1 mm. Shatz and Stryker (300) used electrophysiological methods to confirm this organization for layer IV. Although these studies in the cat were limited to layer IV, studies with a metabolic marker ([^{14}C]deoxyglucose) in monkeys have shown that these ocular-dominance columns indeed extend vertically through all the layers (123, 157, 193). Evidence for orientation columns in area 17 is presented in section II*B2a*.

B. General Functional Features of Retinogeniculocortical Pathways

1. Retina and lateral geniculate nucleus

a) Center/surround organization. Geniculate neurons appear to receive their primary excitatory input either from one retinal ganglion cell or from

very few of the same functional type (40), so that functional properties of geniculate cells are much like those of their retinal inputs. Thus we consider retinal and geniculate neuronal properties together and then point out some of the functional differences between retinal ganglion cells and geniculate neurons.

Kuffler (203) provided the classic description of the receptive-field organization for cat retinal ganglion cells, and Hubel and Wiesel (151) extended this to geniculate neurons. This analysis led to the concept of a concentrically arranged, antagonistic, center/surround receptive-field organization for each cell. Two types were noted: on-center and off-center cells. For on-center cells, the onset of light limited to a small retinal region (i.e., receptive-field center) raises the cell's firing rate, as does cessation of a bright annulus surrounding this region (i.e., receptive-field surround); cessation of light in the center or onset of light in the surround reduces the firing rate. For off-center cells, the reverse is true: cessation of light in the center or onset in the surround raises the firing rate, and onset of light in the center or its cessation in the surround reduces the firing rate. Thus the receptive fields of the cells described by Kuffler (203) and Hubel and Wiesel (151) display no stimulus selectivity other than that for the position and contrast of targets presented to the retina.

b) W-, X-, and Y-cells.[2] Retinal ganglion cells and geniculate neurons can be classified along dimensions other than on- or off-center characteristics, and at least three broad groups can be recognized. Enroth-Cugell and Robson (70) first demonstrated a division of these cells into what they termed X-cells and Y-cells. More recently a third group, called W-cells, has been described.

The W-cells can be distinguished from X- and Y-cells by more slowly conducting axons, sluggish responses to visual stimuli, poor spatial and temporal resolution, poor contrast sensitivity, lower maintained discharge rates, general lack of antagonism in inhibitory interactions between center and surround, poor spatial resolution, and often rather large receptive fields (42, 43, 48, 84, 346, 364, 365, 367, 402). Some W-cells display center/surround receptive-field organization, but many do not. Those lacking center/surround fields form a rather heterogeneous group and include diffuse on-off receptive fields (i.e., cells respond to onset and cessation of light throughout their fields), cells selective to particular directions of stimulus movement, and

[2] For reasons set forth by Rowe and Stone (287), we have followed the noncommittal, and most common, terminology of W-, X-, and Y-cells for these neuron classes. Other names have been used for these cells, and it is not always clear that the cell groups identified by different names represent completely isomorphic classification schemes. With this proviso, the following terms are roughly 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 (35, 40, 42-44, 83, 137, 297, 356).

others as well. It has been suggested that the W-cell class is actually a catchall harboring several further distinct cells types [e.g., Rodieck (281)].

Much more is known about X- and Y-cells, which appear to represent the majority of the retinogeniculocortical pathways. The following is a brief account of the distinguishing characteristics of retinal and geniculate X- and Y-cells (33–35, 40, 70, 83, 137, 138, 148, 207, 297, 356).

1) X-cells display fairly linear spatial summation in their receptive fields, whereas Y-cells display nonlinear summation (70, 137, 138, 297). Tests for linearity typically employ counterphased or drifting sine-wave gratings[3] that can be generated on a cathode-ray tube. Hochstein and Shapley (137, 138) devised a model for X- and Y-cell receptive fields based on a detailed and elegant study of the summation properties of these neurons. The X-cell model is simpler and consists of a center/surround configuration with fairly linear summation properties. That is, a grating position or spatial phase angle can be found at which no response is evoked (i.e., the null position), and the response at other positions occurs at the same temporal frequency as the grating's counterphase rate. The Y-cell model includes a similar, linear center/surround configuration somewhat larger than that for an X-cell. However, superimposed on this and scattered throughout the Y-cell receptive field are small, nonlinear subunits. These provide Y-cells with both their response nonlinearities (typically responses at twice the grating's counterphase rate that are independent of the grating's spatial phase angle) and

[3] Most readers are more familiar with square-wave gratings, which are simple alternating stripes of equally spaced, dark and light regions. A photometer passed across the stripes would show that the luminosity profile of such a grating is a square wave. A sine-wave grating is similar in all repects, except that its luminosity profile is described by a sine wave. Four variables of such gratings are typically altered: contrast, spatial frequency, temporal frequency, and spatial phase angle. Contrast is usually defined as $(L_{max} - L_{min})/(L_{max} + L_{min})$, where L_{max} and L_{min} are, respectively, the maximal and minimal luminance values across the grating. Note that contrast can be changed without changing the mean luminance, which is one-half $(L_{max} + L_{min})$. Spatial frequency is the number of stimulus cycles per degree of visual angle. Temporal frequency (in cycles/s or hertz) is the temporal changes in the grating. This can be achieved in either of two ways: *1*) by drifting the grating, with temporal frequency calculated by the product of spatial frequency (cycles/degree) and speed of drift (degrees/s) or *2*) by counterphasing the grating so 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 a grating; a 180° phase shift means displacement of the grating perpendicular to its orientation by one-half of a spatial cycle; a 90° phase shift, by one-fourth, etc. The theoretical advantages of sine-wave gratings are discussed in detail elsewhere (96, 296). Briefly and simply, Fourier's theorem states that any complex waveform can be described in terms of its component sine waves (Fourier analysis) and that any complex waveform can be created by superposition of appropriate sine waves properly selected for phase, spatial frequency, and amplitude or contrast (Fourier synthesis). Black and white visual scenes can be described as complex waveforms for which light intensity can be plotted as a function of distance across the scene. Such a scene can be analyzed and synthesized in terms of its component sine-wave gratings, although such an analysis needs to be performed in two dimensions. In this context the sine-wave grating can be viewed as a fundamental visual stimulus to which responses can be measured.

their sensitivity to higher spatial frequencies (finer spatial details). At lower spatial frequencies (cruder forms), the linear center/surround component of a Y-cell contributes to and sometimes dominates the response, and this component thus depends on the spatial phase of the grating (i.e., it has a null position) and occurs at the grating's counterphase rate.

2) Axons of X-cells conduct less rapidly than those of Y-cells, both for retinogeniculate axons and geniculocortical axons. X-cell axons in the optic nerve or tract and optic radiation conduct at roughly 15–25 m/s; Y-cell axons conduct at roughly 25–50 m/s (148).

3) For corresponding parts of the visual-field representation, X-cells tend to have smaller receptive-field centers than do Y-cells by a factor of roughly 2. These receptive-field centers tend to increase in size with increasing eccentricity from the area centralis. Earlier studies emphasized that the two populations overlap extensively with regard to the size of their field centers (42, 43, 148, 364). However, recent data suggest no overlap when variability among animals and across the retina is eliminated (41). X-cells typically have field centers less than 1° across, and these can be less than 0.1° in the area centralis.

4) X-cells usually respond to higher spatial frequencies and thus tend to have better spatial resolution than Y-cells. However, this comparison is not straightforward because of the complexity of the Y-cell fields (see point *1* above). When only the linear center/surround components are compared, X-cells have clearly better spatial resolution than Y-cells with virtually no overlap between populations (cf. 41, 330). However, Y-cells are capable of nonlinear responses to much higher spatial frequencies than their linear components can resolve, and these are presumably due to contributions from the nonlinear subunits described by Hochstein and Shapley (137, 138). When these responses are considered, Y-cells have a spatial resolution nearly as good as that seen for X-cells, and considerable overlap occurs between populations (207, 330).

5) X- and Y-cells have different sensitivities to spatiotemporal stimuli (207, 331). This is best illustrated by plotting sensitivity (inverse of contrast needed to evoke a threshold response) against spatial or temporal (counterphase) frequency of the sine-wave grating stimulus.[3] Y-cells monotonically decrease in sensitivity as spatial frequency increases; X-cells have an inverted U-shaped function with peak sensitivity to middle spatial frequencies and reduced sensitivity to higher and lower spatial frequencies. Both X- and Y-cells monotonically decrease in sensitivity as temporal frequency increases. Although under most conditions Y-cells are somewhat more sensitive than X-cells to temporal changes, there is overlap between populations that depends on the spatial frequency of the stimulus. Likewise, although X-cells have slightly higher spatial resolution (i.e., sensitivity to higher spatial frequencies) than Y-cells do, there is overlap between populations that depends on the temporal frequency of the stimulus. Thus the common conclusions that X-cells possess better spatial resolution than Y-cells and that

Y-cells exhibit better sensitivity to temporal patterns than X-cells need to be qualified. The one obvious and dramatic difference between populations is that Y-cells are quite sensitive to low spatial frequencies but X-cells are not. X-cells become relatively more sensitive than Y-cells only as the spatial resolution limit is approached at lower temporal frequencies. The observation that Y-cells are more sensitive to higher temporal frequencies than are X-cells (except at high spatial frequencies) may be consistent with the conclusion that Y-cells respond to faster target motions than do X-cells (40, 148).

6) X-cells tend to respond to appropriate standing-contrast targets (a bright spot in the center for an on-center cell, a dark spot for an off-center cell) with a much more tonic or sustained response than do Y-cells (40, 148). Y-cells cease responding to such a stimulus within a few seconds, whereas X-cells respond for 20 s or more. This distinction appears to hold only under mesopic illumination (287), however, and even then exceptions are common (see also 209).

These properties, to a first approximation, are common to X- and Y-cells in both the retina and lateral geniculate nucleus. Several subtle differences between these populations have nonetheless been detected. First, retinal ganglion cells have receptive fields limited to the eye in which they are located, but most geniculate neurons have binocular fields consisting of the classic center/surround field from the dominant eye and a purely inhibitory field from the nondominant eye (292). Electrical stimulation studies show that each geniculate cell typically receives inhibitory input from each eye (184, 368, 369). Occasional cells receive monosynaptic excitatory input from each eye, although the excitation is subthreshold from the nondominant eye. Second, geniculate neurons possess stronger inhibitory antagonism in their receptive fields than is evident for retinal ganglion cells (151; but see 331). Third, geniculate X-cells have lower rates of spontaneous activity than their retinal counterparts, although no such difference is seen for Y-cells (34). Fourth, Maffei and Fiorentini (230) claimed that receptive-field surrounds of geniculate neurons reacted to dark adaptation differently from those of retinal cells, but this has recently been challenged (182).

c) Distribution and projection of retinal W-, X-, and Y-cells. W-, X-, and Y-cells are found throughout the retina, but their numbers change with retinal location (40, 42–44, 84, 286, 391). The X-cell density peaks sharply at the area centralis. Both Y- and W-cells have a much less marked change in density with retinal location. Y-cells are modestly increased near or in the area centralis, and W-cells have a slight density increase along the visual streak running horizontally through the area centralis. Thus overall ganglion cell density peaks at the area centralis and along the visual streak and declines with eccentricity. Proportionately more Y- and W-cells and fewer X-cells are seen with increasing eccentricity. The most detailed estimates of W-, X-, and Y-cell distributions in the retina depend on anatomical studies of soma size distributions. The validity of the assumed correlations be-

tween soma size and functional (W-, X-, or Y-cell) class is considered in section II*C1*.

Retinal X-cells project almost exclusively to the lateral geniculate nucleus, although some may innervate regions of the mesencephalon apart from the superior colliculus (42, 84, 139). Y- and W-cells innervate both the lateral geniculate nucleus and superior colliculus (84, 139, 191), and most or all Y-cells appear to innervate both structures by way of branching axons (27, 139). W-cells also innervate both the ventral lateral geniculate nucleus (340) and the nucleus of the optic tract in the pretectum (143). Thus, as illustrated in Figure 1, all three classes of retinal ganglion cell project to the lateral geniculate nucleus (for further details of distribution of retinal W-, X-, and Y-cell projections, see 84, 209, 281).

d) Distribution and projection of geniculate W-, X-, and Y-cells. The different cell types are not uniformly distributed within the lateral geniculate nucleus (see Fig. 1; cf. 68, 148, 200, 402). The A laminae contain a mixture of X- and Y-cells. As one moves mediolaterally in these laminae (i.e., from a more central to a more peripheral representation of the visual field), the relative proportion of Y- to X-cells increases, presumably as a simple reflection of the same tendency in the retina. The C laminae contain mostly W-cells, although X- and Y-cells may occasionally be found there as well. There is some evidence that the X- and Y-cells there are limited to lamina C and that ventral to this (laminae C1–C3) only W-cells are found (402). In the medial interlaminar nucleus the vast majority of the neurons are Y-cells, but rare W- and X-cells also have been reported. Although no recordings have been made in the geniculate wing, morphological studies suggest that W-cells (and possibly X-cells) project there (109, 188, 219).

W-, X-, and Y-cells appear to represent three parallel, fairly independent pathways with little overlap in excitatory connections from retina through the lateral geniculate nucleus to cortex. However, Y-cells apparently inhibit X-cells in the lateral geniculate nucleus, and the converse may also be true (148, 324). There is some evidence, mostly physiological, regarding the differential geniculocortical projection patterns of these cell groups. Stone and Dreher (362), recording from geniculate neurons in the A laminae and antidromically activating them from cortical area 17 or 18, concluded that the X-cells project exclusively to area 17 and the Y-cells project to both areas, typically by way of branching axons (see also 91). Both single-unit and evoked-potential recordings of responses to orthodromic stimulation of geniculocortical fibers support the conclusion that X-cells project only to area 17, whereas Y-cells project to areas 17 and 18 (30–32, 118, 240, 326, 377). Even within area 17, the X- and Y-cell projections are separate: X-cell axons terminate in lower layer IV, whereas Y-cell axons do so in upper layer IV (72, 95).

Other evidence of differential functional projections must be inferred from knowledge of W-, X-, and Y-cell distributions in different geniculate laminae and the projections of these laminae to cortex. Since W-cells pre-

dominate among the C laminae, and these laminae project to cortical areas 17, 18, and 19 plus the lateral suprasylvian cortex, W-cell projections probably distribute to each of these areas. Likewise, since the medial interlaminar nucleus is comprised predominantly of Y-cells and projects to cortical areas 18 and 19 (and possibly 17) plus the lateral suprasylvian cortex, Y-cells probably also innervate these cortical areas. W- and Y-cells consequently seem to have a wide distribution of cortical targets. X-cells, by contrast, project exclusively or nearly so to area 17. Some X-cells in the C laminae or medial interlaminar nucleus may project outside of area 17, but this remains to be determined.

The preceding discussion is limited to relay cells, which project to cortex. Most authors agree that interneurons also exist within the lateral geniculate nucleus, and that these neurons have axons that ramify only locally (however, see 80, 81). Unfortunately, exclusively local interneurons, if they exist at all, can presently be identified only from negative evidence such as the failure to transport HRP or the lack of an antidromic response from cortical stimulation. There may be many reasons why true relay cells might present such negative evidence, so one cannot yet be absolutely certain about the identity of intrageniculate interneurons [for further discussion see Friedlander et al. (81)].

2. Cortical area 17

a) Cell classification. Hubel and Wiesel (152, 154) provided the classic and still widely used classification scheme for area 17 neurons. This scheme was formed before knowledge of the W-, X-, and Y-cell classification scheme, and post hoc attempts to relate the two schemes have not been particularly successful (see sect. II*D1*). Hubel and Wiesel (152) originally recognized two basic cell types in area 17: simple and complex cells.

Simple and complex cells differ fundamentally from geniculate neurons in both ocular dominance and orientation (and often direction) selectivity. Whereas geniculate neurons are excited by input from only one or the other eye, depending on the cell's laminar location, most (>80%) simple and complex cells can be excited by appropriate visual stimulation of either retina and are thus binocular (Fig. 2*A*). Cortical neurons tend to have receptive fields for each eye related to roughly corresponding retinal locations. However, finer analysis reveals for most cortical cells a retinal noncorrespondence or disparity between the receptive fields in each eye. A number of investigators have suggested that these disparities provide a neural basis for stereopsis (8, 19, 174, 276).

Another striking feature of simple and complex cells is their orientation selectivity. These cells respond best to an elongated stimulus, such as an elongated rectangle or a contrast border comprising a straight line. The axis orientation of such targets is critical for the generation of a response from

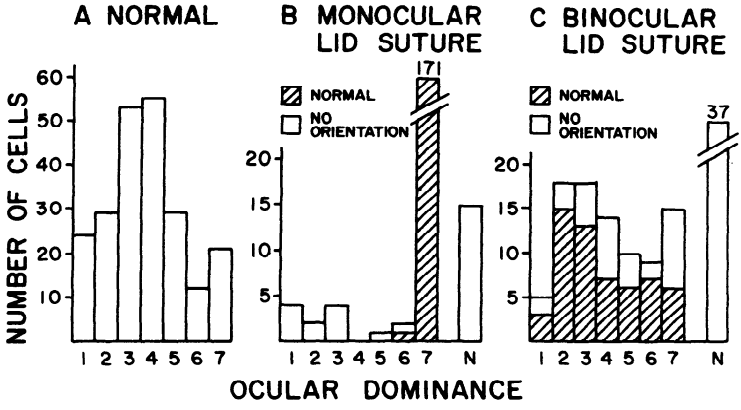

FIG. 2. Ocular-dominance distributions of striate cortex cells in normal and visually deprived cats. Cells of ocular-dominance group 1 are driven only by contralateral eye, group 2 shows a marked dominance by contralateral eye, group 3 has slight contralateral dominance, group 4 cells are driven about equally by either eye, group 5 has a slight dominance by ipsilateral eye, group 6 shows a marked ipsilateral dominance, and group 7 cells are driven only by ipsilateral eye; N indicates cells unresponsive to visual stimulation. *A*: results for normally reared cats. [Data from Hubel and Wiesel (152).] *B*: effects of rearing with monocular lid suture. [Data from Wiesel and Hubel (397).] Recordings were made from 5 kittens reared with monocular deprivation from the time of normal eye opening (~1 wk of age) to 8–14 wk of age. Few cells respond to deprived eye (ocular-dominance groups 1–6), and these cells tend to lack normal orientation selectivity (*open bars*). Cells dominated by nondeprived eye have normal orientation-selective receptive fields (*cross-hatched bars*). Some cells in these animals fail to respond to visual stimulation. *C*: effects of rearing with binocular lid suture. [Data from Wiesel and Hubel (298).] Recordings were made from 4 kittens reared with binocular deprivation from 6–18 days to 2.5–4.5 mo of age. Note flattened shape of ocular-dominance distribution compared with normal cats (i.e., a larger than normal proportion of cells is strongly dominated by 1 eye). Many of the responsive cells also lack normal orientation selectivity (*open bars*), and many cells are unresponsive to visual stimulation (N).

these cortical cells. At the preferred orientation a brisk response generally results, a rotation of 10° causes a noticeably less brisk response, and sufficiently larger rotations lead to absence of an excitatory response. All cells in a column perpendicular to the cortical layering exhibit nearly the same preferred orientation, and as one passes across neighboring columns, one usually sees a gradual, monotonic shift in the preferred orientation. This led to the concept of functional "orientation columns" (152). These have recently been demonstrated anatomically by metabolic labeling (with [^{14}C]deoxyglucose) of cortical neurons active during visual stimulation with a target of a single orientation (3, 295). Presumably these are analogous to the columns described previously (226, 251, 277). A hypercolumn, which contains enough neighboring orientation columns to map all orientations around the clock for both eyes, is roughly 1 mm across. Many of these orientation-selective cells also show direction selectivity such that only certain directions

of target motion through the receptive field will excite the neuron. Geniculate cells exhibit neither obvious orientation nor direction selectivity (48, 402).

Although simple and complex cells share many characteristics, they can be distinguished by several functional properties, some of which are summarized below (18, 115, 124, 152, 154, 252, 275, 311, 399).

1) The optimal stimulus for a simple cell fills the excitatory zone as mapped by small spots, whereas the optimal stimulus for a complex cell is much smaller than the excitatory zone. Thus simple fields display more spatial summation than do complex fields (152).

2) Simple fields are usually comprised of two or more adjoining discharge zones that alternate between dark and light zones. The cell responds when a target darker (brighter) than the background enters a dark (light) zone. In complex fields such separate light and dark zones spatially overlap (311).

3) The discharge zones of simple fields are flanked by suppressive or inhibitory sidebands, the stimulation of which reduces the cell's firing rate. No such zones have been described for complex cells (18, 124, 311).

4) For a given visual-field eccentricity, simple fields tend to be smaller than complex fields (399). Both field types increase in size with increasing eccentricity, but the increase is marked for complex cells and gradual for simple cells. Thus near the area centralis a simple field may be 0.5° across and a complex field 1.5°; at an eccentricity of 50°, typical dimensions are roughly 1° for a simple field and 5° for a complex field.

5) Simple cells tend to be more selective for orientation than are complex cells (152), but this selectivity decreases slightly for both cell types with increasing visual-field eccentricity (399). Near the area centralis a typical simple cell can respond to roughly a 50° range of stimulus orientations (i.e., 25° to either side of the preferred orientation), whereas the range for a typical complex cell is roughly 80°.

6) Movshon (252) reported that simple cells tend to prefer much slower target speeds (about 2°/s) than do complex cells (which prefer speeds of about 20°/s) and furthermore that most simple cells respond poorly if at all to stimulus speeds evoking brisk responses from complex cells (e.g., ~20°/s).

7) Complex cells respond to movements of a stimulus comprised of random dots (white noise), whereas simple cells do not (115).

8) Simple cells tend to have lower spontaneous discharge rates than do complex cells (275).

Two other cell types have also been described. First, some cells (10%) lack orientation selectivity. Because of the waveform of the action potential and because many of these neurons are binocular, they are unlikely to be geniculate axons recorded in cortex [for discussion see Henry (124)]. Second, hypercomplex cells, originally described for areas 18 and 19 (154), are seen occasionally (~10%) but regularly in area 17. These cells are characterized by the requirement that, to excite the cell, an oriented stimulus must not extend above or below the excitatory center along the preferred orientation.

These cells evidently have inhibitory or suppressive zones in these areas and thus are sensitive to the length of a stimulus along the preferred orientation axis. However, it is not clear if such cells actually represent a separate class or if they are merely extremes in a continuum. That is, such inhibitory zones may be common in all simple and complex cells and may range from weak to strong. If so, then cells classified as hypercomplex may be subclasses of simple and complex cells (66, 282, 283, 399; but see 268, 269).

b) Distribution of simple and complex cells. The relative proportion of simple to complex cells varies within area 17 in two ways. First, as one moves with a recording electrode across area 17 from the region in which the area centralis is mapped to a region that maps more peripheral retina, the relative proportion of simple to complex cells drops (399). Second, simple cells tend to be concentrated in deep layer III, layer IV, and layer VI, whereas complex cells are found abundantly in all layers except layers I and IV (93, 152, 217). Also subtle interlaminar differences in response properties have been noted for both simple and complex cells (30–32, 93, 119, 217).

c) Distribution of monocular and binocular neurons. The relatively few monocularly activated neurons in area 17 are more or less concentrated in two locations. First, Albus (2) noted that roughly one-half to two-thirds of both simple and complex cells with receptive fields in the central 4° of visual field (i.e., in or near the area centralis) tend to be monocularly driven. Second, monocularly driven, simple cells increase slightly in layer IV at all eccentricities (300), and most of the binocularly driven cells in this layer can be only slightly excited by one eye as opposed to the nearly balanced ocular-dominance pattern of most cortical neurons in other layers.

3. Cortical area 18

a) Receptive-field properties. The first detailed study of neuronal responses from area 18 of the cat was reported by Hubel and Wiesel (154), who noted certain similarities and differences in neuronal properties between areas 17 and 18. Among the features shared by both areas are neurons selective for stimulus orientation and direction of movement, a similar organization of orientation columns perpendicular to the cortical layering, and binocular neurons. Hubel and Wiesel (154) emphasized two differences: larger receptive fields for area 18 than for area 17 cells and different functional populations between areas. In their sample, no hypercomplex cells were seen in area 17 (cells were all simple or complex) and no simple cells were seen in area 18 (cells were complex or hypercomplex). This last point has been subsequently challenged both by reports of hypercomplex cells in area 17, if indeed these neurons even form a unique cell class (see sect. II*B2a*), as well as many reports of simple cells in area 18 (67, 254, 266, 267, 377). The other observations of Hubel and Wiesel (154) have been largely confirmed and somewhat extended in many laboratories (61, 67, 254, 266, 267, 301, 377).

Several studies have emphasized that, compared with cells in area 17,

not only are receptive fields of area 18 neurons larger, but they also respond to and often prefer much higher stimulus speeds (67, 266, 267, 377). Two further observations may be related to this. First, Tretter et al. (377) orthodromically activated neurons in areas 17 and 18 from electrical stimulation of the optic chiasm or radiations. Based on measurements of conduction latencies for such neuronal activation, they concluded that area 17 neurons are activated by geniculate X- or Y-cell afferents and area 18 neurons are activated only by Y-cell afferents [see also sect. II*B1d*; Stone and Dreher (362)]. Because Y-cells tend to have larger receptive fields and better responsiveness to faster target movements than do X-cells, these differences in afferentation are consistent with the described receptive-field differences between areas 17 and 18. Second, Movshon et al. (254) measured the responsiveness of cortical cells to sine-wave gratings of various spatial and temporal frequencies. Compared with cells in area 17, those in area 18 respond to a range of lower spatial and slightly higher temporal frequencies. Responsiveness to lower spatial frequencies is often associated with large receptive fields, and responsiveness to higher temporal frequencies, with responsiveness to faster target movements.

b) Effect of area 17 removal. Although many properties of area 18 neurons can be explained by their geniculocortical Y-cell input (254), Hubel and Wiesel (154) argued that the functional properties of area 18 cells are best explained by inputs from area 17 and that different visual cortical areas represent different hierarchical levels in a single chain of neural processing (this theory is further elaborated in sect. II*D1*). Several studies were designed to test this explanation by comparing neuronal properties in area 18 before and after elimination of area 17.

Donaldson and Nash (61) surgically ablated area 17 and found little observable effect on area 18 neurons that could be activated. However, they emphasized the many unresponsive cells not seen preoperatively in area 18 but that constitute the postoperative majority. Their postoperative study followed a 1- to 11-wk period after the ablation. Dreher and Cottee (67) recorded postoperatively within minutes of the ablation and found little difference between pre- and postoperative neuronal responses in terms of either receptive-field features or numbers of responsive cells. The area 17 lesion seemed only to reduce responsiveness of area 18 cells to slow target movements. Sherk (301) reinvestigated the question more recently with the more elegant approach of reversible cooling of area 17. Her results tend to confirm the observations of Dreher and Cottee (67). The postoperative lack of responsive neurons reported by Donaldson and Nash (61) may be related to the relatively long period between the ablation and recording. For instance, individual neurons projecting to both areas 17 and 18 by means of a branching axon (e.g., geniculocortical Y-cells) may be affected by an area 17 lesion so that eventually their synaptic inputs to area 18 become ineffective. Soon after the lesion, these geniculocortical inputs can still activate cells, but within days or weeks, they no longer can. In any case, it seems

clear that acute removal of area 17 has little obvious effect on response properties of area 18 neurons. Other inputs to area 18, such as geniculate Y-cells, are sufficient for these response properties.

C. Structure-Function Correlations of Retinogeniculocortical Pathways

1. Retinal ganglion cells

Roughly a century ago, Cajal emphasized the morphological variety of retinal ganglion cell types seen with Golgi-impregnation methods [see translation in Rodieck (280)]. Boycott and Wässle (28) recently analyzed such Golgi-impregnated cells in cat retinal whole-mount preparations and provided a morphological classification scheme related to W-, X-, and Y-cells. They described three main structural classes: α-cells have the largest somata and dendritic trees, β-cells appear to be smaller than α-cells with a denser dendritic arbor. In any limited patch of retina there is little or no overlap in soma or dendritic-field diameter between α- and β-cells. The γ-cells are distinguished not only by their small somata (the smallest among retinal ganglion cells) but also by their dendritic geometry. The dendrites of γ-cells have few branches, but the extents of their dendritic trees are roughly similar to those of α-cells. Nevertheless soma sizes of β-cells overlap somewhat with those of γ-cells. Other rare morphological types were described. Boycott and Wässle (28) proposed that α-cells are Y-cells, β-cells are X-cells, and γ-cells are W-cells. Note that this morphological classification scheme is incomplete: Boycott and Wässle (28) described one other structural type (δ-cells), and a large variety of other types has also been found [see translation of Cajal's work (280); see also Leventhal et al. (219, 220)]. This tends to weaken any exact correspondence between W-, X-, and Y-cells, respectively, with γ-, β-, and α-cells.

The capriciousness and uncontrolled staining biases of the Golgi method make it difficult to determine the retinal distribution of α-, β-, and γ-cells with this approach. However, because of differences in their soma sizes, these distributions can be estimated from standard Nissl-stained material. The distribution and number of small, medium, and large somata match fairly well those of W-, X-, and Y-cells sampled in the retina with microelectrodes, if one assumes electrode biases that strongly select for large somata (e.g., 84, 221, 286, 359). That is, the density of the largest somata (α- or Y-cell?) displays a slight increase around the area centralis and a shallow decline with retinal eccentricity, that of the medium-sized somata (β- or X-cell?) peaks sharply at the area centralis and declines steeply with increasing retinal eccentricity, and that of the smallest somata (γ- or W-cell?) is fairly flat across the retina except for a moderate increase along the visual streak. Furthermore the central projections of small, medium, and large retinal ganglion cells, as revealed by HRP retrograde tracing tech-

niques, correspond reasonably well with what is known of W-, X-, and Y-cell projections (191; but see 219, 220). Finally, Cleland et al. (45) were able, in a limited patch of retina, to match each large soma with the position of an extracellularly recorded Y-cell, although a few Y-cells could not be matched to large somata. They concluded that, roughly speaking, the largest somata (and thus presumably Y-cells) represent only about 5–10% of the retinal ganglion cells, whereas the medium-sized and smallest soma classes (presumably X- and W-cells, respectively) exist in approximately equal numbers.

Therefore there is considerable indirect evidence consistent with the suggestion of Boycott and Wässle (28) that Y-cells are α-cells, X-cells are β-cells, and W-cells are γ-cells. However, three notes of caution are worth raising. First, nearly all the correlations between physiological and anatomical distributions require assumptions, both about electrode sampling biases and also about the relationship between Nissl-stained and Golgi-impregnated material. Different laboratories have been unable to agree on the identity and number of retinal ganglion cells in Nissl-stained material (158–160, 286, 360, 361). Further, Leventhal et al. (219, 220) have recently presented data that complicate these relationships. These authors identified a population of retinal ganglion cells, called ϵ-cells, with medium-sized somata in the β-cell range but a dendritic arbor more like γ-cells. This new type, which in Nissl-stained material presumably would have been identified as a β-cell and therefore an X-cell, projects to the C laminae and geniculate wing. Leventhal et al. (219) consequently proposed that these are W-cells. Morphological and functional classes of retinal ganglion cells identified by soma size alone may thus lead to some false conclusions. Second, and perhaps related to the first note of caution, Boycott and Wässle (28) described rarely encountered morphological types other than α-, β-, and γ-cells. The capriciousness of the Golgi method raises the possibility that this classification scheme is incomplete and that other major types have not been identified, a possibility that Boycott and Wässle (28) clearly acknowledge. Third, most of the evidence, though based on high-quality data, is indirect and circumstantial. This last point is raised again below in our consideration of structure-function relationships for geniculate neurons, because similar assumptions and conclusions there have been challenged by a more direct approach to structure-function correlations.

2. Lateral geniculate nucleus

Guillery (105) used Golgi-impregnation techniques to elucidate the morphology of geniculate neurons in the cat. He described three morphological classes (classes 1, 2, and 3) in the A laminae and lamina C, and another (class 4) in the ventral C laminae. Class 1 cells are large, with thick, cruciate dendrites and few dendritic appendages that tend to be simple, spinelike

structures. Dendrites of these cells typically cross laminar borders. Class 2 cells are intermediate in size, with thin, sinuous dendrites. Numerous grape-like appendages are clustered at or near the dendritic branch points of these cells. These appendages are always located in the same lamina as the soma, although the dendrites occasionally cross laminar borders. Class 3 cells are small, with thin, tortuous dendrites contained within a single lamina, and many complex appendages occur along these dendrites. Class 4 cells are intermediate in size and are characterized by a dendritic arbor oriented parallel to the geniculate lamination. Based on this classification scheme, a number of investigators have suggested rather detailed structure-function correlates for W-, X-, and Y-cells and for interneurons (e.g., 211, 402). These correlates derive from indirect approaches analogous to those described above for retinal ganglion cells, and they probably suffer from similar drawbacks. For instance, Guillery (105) emphasized that the plurality (40%) of his neuronal sample could not be placed into one of his major classes, and this leaves open the problem of how to relate these numerous morphologically unclassified cells to the known physiological classes.

LeVay and Ferster (211) also proposed a correlation based on soma size and the presence in some cells of a "cytoplasmic laminated body" (see also 63, 180, 250, 294). Such cytoplasmic structures have been found in many neural regions outside of the lateral geniculate nucleus (e.g., 129, 202, 249, 257, 332, 403). The type 1 cell has a large soma, no cytoplasmic laminated body, and seems equivalent to Guillery's (105) class 1 cell. The type 2 cell has a medium-sized soma, a cytoplasmic laminated body, and is probably equivalent to Guillery's (105) class 2 cell. The type 3 cell has a small soma, no such cytoplasmic structure, and seems equivalent to Guillery's (105) class 3 cell. LeVay and Ferster (211) utilized several converging lines of indirect evidence to suggest that type 1 cells are Y-cells and comprise roughly 33% of the A laminae neurons, that type 2 cells are X-cells and comprise roughly 40% of the neurons, and that type 3 cells are interneurons representing roughly 25% of the cells.

Friedlander et al. (80, 81) and Stanford et al. (346) recently employed a direct means of relating structure and function to describe the morphology of W-, X-, and Y-cells in the A and C laminae of the lateral geniculate nucleus. These authors used HRP-filled micropipettes to record intracellularly from and iontophorese HRP into neurons identified as W-, X-, or Y-cells, providing a detailed morphological picture for each functionally characterized neuron. Although morphological heterogeneity exists within each functional class, characteristic structural features can nonetheless be listed for these cells.

Y-cells were found in the A and C laminae, and they have large somata (mean cross-sectional area, 490 μm^2; range, 238–935 μm^2). Each has thick, cruciate dendrites with few appendages. The dendritic arbor is roughly radially symmetric, for most cells, and part of it always crosses the laminar borders. X-cells were found only in the A laminae, and they have smaller

somata (mean area, 219 μm^2; range, 68–420 μm^2) and finer, sinuous dendrites usually with numerous, complex appendages. The dendritic arbor of most X-cells is oriented perpendicular to the laminar borders and is always confined within a single lamina. The soma sizes of X-cells overlap to an extent with those of Y-cells. W-cells were found only in the C laminae, and they have smaller somata (mean area, 188 μm^2; range, 75–322 μm^2). The numerous, fine dendrites of W-cells are oriented more or less parallel to the laminar borders, and complex dendritic appendages are seen for some W-cells. In many ways W-cells resemble X-cells rotated through 90°C in the coronal plane.

Friedlander et al. (81) drew two further conclusions for A laminae by comparing the soma size distribution of HRP-filled cells with that from Nissl-stained material. First, there was no suggestion of electrode sampling biases based on soma size[4], and they concluded that the ratio of X-cells to Y-cells in the A laminae is roughly 3:2. This is much lower than the suggested retinal ratio of 5–10:1, and it led Friedlander et al. (81) to suggest a relative amplification of Y-cell numbers due to divergence in retinogeniculate connections. Second, virtually all the HRP-filled cells are confirmed relay cells, and the similarity of the HRP and Nissl soma size distributions suggested the presence of very few, if any, interneurons. Indeed Friedlander et al. (81) described several relay cells with morphological features thought to represent interneurons [i.e., class 3 cells of Guillery (105)]. The entire concept of a separate and unique class of interneurons in the A laminae should be reconsidered.

3. Cortical area 17

Area 17 is the only area of visual cortex in which a structure-function correlation has been attempted at the single-cell level. Again this was ini-

[4] There is good reason to believe that electrode sampling biases are a genuine problem among somata (162) and, more specifically, that different electrodes can sample different proportions of W-, X-, and Y-cells among the same neuronal population (84, 221, 359). What is not entirely clear as a general maxim is that these biases are related simply and reliably to soma size and that larger somata generate larger extracellular potential fields through which an electrode might pass. This would be true if the geometry of extracellular potential fields generated by a neuron simply reflected soma geometry. To the extent that the cell's dendrites and/or nearby elements contribute to or distort the geometry of these potentials, however, it may be difficult to predict electrode sampling biases on the basis of soma size alone. Indeed Friedlander et al. (81) found no evidence for electrode sampling biases of geniculate somata related to their sizes. Sampling biases do seem to occur more among fibers. Until recently most physiological studies of cat retinal ganglion cells were based on optic tract recordings, and the population of W-cells was effectively missed. Presumably this occurred because these cells have the slowest conducting fibers and thus probably the thinnest axons; if so, then these thin axons would be difficult to isolate with conventional recording techniques. Not until the use of intraretinal recording, whereby the electrode tip is placed among retinal ganglion somata, were W-cells recognized as a large population of retinal ganglion cells.

tially based on morphological classes seen in Golgi-impregnated material. Two basic types are seen (227, 264, 314, 372): pyramidal and stellate cells, although other forms have been described. Pyramidal cells tend to have large, pyramid-shaped somata, long apical dendrites that often approach the pial surface, and basal dendrites that fan out from the base of the soma parallel to the layering. Stellate cells tend to have small, spherical somata, with profusely branching dendrites radiating in all directions. Both cell types are found in all layers, but pyramidal cells occur most frequently in layers II, III, V, and VI, and stellate cells, in layers II and IV.

Kelly and Van Essen (192) tried to establish a structure-function relationship by intracellular recording, classification of the cell as simple or complex, and injection of the dye Procion yellow. They concluded that most simple cells are stellate and most complex cells are pyramidal, but many exceptions were noted. More recent experiments with the more sensitive procedure of HRP filling emphasize the failure of correlation between these functional and structural classes (95, 222). Therefore a precise structure-function relationship for cortical neurons is still lacking.

D. Functional Organization of Retinogeniculocortical Pathways

Sections II*A–C* present a survey of the normal retinogeniculocortical pathways in the cat. The functional organization and interrelationships of these pathways are not completely understood, but several hypotheses have been generated and are briefly considered here.

1. Serial versus parallel processing

Hubel and Wiesel (154) proposed a serial-processing theory for the functional organization of the retinogeniculocortical pathways. In short, they suggested that information processing for a visual scene is accomplished by single neuronal chains that ascend a hierarchy from retina through the lateral geniculate nucleus to and through area 17. Each chain extracts information by requiring more complicated stimulus configurations for neuronal activation as the hierarchy is ascended. From the pattern of activity at the top of the hierarchy, it is presumed possible to infer the visual stimulus. Thus a homogeneous population of retinal ganglion cells relay through a similarly homogeneous population of geniculate neurons, which project to cortical simple cells, which in turn project to complex cells, then on the hypercomplex cells, etc.

This compelling and simplifying hypothesis has largely been inferred from receptive-field properties. However, not all cortical response properties are explicable by such a simple hierarchy, and certain receptive-field features seem to contradict such a strict interpretation of this serial-processing scheme. For example, complex cells typically respond vigorously to certain

stimulus parameters, such as fast-moving targets and random-dot visual noise, that do not effectively activate simple cells (115, 252). Also Sillito (318) has shown that local iontophoretic application of bicuculline (an antagonist of γ-aminobutyric acid, a presumed neurotransmitter in the central nervous system) during single-cell recording greatly reduces or abolishes direction selectivity for all simple and many complex cells. Sillito (319) more recently showed that bicuculline also abolishes orientation selectivity for many complex cells. He concluded that many complex cells must receive excitatory inputs from neurons nonselective for direction and orientation (i.e., not from simple cells), since bicuculline application effectively isolates the excitatory inputs to a neuron. This last assumption, however, has not been directly tested.

Perhaps a more fundamental problem with a strict interpretation of serial processing is that it ignores the existence of W-, X-, and Y-cells and their pathways. Of course this is not at all surprising, because Hubel and Wiesel (154) proposed the theory before these cell types and pathways were recognized. One of the more intriguing and controversial questions in this field is: How are the area 17 cell types (simple, complex, etc.) related to geniculocortical cell types (W-, X-, and Y-cells)? To answer this, Stone, Henry, and their colleagues (30–32, 118, 119, 147, 287, 358, 362, 363) proposed the parallel-processing scheme. This suggests that W-, X-, and Y-cells represent three parallel, fairly independent pathways to and through area 17 such that each cortical neuron is a link in one or another of these chains. Presumably each pathway (W-, X-, or Y-cell) processes somewhat different aspects of the visual scene in parallel (see below), and these are combined at some neural site to analyze the visual input. Stone et al. (363) have recently reviewed the arguments in favor of this hypothesis.

Most of the evidence for parallel processing stems from measurements of the conduction velocity of geniculocortical afferents. That is, the difference in conduction latency of a cortical cell's response to stimulation of two or more afferent sites, including optic chiasm and several sites in the optic radiations, often can be used to indicate whether W-, X-, or Y-cells provide afferentation, because axons of these cells possess different conduction velocities. Most studies have focused on X- and Y-cell afferents; because geniculate W-cells were only recently identified, they are thought to represent a minority of geniculate input to area 17, and their slowly conducting monosynaptic input to cortex is hard to distinguish from multisynaptic pathways involving rapidly conducting X- or Y-cells.

This approach was first employed by Hoffmann and Stone (147) and Stone and Dreher (362). They concluded that simple cells receive X-cell input and that complex cells receive Y-cell input (but see 30–32, 326). It seems clear that many complex cells receive monosynaptic input from geniculate Y-cells, a point that belies a strict interpretation of serial processing, which places complex cells at a disynaptic position with respect to geniculate afferents. More recently Bullier and Henry (30–32) strengthened the arguments for

parallel processing with some revision of the above scheme. They concluded that cortical area 17 neurons receive input from only one of the W-, X-, or Y-cell pathways, with little or no mixing, and that complex cells tend to be part of the Y-cell pathway but simple cells can receive input from either X- or Y-cells. These authors found that many complex cells are monosynaptic from geniculate input and that many simple cells cannot be monosynaptically driven from geniculate input. These electrical stimulation data thus indicate no systematic or dramatic difference between simple and complex cells in their position within the cortical hierarchy. Again cells that are part of the W-cell pathway are rare and/or difficult to identify (see also 363).

Harvey (118) recently extended this analysis to area 18. He argues that these cortical neurons receive essentially only Y-cell input mono- or polysynaptically from the optic radiations. Simple cells tend to receive the monosynaptic input, and complex cells, the polysynaptic input, although exceptions were noted.

Although most of the above evidence for area 17 derives from electrical stimulation studies, certain receptive-field data are also consistent with this hypothesis of parallel processing. Leventhal and Hirsh (218) and Citron et al. (38) reported strong receptive-field similarities between classes of area 17 neurons and X- or Y-cells. However, Movshon et al. (254) suggested a different form of parallel processing based on their receptive-field studies: X-cell input dominates area 17, and Y-cell input dominates area 18.

This discussion represents extreme views of serial and parallel processing in order to highlight their differences. Combinations of the two schemes are also possible, and parallel processing could be viewed as a special case of serial processing involving several hierarchical units instead of one.

2. Functional role of various cell types

Another question of general interest concerns the role these various cell types and pathways play in vision. No unequivocal answer presently exists, and here we only consider several of the many possible hypotheses. These hypotheses all rest on a number of assumptions, and they should not be mistaken for a genuine understanding. Nevertheless they can serve as a useful theoretical framework on which to place considerations of developmental studies.

a) Serial processing. The functional implication of the serial-processing scheme is relatively straightforward (sect. II*D1*). As the hierarchy is ascended, cells become increasingly selective for stimulus parameters. Thus the pattern of active cells near the top of the hierarchy is sufficient to document the visual scene.

b) W-, X-, and Y-cells. The theory of parallel processing suggests that each of these cells and pathways is involved in a relatively independent and parallel analysis of different components of the visual scene. The most dif-

ficult with which to deal and for which to assign a special function is the W-cell geniculocortical pathway. W-cells are poorly understood and seem relatively insensitive (compared with X- and Y-cells) to most spatiotemporal visual patterns (sect. II*B1b*). Most theories of functional significance of these parallel pathways thus concentrate on X- and Y-cells and tend to sweep W-cells under the rug like some evolutionary debris. This weakness in the hypotheses noted below must be understood, and they might have to be altered or abandoned as we learn more about W-cells.

A number of theories have emerged concerning the role of X- and Y-cells, and they all derive more or less from distinctions in their receptive-field properties. Three are considered here, but many more are possible. The most common is that X-cells analyze spatial patterns or forms and that Y-cells analyze temporal patterns and are responsible for flicker sensitivity (166, 204, 363). X-cells seem ideally suited for a spatial analysis because of their relatively sustained and linear responses, small receptive fields, preference for stationary or slowly moving targets, and marked concentration in the area centralis. Y-cells seem equally suited for a temporal analysis because of their relatively transient and nonlinear responses, larger receptive fields, and sensitivity to rapid target movements. A second, related suggestion is that Y-cells are involved in a fixation role, whereby targets of interest are brought by head and eye movements into the area centralis for a more detailed spatial analysis by X-cells (363).

The third hypothesis suggests a very different functional dichotomy for X- and Y-cells (and also ignores W-cells). This is based on contrast-sensitivity functions of geniculate X- and Y-cells (207, 304, 305). These functions plot the contrast threshold necessary for a sine-wave grating to evoke a response at a range of spatial and temporal frequencies. The major difference between X- and Y-cells lies in sensitivity to low spatial frequencies: X-cells are fairly insensitive to such stimuli, whereas Y-cells are quite responsive (sect. II*B1b*). Compared to this, differences between the cells in temporal sensitivity or spatial resolution are minimal, although most X-cells can respond to slightly higher spatial frequencies than can most Y-cells, and the converse is true for temporal frequencies. A number of psychophysical studies (96, 97, 130–132, 175) have shown that low spatial frequencies are sufficient for recognition of spatial patterns. In fact patterns from which the high spatial frequencies have been removed (by defocusing, etc.) are readily recognized, and only fine details are lost. Basic spatial information is carried by the low spatial frequencies; the high frequencies add the detail. Since Y-cells are much more sensitive than X-cells to low spatial frequencies, Y-cells may be involved in the basic spatial analysis of form, whereas X-cells signal certain other spatial parameters, such as fine detail, stereopsis, etc.

There is some behavioral evidence based on cortical lesions in the cat consistent with this view. Removing area 17 and parts of area 18 with minimal damage to other cortex produces an animal with little or no cortical representation of the X-cell pathway but with many Y-cell (and W-cell)

projections intact (118, 362; see also 363). Such an animal displays excellent pattern discrimination with only a mild acuity loss (10). Presumably a brain with cortical representation of Y-cells (and W-cells) but few or no X-cells is capable of extensive spatial pattern analysis. This observation is consistent with, but by no means proves, the hypothesis that Y-cells play a major role in spatial pattern analysis.

E. Extrageniculate Visual Pathways

In addition to its projection to the dorsal lateral geniculate nucleus, the retina projects to a number of diencephalic and mesencephalic structures in the cat. Only two of these structures have been studied in visually deprived animals: the pretectal nucleus of the optic tract and the superior colliculus. Likewise, among the many visual cortical areas outside areas 17 and 18 (121, 271, 383, 385), only the lateral suprasylvian visual area has been studied in visually deprived animals. Although Hoffmann (140) described effects of lid suture on the nucleus of the optic tract, we omit this from further discussion to maintain focus. As a background to our later discussion of the effects of visual deprivation in the superior colliculus and lateral suprasylvian cortex, these areas are described briefly in this section (see Figs. 3 and 4).

1. Superior colliculus

a) Inputs. The cat's superior colliculus can be divided into seven major layers on the basis of its cytoarchitecture and myeloarchitecture (181). Cells in the upper three layers receive direct retinal inputs as well as descending projections from visual areas of cortex (4, 86, 103, 117, 190, 206, 387), and these cells respond exclusively to visual stimulation (98, 348, 366). In contrast, cells in the lower four layers receive auditory and somatic inputs, with only a sparse retinal projection (4, 86, 103, 117, 206, 248, 357), and these cells respond to stimulation of all three sensory modalities (98, 348, 352, 366). Studies of visual deprivation in this structure have been restricted almost entirely to the purely visual upper layers. Therefore the overview that follows is confined to consideration of only the upper three layers of the superior colliculus.

The retinal projections to the superior colliculus (i.e., retinotectal pathways) arise nearly exclusively from the contralateral eye although a small projection exists as well from the ipsilateral eye (4, 103, 117, 206). The nasal hemiretina projects exclusively to the contralateral superior colliculus. However, the temporal hemiretina projects bilaterally to both superior colliculi (84, 117). Both W- and Y-cells, but not X-cells, contribute to the retinotectal pathways (sect. II*B2c*).

In addition to the retinotectal inputs, the superior colliculus receives a substantial projection from corticotectal pathways. These arise from large

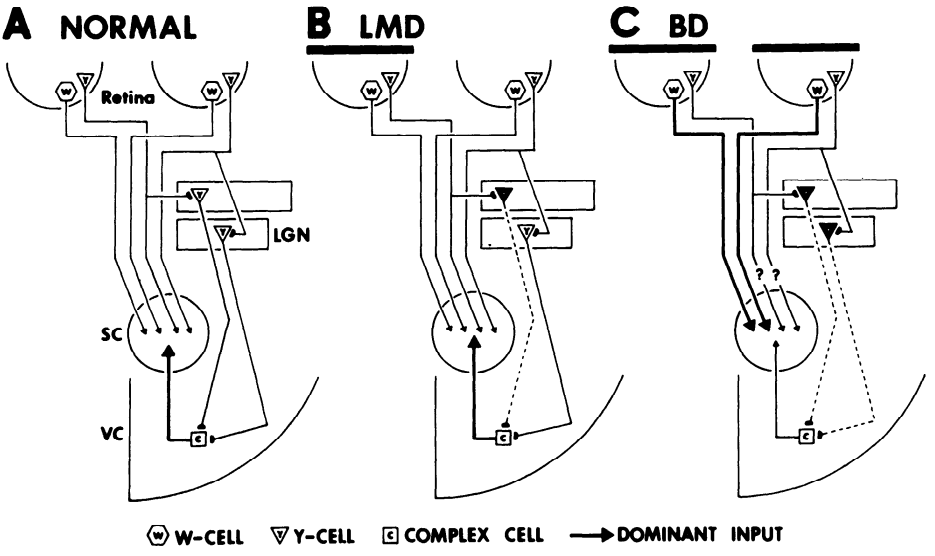

FIG. 3. Schematic summary diagram of afferents to superior colliculus (SC) in a normal, left monocularly deprived, and binocularly deprived cat. *A*: normal pathways, including an extensive direct retinotectal W-cell pathway, a minor direct retinotectal Y-cell pathway, and an extensive indirect Y-cell pathway. The last includes retinal Y-cell input to the lateral geniculate nucleus (LGN), geniculate Y-cell input to visual cortex (VC), and corticotectal input from complex cells. Y-cell indirect pathway seems to be the dominant input to superior colliculus. No X-cell afferentation to superior colliculus has yet been detected. *B*: pathways in a left monocularly deprived cat. All pathways from right (nondeprived) eye and retinotectal pathways from left (deprived) eye seem to develop normally. However, deprived Y-cell indirect pathway fails to develop normally, presumably due to a failure of deprived geniculate Y-cells to develop normally. Dominant input to superior colliculus seems to be Y-cell indirect pathway, which in turn is dominated by nondeprived (right) eye. *C*: pathways in a binocularly deprived cat. W-cell retinotectal pathway develops normally. Y-cell retinotectal pathway may develop with some abnormalities, but small size of this pathway in normal cats makes evaluation of possible abnormalities difficult. Indirect retinogeniculocorticotectal pathway involving Y-cells completely fails to develop. This seems to involve a developmental failure of geniculate Y-cells, an essential link in this pathway, because responsiveness of collicular neurons to electrical stimulation of visual cortex develops normally. Dominant input in these cats appears to be the (W-cell) retinotectal pathway (see text for details). [From Hoffmann and Sherman (145).]

regions of cortex including areas 17 and 18 (86, 149, 186, 190, 232, 387). The corticotectal neurons reside in layer V of cortex and most have complex receptive fields (119, 139, 149, 186, 232, 270, 326, 376). These corticotectal complex cells have large receptive fields that lack clear spatial summation, are driven about equally by both eyes, are direction selective, and respond well to fast stimulus movement. Many or all of these corticotectal cells receive monosynaptic inputs from geniculate Y-cells and are thus part of an indirect Y-cell input to the superior colliculus (139; but see 119). This indirect input travels from retinal Y-cells to lateral geniculate Y-cells to cortical complex cells to the superior colliculus. Hoffmann (139) used electrical ac-

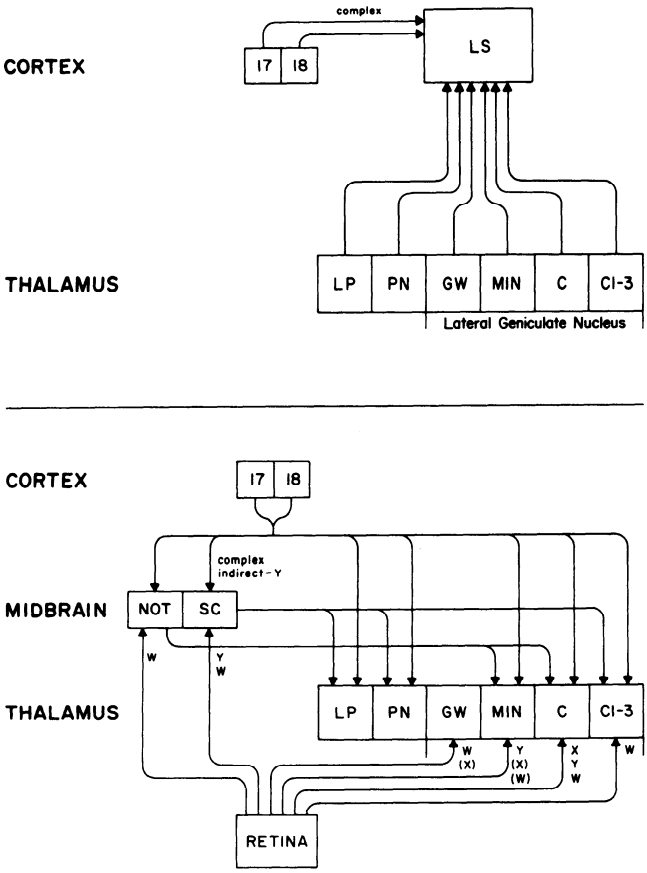

FIG. 4. Visual inputs to lateral suprasylvian visual area of cortex and to extrageniculate regions of visual system studied in visually deprived cats. *Upper panel*: major thalamocortical and corticocortical visual inputs to lateral suprasylvian cortex. *Lower panel*: major inputs to subcortical structures that directly or indirectly innervate lateral suprasylvian cortex. LS, lateral suprasylvian cortex; PN, posterior nucleus; LP, lateral posterior nucleus; NOT, nucleus of optic tract; SC, superior colliculus. *Complex* refers to complex cells in area 17 that provide inputs to lateral suprasylvian cortex or superior colliculus (different populations of complex cells from different cortical layers project to each area). *Indirect-Y* refers to indirect Y-cell pathway from retina to lateral geniculate nucleus to complex cells of area 17 to superior colliculus. Other abbreviations as in Fig. 1.

tivation to identify afferents to collicular neurons (see Fig. 3). He estimated that 73% receive retinotectal W-cell input; 9%, retinotectal Y-cell input; and 18%, indirect Y-cell (corticotectal) input.

b) Receptive-field properties. In normal cats, superior colliculus cells have large receptive fields, and many have internal or surround receptive-field inhibition that limits the optimum stimulus size (12, 98, 285, 354). Unlike cells in areas 17 and 18, colliculus cells are not orientation selective (12, 285,

354). Most colliculus cells respond better to moving than to stationary flashing stimuli, however, and 60% or more are direction selective (139, 237, 345, 348, 354, 366). These neurons typically respond to a wide range of stimulus velocities, although some respond best to slowly moving stimuli (5–10°/s) and others respond best to rapidly moving stimuli (50–100°/s). About 90% of superior colliculus cells are driven by both eyes, with a slight dominance by the contralateral eye (12, 139, 285, 354). The ocular-dominance pattern of collicular neurons thus closely resembles that for cortical area 17 neurons.

c) Removal of visual cortex. Lesion experiments indicate that different aspects of these receptive-field properties are provided by the retinotectal and corticotectal inputs. Removal of cortical area 17 and parts of area 18 markedly decreases the proportion both of direction-selective cells and of cells responding to the ipsilateral eye, and many collicular cells respond well to stationary flashing stimuli after such a lesion (12–14, 242, 285, 347, 394). Therefore the indirect Y-cell pathway through cortical areas 17 and 18 apparently provides most superior colliculus cells with direction selectivity, responsiveness to the ipsilateral eye, and inhibition of responsiveness to stationary flashing stimuli. The direct retinal Y-cell and W-cell inputs, in the absence of visual cortex, seem to provide collicular neurons with a variety of nonselective receptive-field properties from the contralateral eye and rather little functional input from the ipsilateral eye.

2. Lateral suprasylvian cortex

The presence of a visual area on the medial bank of the cat's lateral suprasylvian sulcus was first described by Marshall et al. (234) and later by Clare and Bishop (39). Subsequent anatomical (121) and electrophysiological (155, 271, 333, 381, 382) experiments demonstrated that the lateral suprasylvian visual area, or lateral suprasylvian cortex, is quite large. It extends along the entire medial bank of the middle suprasylvian sulcus and continues for several millimeters along the caudal (or ventral) bank of the posterior suprasylvian sulcus. Throughout most of its length, the lateral suprasylvian cortex extends from the dorsal lip of the sulcus down to the fundus. On the basis of visuotopic mapping studies, Palmer et al. (271) have suggested that the lateral suprasylvian cortex actually consists of three separate visual areas. However, the afferents to these three subareas and the receptive-field properties of their neurons are very similar, if not identical (121, 179, 185, 258, 284, 293, 315, 333, 334, 381). Therefore the interpretation that these are three separate areas is open to question. In any case, all studies of visually deprived cats and most studies of normal cats have concentrated on the region of the lateral suprasylvian cortex that lies along the posterior two-thirds of the medial bank of the middle suprasylvian sulcus [the PMLS subarea described by Palmer et al. (271)]. The following overview is thus confined to this region of the lateral suprasylvian cortex.

a) Inputs. The lateral suprasylvian cortex is an area of convergence of inputs from the geniculostriate system, direct inputs from the lateral geniculate nucleus, and extrageniculate pathways (Fig. 4). The direct geniculate pathway consists of projections from three regions of the lateral geniculate nucleus: the C laminae, the medial interlaminar nucleus, and the geniculate wing (17, 94, 121, 161, 179, 194, 213, 219, 229, 278, 284). There have been no studies directly concerned with the extent to which geniculate W-, X-, or Y-cells project to the lateral suprasylvian cortex. However, since the medial interlaminar nucleus is comprised almost entirely of Y-cells, and the C laminae (and probably the geniculate wing) are comprised largely of W-cells, it seems likely that this cortex receives both W- and Y-cell input in substantial amounts. An additional small X-cell input cannot be ruled out entirely.

The lateral suprasylvian cortex also receives inputs from the lateral posterior nucleus and posterior nucleus of the thalamus[5] (17, 94, 101, 121, 161, 179, 194, 213, 229, 258, 284). These nuclei, along with the C laminae of the lateral geniculate nucleus, receive inputs from the upper layers of the superior colliculus[6] (5, 99, 100, 102, 189, 260). Therefore a source of afferents to the lateral suprasylvian cortex derives from retinotectothalamic pathways. Recent experiments also indicate that the pretectal nucleus of the optic tract projects to the medial interlaminar nucleus and C laminae of the lateral geniculate nucleus (104), thereby providing a retinopretectothalamic pathway to the lateral suprasylvian cortex.

Finally, this cortical area receives direct corticocortical projections from areas 17, 18, and 19 of both hemispheres (86, 94, 121, 185, 229, 293, 315–317, 401). Anatomical studies indicate that these corticocortical projections arise

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[5] Niimi and Kawahara (259) have suggested that the cat's lateral posterior nucleus and posterior nucleus are homologous to the primate's inferior pulvinar and medial pulvinar, respectively. Likewise these authors suggest that the cat pulvinar is homologous to the primate lateral pulvinar. We retain the older nomenclature of Rioch (279) and Jasper and Ajmone-Marsan (170) (i.e., lateral posterior nucleus, posterior nucleus, and pulvinar) to avoid confusion, because most anatomists and physiologists working in the cat's visual system have used these designations to describe their results.

[6] Recent anatomical studies have shown that the medial thalamus (including posterior nucleus, lateral posterior nucleus, and pulvinar) can be partitioned on the basis of its afferents into a corticorecipient zone, tectorecipient zone, and pretectorecipient zone (11, 17, 99, 100, 187, 190, 387). These recipient zones lie adjacent to each other in relatively nonoverlapping slabs, and they cut across the cytoarchitecturally defined borders of the thalamic nuclei. The cortical projections of each of these recipient zones have not been fully worked out, largely because the zones are relatively thin, they are angled obliquely across the thalamus (from dorsomedial to ventrolateral), they change their position slightly from anterior to posterior in the thalamus, and they are not clearly delineated by cyto- or myeloarchitectural landmarks. As a result it is difficult to be sure if lesions or injections (in anterograde tracing studies) or labeled cells (in retrograde labeling studies) are entirely within one or another of these thalamic recipient zones. Nevertheless the position of retrogradely labeled cells after HRP injections into the lateral suprasylvian cortex (17, 161, 179) suggests that the tectorecipient zone of the lateral posterior and posterior nuclei includes some neurons that project to the lateral suprasylvian cortex.

from cells in layers II and III (94, 229), and electrophysiological recording from area 17 cells driven antidromically by electrical stimulation of the lateral suprasylvian cortex supports this observation (128). These experiments also indicate that most of the neurons that project from layers II and III of area 17 to the lateral suprasylvian cortex belong to a particular subtype of complex cells. These cells have smaller receptive fields than other complex cells, respond to more slowly moving stimuli, have little or no spontaneous activity, and give a sustained response to stationary flashing stimuli (128). Unfortunately, geniculate inputs to these area 17 cells are unknown.

In addition to their direct projections to the lateral suprasylvian cortex, areas 17 and 18 innervate the nucleus of the optic tract, the superior colliculus, and most of the thalamic structures that project to the lateral suprasylvian cortex (17, 121, 190, 386, 387). Thus both direct and indirect pathways from cortical areas 17 and 18 to lateral suprasylvian cortex exist.

b) Receptive-field properties. The receptive-field properties of cells in the lateral suprasylvian cortex are similar in many respects to those of superior colliculus cells, and they differ significantly from those of cells in cortical areas 17 and 18 (37, 155, 333, 381, 407). In the lateral suprasylvian cortex, cells have large receptive fields, are sensitive to stimulus size, and lack orientation selectivity.[7] Most of these cells respond poorly to stationary stimuli flashed on or off but give brisk responses to moving stimuli over a broad range of stimulus velocities (i.e., from 5–10°/s to over 200°/s) and little or no response to more slowly moving stimuli (37, 327, 333, 381). Roughly 80% of these cells display direction selectivity, and over 70% are binocularly driven with an overall dominance by the contralateral eye (155, 327, 333).

c) Removal of visual cortex. Lesion experiments interpreted like the analysis for superior colliculus indicate that different aspects of receptive-field properties for lateral suprasylvian neurons are provided by the corticocortical and thalamocortical inputs (Fig. 5). Removal of cortical areas 17 and 18 markedly decreases the proportion both of direction-selective cells and of cells that respond to the ipsilateral eye, and many of the cells respond best to stationary flashing stimuli after such a lesion (334, 335, 338). These

[7] Two early reports stated that cells in the lateral suprasylvian cortex are orientation selective and that their receptive fields resemble those of complex and certain hypercomplex cells in visual cortical areas 17, 18, and 19 (155, 407). However, both studies tested the responses of these lateral suprasylvian cortex cells only with moving light slits or dark bars. Thus these studies failed to distinguish among the influences of stimulus size, orientation, and direction of movement. Tests designed to distinguish among these stimulus parameters indicate that the relevant parameters are stimulus size and direction of movement but not orientation (37, 333). Thus, although cells in the lateral suprasylvian cortex respond well to oriented light slits or dark bars, they respond equally well to circular spots of light. In addition changes in spot diameter (within the receptive-field-activating region) have the same effect as changes in slit length. For direction-selective cells, directional tuning (range of movement directions that produces a response) is the same for spots as for oriented slits. Finally, cells that respond to stationary flashing slits of light produce equal responses at all orientations. Thus these cells usually are direction selective but not orientation selective.

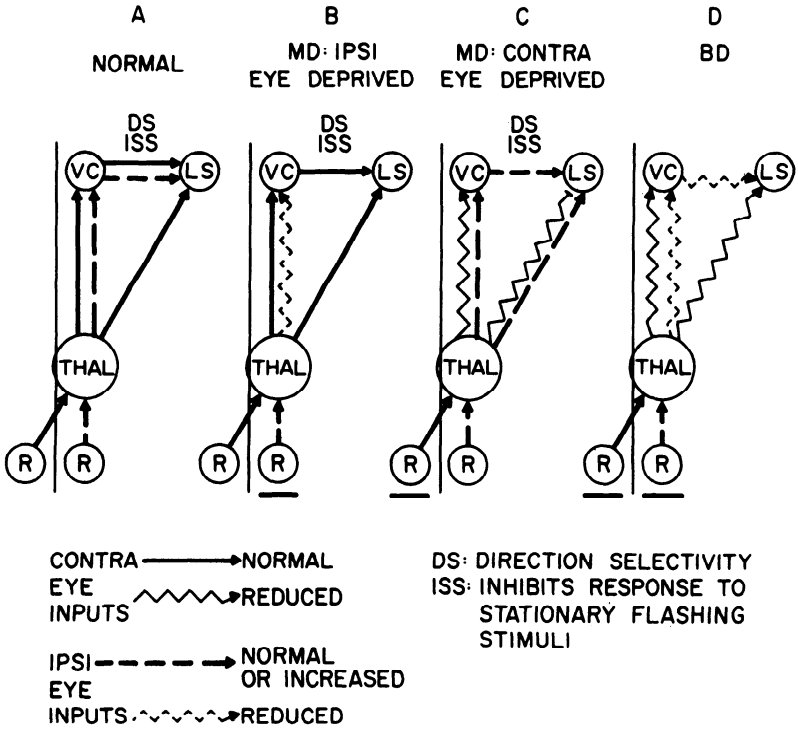

FIG. 5. Schematic representation of functional inputs to lateral suprasylvian cortex in normal cats and in each hemisphere of visually deprived cats. Each diagram shows the 2 eyes (R), plus thalamus (THAL), visual cortical areas 17 and 18 (VC), and lateral suprasylvian visual cortex (LS) of 1 hemisphere. *Vertical line* indicates midline. Details of pathways by which certain functional information reaches lateral suprasylvian cortex are not known in all cases. For example, functional properties provided by visual cortex to lateral suprasylvian cortex may arrive by direct corticocortical connections or by more indirect routes (e.g., a corticothalamocortical pathway). Purpose of diagrams is simply to show functional information provided to lateral suprasylvian cortex neurons by primary geniculocortical pathways (directly or indirectly) and by thalamic pathways to lateral suprasylvian cortex that are independent of visual cortex. Specific thalamic nuclei and details of their projections have been omitted for clarity; they are shown in Fig. 4. *A*: functional inputs to lateral suprasylvian cortex in either hemisphere of normally reared cats, determined by experiments in which visual cortex has been removed from animals. [Data from Spear and Baumann (333, 334).] *B*: inputs in hemisphere ipsilateral to deprived eye in monocularly deprived cats. *C*: inputs in hemisphere contralateral to deprived eye in monocularly deprived cats. *Short bar* at termination of thalamic pathway to lateral suprasylvian cortex for contralateral eye indicates that these inputs are suppressed by those from visual cortex. [Data in *B* and *C* from Spear and Tong (341, 373).] *D*: inputs in either hemisphere of cats reared with binocular lid suture. [Data from Tong et al. (374).]

changes do not result from the elimination of corticotectal pathways with the consequent alteration of the tectothalamic input to lateral suprasylvian cortex (327). Cortical areas 17 and 18 thus provide most neurons in the lateral suprasylvian cortex with direction selectivity, responsiveness to the ipsilat-

eral eye, and inhibition of responsiveness to stationary flashing stimuli. The remaining thalamic inputs, in the absence of cortical areas 17 and 18, provide these cells with a variety of nonselective, receptive-field properties from the contralateral eye and little functional input from the ipsilateral eye.

III. GENERAL NONCOMPETITIVE AND COMPETITIVE MECHANISMS OF VISUAL DEVELOPMENT

During development, neurons can form synapses, maintain synapses, and/or degenerate and lose synapses. The mechanisms by which these processes occur can be divided into two broad categories, termed "noncompetitive" and "competitive." Many visual-deprivation studies have been aimed at elucidating these mechanisms. Therefore we define them briefly and outline the strategies employed to determine their presence.

A. Definitions of Noncompetitive and Competitive Mechanisms

At a simple level, imagine two neurons, A and B, that develop axons to innervate neuron C. If this development were controlled by a noncompetitive mechanism, the synaptic development from neuron A onto neuron C would be independent of that from neuron B onto neuron C. The number of synapses formed by neurons A or B onto neuron C might relate to factors such as the amount or pattern of neural activity each exhibits during development. On the other hand, a competitive mechanism implies that neurons A and B compete for limited synaptic space onto neuron C. The success of neurons A or B in this competition would depend on the relative neural activity each exhibits during development.

If neuron A had normal activity during development but neuron B did not, the final pattern of development would depend on which mechanism operated. The noncompetitive mechanism would result in a normal number of synapses from neuron A and fewer from neuron B. The competitive process would create fewer from neuron B and correspondingly more from neuron A. It should be noted that for either mechanism the effect could be observed at the postsynaptic site (e.g., neuron C) and/or among presynaptic elements (e.g., neuron B).

In general, noncompetitive mechanisms thus control neuronal development on the basis of afferent input to the neurons in question and/or the ability of these neurons to develop or maintain functional efferent connections. This mechanism implies that development of the neuron in question progresses without regard to the development of any other neuron that is not a source of its afferent input. In contrast competitive mechanisms control development by interactions among cells. Such a mechanism requires cells to compete with one another for the development and/or maintenance of synapses. Normal visual stimuli during development evoke normal activity

in these cells and lead to competitive interactions that produce what is defined as normal pathways in the adult. Visual deprivation, by creating abnormal activity in these cells, changes the efficiency with which they can compete with other cells for central connections.

Both normal and abnormal development could result from the action of these noncompetitive and competitive mechanisms acting alone or in combination. A consideration of whether or not binocular competition plays a role in development of the central visual pathways can serve to clarify this distinction between noncompetitive and competitive mechanisms of development, and it can also serve to illustrate the experimental strategies required to determine their presence.

B. Binocularly Noncompetitive and Competitive Mechanisms of Development

A developmental mechanism of binocular competition can be thought of as a process of competitive interactions between central pathways related to each eye resulting in the formation and/or maintenance of synapses related to each eye. For instance, a relay cell from lamina A might compete with one from lamina A1 for synaptic space on a cortical neuron. A binocularly noncompetitive mechanism means that the central (geniculocortical) connection in question related to a given eye develops without regard to the development and activity of pathways related to the other eye. Taken alone, the observation in monocularly sutured cats that deprived geniculate laminae have smaller somata than do nondeprived laminae, or that in area 17 practically all neurons can be influenced only by the nondeprived eye, does not permit one to distinguish between a binocularly competitive or noncompetitive mechanism as the cause. Either process could be responsible. The obvious and crucial question is: How does one experimentally distinguish between these alternatives of binocularly competitive and noncompetitive development? Two general strategies (described next) have been used in studies of visual deprivation.

1. Monocular versus binocular suture

Eyelid suture creates serious abnormalities in the developing geniculocortical pathways (for details, see sect. IV and V). To distinguish binocularly competitive from noncompetitive mechanisms, a bilaterally symmetrical (binocular) deprivation can be compared with an asymmetrical (monocular) one. Historically this was indeed how a distinction between the two mechanisms was first identified (398). Abnormalities produced by monocular suture were regarded as due to an unbalanced competitive interaction if analogous abnormalities after rearing with binocular suture were less severe. Wiesel and Hubel (398) found that monocular suture produces striking ab-

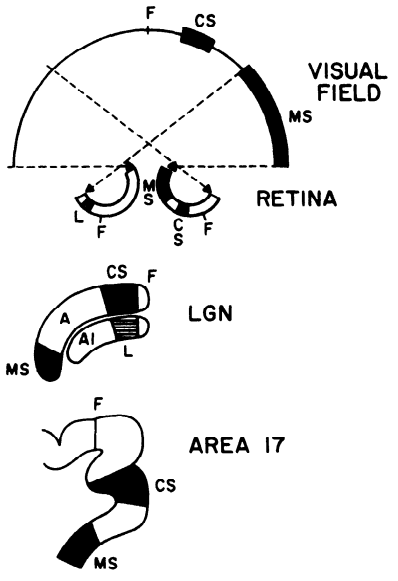

FIG. 6. Natural and artificial monocular segments (MS and CS, respectively) illustrated for right eye and left half of brain. Natural monocular segment includes a peripheral region of right visual field that can be viewed only by right eye, because nasal retina in right eye extends beyond homonymous representation of temporal retina in left eye. Because of precise retinotopic representation of visual field in lateral geniculate nucleus (LGN) and cortical area 17, monocular segments of these structures can be readily identified. This segment has not yet been identified for study in cortical area 18. Same relationships apply to monocular segment in left hemifield. Finally, if a small retinal lesion is placed in left retina, an artificial monocular segment is created for homonymous region of right retina, and this region is retinotopically represented in each central structure. F, fixation point in visual field and its representation in each neuronal structure; L, retinal lesion and its representation in lateral geniculate nucleus.

normalities in cortical response properties and that binocular suture does not produce comparable changes. For instance, monocular suture leads to a condition in which only about 10% of the cells can be activated via the deprived eye. If this were due to a noncompetitive effect, one might predict that binocular suture would produce very few cortical cells that either eye could activate (i.e., twice the effect of monocular suture). Instead, rearing with binocular suture results in cortical neurons that both eyes can activate, and relatively few visually unresponsive cells are encountered. Because these alterations seem less severe than those after monocular suture, the effects of monocular suture can reasonably be ascribed to unbalanced competitive interactions (but see sect. VII*A*).

2. Monocular versus binocular segment

A second method for distinguishing binocularly competitive from noncompetitive mechanisms was proposed by Guillery and Stelzner (111). They used monocularly deprived animals and compared the abnormalities in the deprived binocular segment of the lateral geniculate nucleus with those in the deprived monocular segment. Figure 6 illustrates the division of the central visual pathways into binocular and monocular segments. Guillery and Stelzner (111) measured the size distribution of geniculate somata from laminae A and A1. The effects of any binocularly noncompetitive deprivation are seen in the monocular segment, where there is no possibility of binocular interactions, whereas the combined effects of binocularly competitive and noncompetitive processes can be seen in the binocular segment. This provides

the second strategy for discriminating binocularly competitive from noncompetitive mechanisms in monocularly sutured cats, although a caveat is noted below. If abnormalities are equally severe in deprived binocular and monocular segments, a noncompetitive mechanism is suggested; if abnormalities are limited to the deprived binocular segment, binocular competition is likely; and a combination of mechanisms would result in abnormalities that occur in both segments but that are more severe in the binocular than in the monocular segment. This strategy has the virtue that the comparisons are within individual subjects exposed to a single rearing condition.

The caveat is that differential effects of visual deprivation on the binocular and monocular segments are potentially explicable by differences between these segments other than ocularity. For instance, cells in the monocular segment might be less sensitive to deprivation because the visual periphery is less concerned with detailed forms, because the relative ratios of cell types (i.e., X-cells vs. Y-cells) differ between these segments, because the two segments might have different cortical projections [e.g., Tusa et al. (384, 385) state that the monocular segment is well represented in area 17 but not in area 18], because the two segments possibly develop at different rates, etc. Unless these other differences between the segments can be ruled out as factors in differential effects of visual deprivation, conclusions about binocular competition cannot be confidently drawn.

Guillery (106) designed an elegant experiment to deal with this problem. He created an artificial monocular segment ("critical segment") by placing a neonatal retinal lesion in one eye of a kitten at the same time the lids of the other eye were sutured. Now the deprived eye and its central connections have two monocular segments (see Fig. 6): the natural one representing extreme nasal retina and the artificial one representing the homonymous region of the retinal lesion in the open eye. This second segment can be placed at various eccentricities by varying the location of the lesion and thus placing an artificial monocular segment in a region that otherwise would develop as a binocular segment. To the extent that the two deprived monocular segments (natural and artificial) develop in the same manner, one can draw fairly firm conclusions about binocular competition. For instance, if both deprived monocular segments develop normally along some dimension, whereas the deprived binocular segment does not, one can clearly conclude that binocular competition plays an important role in the development of this dimension.

Actually the logic behind the comparison of binocular and monocular segments and that behind the comparison of binocular and monocular deprivation are rather similar. Both suffer from certain flaws that to some extent limit the conclusions drawn from them. These are considered in section VII*A* in the context of data obtained in experiments with these two strategies. However, both strategies are useful and, when applied in combination, can provide information about the role and nature of competitive and noncompetitive mechanisms.

C. Other Noncompetitive and Competitive Mechanisms

Thus far we have discussed noncompetitive and competitive developmental mechanisms only in terms of the afferents for the two eyes. However, these are general classes of mechanisms that can apply to almost any grouping of cells. For example, there may be competition between afferents from different structures (e.g., the A laminae of the dorsal lateral geniculate nucleus vs. the medial interlaminar nucleus) or even between different cell types within a structure (e.g., X-cells vs. Y-cells, on-center cells vs. off-center cells). Unfortunately it is not yet possible to determine if competition of this sort occurs. For example, to determine if Y-cell abnormalities occur because of competition with X-cells, one requires a preparation in which one population of deprived Y-cells has potentially competitive X-cells present while another population of deprived Y-cells does not. Such preparations are not presently available. Consequently nearly all of our conclusions regarding competitive mechanisms of development derive from studies that concentrate on the presence or absence of binocular competition. These other forms of competitive interactions may nonetheless occur, even if they are presently difficult to detect. An appreciation of the possibility of such competitive interactions is the first step in designing experiments to elucidate and study them.

IV. MONOCULARLY SUTURED CATS

In this section we review studies of cats reared with monocular suture during the postnatal critical period. Unfortunately the extent and relative dynamics of this critical period are not completely understood. Hubel and Wiesel (156) concluded that this period begins during the 4th wk after birth, peaks during the next few weeks, and ends gradually during the 3rd or 4th mo (see also 22). However, there is evidence that the critical period begins during the first 3 wk (389) and extends beyond the 6th mo (58, 173). Since relatively few experiments are designed to study cats reared with eyelid suture from the 2nd wk after birth until at least 6 mo, some of the confusing or contradictory conclusions in the literature may be due to rearing conditions that involve different portions of the critical period. Therefore we note any unusual periods of lid suture employed in certain studies, particularly when these seem a possible source of conflicting data.

A. Retina

Studies of the deprived retina and optic tract in cats reared with monocular lid suture have consistently produced results within the normal range. Deprived retinal ganglion cells have normal soma sizes (310), qualitatively normal response properties (396), and a normal complement of W-, X-, and

Y-cells (310). Furthermore deprived retinal X- and Y-cells display normal spatial and temporal contrast-sensitivity functions, including normal spatial resolution for the deprived X-cells (196). This was confirmed and extended by the recent demonstration that even deprived retinal X-cells in the area centralis have normal spatial resolution, and area centralis X-cells possess the highest spatial resolution of any ganglion cells in the cat[8] (46). Jones (171) also found no evidence of retinal abnormalities from evoked potentials recorded in the optic tract. These potentials were evoked by a patch of light temporally modulated at different rates, and no differences were found between stimulation of the deprived or nondeprived retina. It consequently appears that any deficits that develop during rearing with monocular lid suture occur central to the optic tract. Of course this conclusion must be limited to properties specifically tested.

B. Lateral Geniculate Nucleus

Obvious effects of rearing with monocular suture can be found in the lateral geniculate nucleus, and both morphological and physiological abnormalities have been found there. Since the optic tract seems normal in monocularly deprived cats, these changes in the lateral geniculate nucleus represent one of the most peripheral sites in the visual pathways in which effects of monocular deprivation can be found.

The available evidence suggests that the abnormalities of geniculate neurons in deprived laminae have a postsynaptic origin. Ultrastructural studies of monocularly sutured cats have revealed no differences in the size or distribution of optic tract terminals between the deprived and nondeprived A laminae (404–406). Also the geniculate abnormalities are not due to any detectable change in neuronal numbers, because no difference in this parameter was seen between deprived and nondeprived regions of the medial interlaminar nucleus (201) or A laminae (177).

1. Effects of lid suture on morphology

a) Lack of soma growth in deprived A laminae. Wiesel and Hubel (396) first pointed out that somata in the deprived A laminae (i.e., those receiving

[8] Cleland et al. (46) presumably were encouraged to concentrate on the deprived area centralis in their study because of the report by Ikeda and Tremain (165) that cats reared with convergent strabismus fail to develop normal spatial resolution among area centralis X-cells in the retina. It seems puzzling that strabismus could affect any retinal response properties that are unaffected by lid suture. However, Cleland et al. (47) recently reported normal spatial resolution for all retinal ganglion cells, including X-cells in the area centralis, of cats reared with convergent strabismus, and this contradicts the claim of Ikeda and Tremain (165). Because of this discrepancy, conclusions regarding the effect of lid suture on the spatial acuity of retinal X-cells should be somewhat qualified.

retinal afferents from the sutured eye) are only about two-thirds as large, on average, as their nondeprived counterparts. This finding has since been confirmed by many investigators. Guillery and Stelzner (111) extended these observations in an important direction. These authors confirmed the difference in cell size between deprived and nondeprived laminae but observed that these abnormalities are limited to the binocular segment of the nucleus, at least for the A laminae. The deprived monocular segment of lamina A, which suffered from the same visual deprivation as did the binocular segment, has somata approximately equal in size to its nondeprived counterpart in the opposite hemisphere. Guillery (106) extended these observations by studying cats raised with an artificial monocular segment (see Fig. 6 and sect. III*B2*). He found approximately normal geniculate cell sizes in deprived laminae both in the natural and the artificial monocular segments. These experiments convincingly demonstrate that, in monocularly sutured cats, binocular competition plays a key role in the development of geniculate cell sizes for the A laminae.

More recent experiments have raised the possibility that noncompetitive mechanisms also play a role in geniculate cell growth. Hickey et al. (135) reported a slight difference between the deprived and nondeprived monocular segments of lamina A (the former being roughly 10% smaller than the latter), although this is less than the difference found between binocular segments of the A laminae (30–49%). This is illustrated in Figure 7. Since binocular competition cannot occur in the monocular segment, Hickey et al. (135) concluded that both a noncompetitive mechanism and binocular competition are involved in the development of soma sizes. Kalil (177) subsequently demonstrated that when monocular segments are measured relatively near the binocular segment (i.e., dorsomedially) in lamina A of each hemisphere, differences in cell size (about 20%) may be nearly as large as those found in the binocular segment. However, with measurements farther from the binocular segment border (i.e., ventrolaterally in the monocular segment), no effects of monocular deprivation were detected. Thus there appears to be a gradient in the effects of monocular deprivation on monocular segment cells, with greater effects near the binocular segment border than away from it. The reasons for this are not clear, but possibly the border between binocular and monocular segments is irregular or gradual or there may be interactions between the two segments (see sect. VII). In any case the effects of monocular deprivation are clearly less in the monocular segment as a whole than in the binocular segment.

b) Hypertrophy in nondeprived A laminae. Guillery (106) suggested that if binocular competition causes deprived cells to grow less, it might also cause nondeprived cells to hypertrophy. That is, if the victors in a competitive battle (i.e., nondeprived cells) take over synaptic zones in cortex ceded by the losers (i.e., deprived cells), then the nondeprived cells would develop abnormally large terminal arbors in cortex and/or excessive numbers of geniculocortical synapses. If soma sizes reflect the extent of geniculocortical

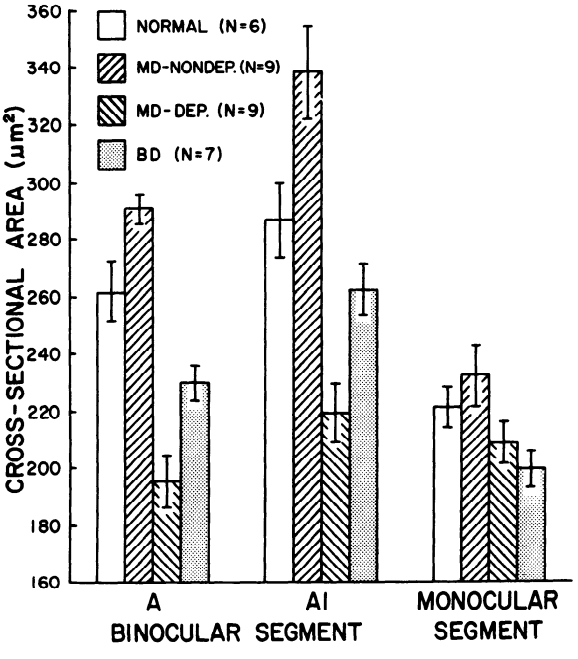

FIG. 7. Cross-sectional areas of dorsal lateral geniculate cells in normal and visually deprived cats. Deprived cats received monocular (MD) or binocular (BD) lid suture from before normal eye opening to at least 4 mo of age. For each cat 100 cells were measured in each region of nucleus (binocular segment of laminae A and A1, and monocular segment of lamina A), and mean cell size was calculated for each region. Each bar represents mean ± 1 SE for individual cats; n is number of cats in each group. In binocular segment of monocularly deprived cats, cells in nondeprived (nondep.) laminae are slightly larger than normal and cells in deprived laminae (dep.) are much smaller than normal. By contrast, cells in binocularly deprived cats are similarly reduced in size throughout the binocular segment; they are slightly smaller than normal and are somewhat larger than those in deprived laminae of monocularly deprived cats. In monocular segment, they are smaller than normal and similar in size or slightly smaller than those in monocularly deprived cats. [Data from Hickey et al. (135) and Spear and Hickey (337).]

arbors, then nondeprived geniculate somata would hypertrophy. In fact studies such as those of Wiesel and Hubel (396) and Guillery and Stelzner (111) could hypothetically be interpreted solely on the basis of hypertrophy of nondeprived somata with no size abnormality of deprived somata.

Hickey et al. (135) obtained the first direct measure of lack of growth in deprived laminae and hypertrophy in nondeprived laminae by comparing soma sizes from monocularly deprived cats with those from normal cats (see Fig. 7). They reported a 20–25% reduction of soma size for deprived somata and a 10–15% hypertrophy for nondeprived neurons compared with sizes in normal cats. Kalil (177) performed a similar analysis and found a similar lack of growth for deprived cells; however, he concluded that no hypertrophy occurs for nondeprived somata. Both studies relied on intersubject comparisons, and normal variation in cell sizes among cats could possibly obscure any existing hypertrophy.

c) Differences in soma growth between A laminae. Hickey et al. (135) concluded that, in the binocular segment, deprived lamina A neurons are 33% smaller than those in nondeprived laminae A, and a similar comparison for lamina Al gave a 35% difference. Therefore cell growth in laminae A and Al seems equally affected by lid suture.

More recently, however, Hickey (133) described two patterns of geniculate soma sizes in monocularly deprived cats. In 32 of 38 such cats, soma sizes were affected roughly equally in laminae A and A1. In the remaining six cats, deprived lamina A showed little or no evidence of an abnormal soma size distribution, although deprived lamina A1 somata were considerably smaller than normal. Because the pattern in these six cats seems similar to that described in monocularly deprived Siamese cats (108), Hickey (133) suggested that cats can be affected variably by rearing with monocular deprivation: common cats typically show a pattern in which laminae A and A1 are fairly equally affected, whereas another extreme is represented by some common cats and Siamese cats in which the deprivation effects are largely limited to lamina A1.

d) Soma growth in C laminae. Hickey (133) used autoradiographic tracing techniques to delineate laminae C, C1, and C2 in cats raised with monocular suture. His measurements of soma size in these laminae indicate that significant changes are limited to lamina C. That is, compared with cells in nondeprived laminae of the other hemisphere, deprived lamina C cells were 23% smaller; lamina C1, only 8% smaller; and lamina C2, only 3% smaller. This suggests that W-cell soma sizes are largely unaffected by monocular lid suture. Since measurements in lamina C were not made separately for binocular and monocular segments, it is not clear whether or not these cell size changes in deprived cats are due to binocular competition.

e) Soma growth in medial interlaminar nucleus. Kratz et al. (201) also used autoradiographic tracing techniques to delineate the deprived and nondeprived regions of the medial interlaminar nucleus in cats raised with monocular suture. Deprived somata there were 34% smaller than nondeprived somata. Monocular and binocular segments were not identified for independent analysis, so it is unclear whether or not binocular competition plays a role in development of cell size in the medial interlaminar nucleus.

f) Cytoplasmic laminated bodies. LeVay and Ferster (211) proposed that, in normal cats, type 1 cells (large somata, no cytoplasmic laminated bodies) are Y-cells, type 2 cells (intermediate size somata, cytoplasmic laminated bodies) are X-cells, and type 3 cells (small somata, no cytoplasmic laminated bodies) are interneurons (sect. II*C2*). These authors also showed that lid suture seems to affect development of type 1 cells the most, type 2 cells less, and type 3 cells not at all. A slight reduction in the proportion of type 1 cells was noted in deprived laminae (a ratio of type 1 to type 2 of 0.8 vs. 1.0 in nondeprived laminae). More striking is the effect of deprivation on soma size. Deprived type 1 cells are only 58% as large as nondeprived type 1 cells, whereas deprived type 2 cells are 80% as large as their nondeprived counterparts. Thus, although the larger (type 1) cells are more affected by lid suture than are the smaller (type 2) cells, the type 2 somata still are only 78% as large as type 1 somata in deprived laminae. Type 3 cells are essentially unaffected by the deprivation.

g) Cells projecting to cortical areas 17 or 18. The differential effects of monocular suture on geniculate neurons that project to areas 17 and 18 were

studied by retrograde labeling of geniculate neurons with HRP. This was done by injecting HRP into one or the other cortical area and studying the neuronal labeling in the lateral geniculate nucleus.

Labeled relay cells in the deprived A laminae are smaller than their nondeprived counterparts, regardless of the cortical projection zone. However, the effect is larger for neurons that project to area 18 than for those that project to area 17 (85, 224). Furthermore there are fewer labeled cells in deprived laminae A or A1, but again the difference is relatively larger after area 18 injections. The mean percentages of labeled cells reported in nondeprived versus deprived laminae were 77% vs. 66% after area 17 injections and 15% vs. 5% after area 18 injections (224). Thus, although the *absolute* loss of labeled cells is roughly the same for each cortical area, the *relative* loss is much greater for area 18 than for area 17 (60% fewer vs. 14% fewer). Lin and Sherman (224) also showed that, after injections of HRP into extensive areas of visual cortex, labeled neurons in deprived regions of the medial interlaminar nucleus are smaller and fewer than those in nondeprived regions.

The projection to area 18 from the A laminae is from Y-cells, whereas the X-cells project to area 17, and the medial interlaminar nucleus is comprised mostly of Y-cells (sect. II*B1d*). Consequently the patterns of HRP retrograde labeling suggest a fairly selective effect of deprivation on development of Y-cell geniculocortical projections. Unfortunately the interpretation of HRP labeling is far from clear. The failure to label cells could be due to physically absent or relatively inactive cells, axons, or terminals or even to other factors that may or may not bear on the issue of the functional integrity of deprived geniculate Y-cells.

2. Effects of lid suture on physiology

Although Wiesel and Hubel (396) found large differences in soma size between deprived and nondeprived laminae, they reported only subtle abnormalities in response properties for these deprived neurons. Nonetheless 4 of 20 (20%) deprived cells studied in detail were judged to have abnormal receptive-field properties (396). Other early studies (113, 309) also reported only subtle abnormalities due to deprivation. However, this apparent paradox between abnormal morphology and relatively normal physiology seems to have been at least partially resolved once the parallel W-, X-, and Y-cell pathways were appreciated. To date no studies of identified geniculate W-cells have been reported for visually deprived cats. The discussion here is thus limited to X- and Y-cells.

a) Y-cells. Sherman et al. (308) recorded an abnormal distribution of Y-cells in deprived laminae. X-cells were found at roughly the normal rate in cells per millimeter of electrode traverse, and they had grossly normal response properties (but see sect. IV*B2b*). Y-cells, on the other hand, were recorded only rarely throughout the deprived binocular segment but were

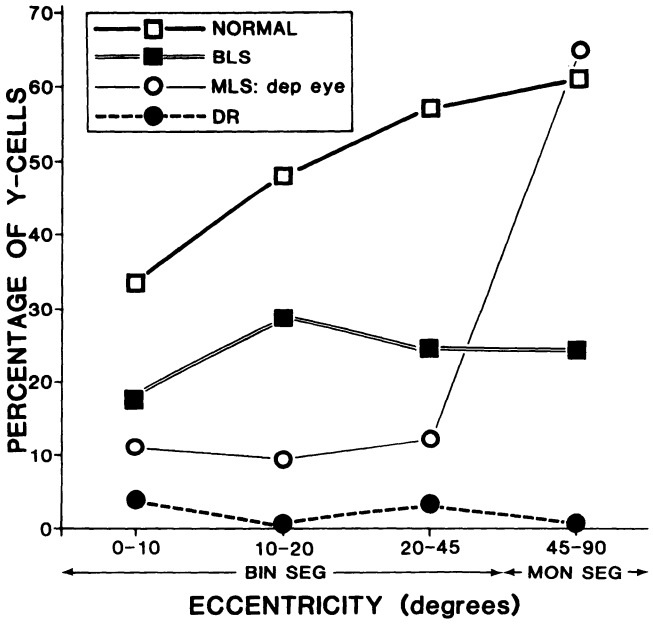

FIG. 8. Percentage of Y-cells in laminae A and A1 recorded electrophysiologically as function of eccentricity of their receptive fields from area centralis (unpublished data from Sherman's laboratory based on from 62 to over 300 neurons for each data point). Over 95% of neurons in A laminae can be readily identified as X- or Y-cells, and thus the percent fraction of X-cells can be estimated reasonably accurately from these data. Neurons are divided into 4 eccentricity groups: 3 in binocular segment (BIN SEG) and 1 in monocular segment (MON SEG). In normal cats, Y-cell percentage increases monotonically with eccentricity. Although not illustrated, function found in nondeprived laminae of monocularly sutured cats seems quite normal. In deprived laminae of these cats (MLS: dep eye), few Y-cells can be recorded in binocular segment, but normal proportion is found in monocular segment. X-cells are located with normal frequency and response properties, except for reduction in spatial acuity. In binocularly sutured cats (BLS), a moderate loss in recorded Y-cell percentage was seen at all eccentricities. In dark-reared cats (DR), few Y-cells could be found at any eccentricity. Note that Y-cell percentages are normal in monocular segment for monocularly sutured but not binocularly sutured or dark-reared cats.

found in normal numbers in the deprived monocular segment. In the binocular segment of the A laminae, roughly 10–15% of the deprived neurons were Y-cells, whereas Y-cells constituted approximately 50–60% of the neural sample in nondeprived laminae (Fig. 8). These authors also reported difficulty in recording deprived Y-cells in the C laminae.

Sherman et al. (313) extended this analysis to monocularly deprived cats reared with a deprived, artificial monocular segment (see sect. III*B2*) and reported that recorded Y-cell numbers also were normal in that segment. Finally, Lehmkuhle et al. (208) reinforced these observations with more quantitative receptive-field data based on contrast-sensitivity functions. These authors found that the deprived Y-cells in the monocular segment

respond to all tests completely normally. These data indicate that some form of binocular competition dominates the development of Y-cells and that the Y-cells developing at a competitive disadvantage become unresponsive, abnormal, or difficult to isolate with most conventional microelectrode techniques.

Kratz et al. (201) recently extended this study to the medial interlaminar nucleus in which practically all neurons are Y-cells in normal cats. They found that, in nondeprived portions of this nucleus in monocularly deprived cats, 95% of the neurons are normal Y-cells, but only 43% of the neurons in deprived portions are normal Y-cells. The remaining 57% have grossly abnormal response properties, including large, diffuse receptive fields, poor responsiveness to visual stimulation, and poor responsiveness to electrical stimulation of the optic chiasm. Also sampling density is markedly reduced in the deprived regions: 5.2 cells/mm (including 5.1/mm for normal Y-cells) were found in nondeprived regions compared with 2.8 cells/mm (including 1.0/mm for normal Y-cells) in deprived regions.

Although the inability to record deprived geniculate Y-cells in monocularly sutured cats has subsequently been observed in a number of other studies (cf. 71, 92, 141, 142, 233, 256, 408) and seems to correlate generally with some of the morphological abnormalities mentioned, the interpretation of these physiological data is far from clear. Two general explanations have been offered. *1*) The results could be caused by electrode sampling biases (e.g., 71, 298, 308); that is, microelectrodes may selectively isolate larger somata. According to this explanation, in normal laminae the Y-cells are larger than the X-cells and are readily recorded; in deprived laminae, the presumably smaller size of Y-cells reduces their recordability, and this could occur without any physiological abnormalities among deprived geniculate neurons. *2*) The loss of recorded Y-cells could reflect a severe functional deficit and cannot be explained completely by electrode sampling characteristics.

Although most anatomical and physiological evidence apparently supports the latter interpretation of a true functional deficit for deprived geniculate Y-cells, a definitive understanding of these phenomena is presently not possible. Also the interpretation of virtually all electrophysiological studies, including those discussed in this review, are plagued by the specter of electrode sampling artifacts. Since data relevant to this issue have also been produced from studies of binocularly deprived cats and young kittens, we delay discussion of this point for a more complete consideration in section VII.

b) X-cells. As mentioned previously, X-cells in deprived laminae were thought to develop fairly normally (308). However, more subtle measures of receptive-field properties have revealed a loss of spatial resolution for deprived X-cells to roughly half the normal value (146, 208, 256; see also 231). Shapley and So (298) recently challenged this finding with a report that no difference in mean spatial resolution could be found between deprived and

nondeprived X-cells, although the actual values they reported are roughly comparable to the values reported earlier for deprived X-cells. More data are needed to resolve this discrepancy. In any case the deficit reported for deprived X-cells by Lehmkuhle et al. (208) is just as large in the monocular as in the binocular segment. This suggests that the resolution deficit for X-cells, if it indeed exists, develops without the obvious influence of binocular competition. The deficits described for deprived geniculate X- and Y-cells thus result from different mechanisms.

c) Interneurons. Mooney et al. (244) recorded from presumed interneurons in deprived geniculate laminae and found fairly normal properties, leading them to conclude that deprivation affects relay cells fairly exclusively. However, Friedlander et al. (81) have questioned whether it is possible to identify interneurons with the electrophysiological criteria used.

d) Evoked-potential studies. Evoked-potential studies of the lateral geniculate nucleus after early monocular suture tend to underscore the presence of abnormalities in deprived laminae. Jones (171) reported both little abnormality in deprived laminae for potentials evoked by a light flickering at a low temporal rate (for which X-cells are most sensitive) and a rather large reduction for potentials evoked by high rates (for which Y-cells are most sensitive). However, Mitzdorf and Neumann (239) argued that an equally large reduction in retinogeniculate transmission occurs for X- and Y-cells in deprived laminae. These latter authors calculated current-source density from the second spatial derivative of field potentials evoked from electrical stimulation at each optic disk, and from the latency of various current sources and sinks they ascertained whether X- or Y-cells were involved.

Both of these studies indicate deficits for deprived Y-cells but disagree on whether evidence for an X-cell deficit exists. Even without this lack of agreement, it is not at all clear how the evoked potentials (or their 2nd spatial derivative) relate to functional properties of the visual pathways.

3. Structure-function correlations

Friedlander et al. (82) have obtained preliminary evidence for the structure-function relationships of individual geniculate neurons in the A laminae of monocularly sutured cats. This was accomplished by intracellular injection of HRP into physiologically identified neurons. As might be expected, they found normal structure-function relationships for nondeprived neurons. However, a number of unusual features were noted in the deprived laminae. Some deprived X- and Y-cells have normal morphological features except for somewhat shrunken somata. Some deprived cells with poor or abnormal responsiveness, most of which were judged to be abnormal Y-cells, have unusual morphological features never seen in normal cats. These include an extremely dense and complex dendritic arbor comprised of very thin, sinuous,

and varicose dendrites. Most striking, however, is the appearance of a number of neurons with physiology characteristic of X-cells that have morphology typical of normal Y-cells, including fairly large somata and thick, cruciate dendrites arranged in a spherically symmetrical arbor. This last observation led Friedlander et al. (82) to suggest that perhaps some geniculate neurons, which under normal conditions develop as Y-cells (i.e., retain or accept retinal input only from Y-cells), instead develop during deprivation as X-cells (i.e., retain or accept input from retinal X-cells). In any case it seems clear that deprived neurons develop most unusual structure-function relationships.

C. Cortical Area 17

1. General physiological effects

The effects of early monocular deprivation on response properties of cat striate cortex neurons are perhaps the best documented and least controversial of any observation in the literature on visual deprivation. If kittens are raised with monocular lid suture until adulthood, the deprived eye is able to drive only about 5–10% of the cells in the binocular segment of cortical area 17 (141, 199, 300, 322, 328, 339, 397, 398, 400). Figure 2*B* illustrates this result, which is extremely consistent from animal to animal. Moreover similar results are seen over a wide range of visual-field locations in the binocular segment, from the area centralis representation to at least 30° eccentric (141, 339, 400). Among the few cells that can be driven by the deprived eye in the binocular segment, the receptive-field properties generally are very abnormal. The cells typically lack direction selectivity, very few are orientation selective, and the responses tend to be weak and inconsistent (141, 300, 322, 339, 398, 400).

The effects of monocular deprivation in the deprived monocular segment of cortical area 17 are much less severe than those in the binocular segment (400). This is shown in Figure 9. In the deprived monocular segment, about 67% of the cells respond to the deprived eye, and over half of the responsive cells appear to have normal receptive fields. Interestingly, nearly all these are simple cells. An experiment in which multiple-unit recordings were made in an artificial monocular segment (or critical segment) in the central visual-field representation of striate cortex confirms this finding. Again the deprived eye is able to drive a much larger proportion of cells in the artificial monocular segment than in the surrounding binocular segment (307). Taken together the results in the natural and artificial monocular segments indicate that binocular competition is important in the inability of the deprived eye to drive striate cortex cells after monocular deprivation.

Although the monocular segment of area 17 is less affected than the binocular segment of striate cortex, the monocular segment nevertheless is

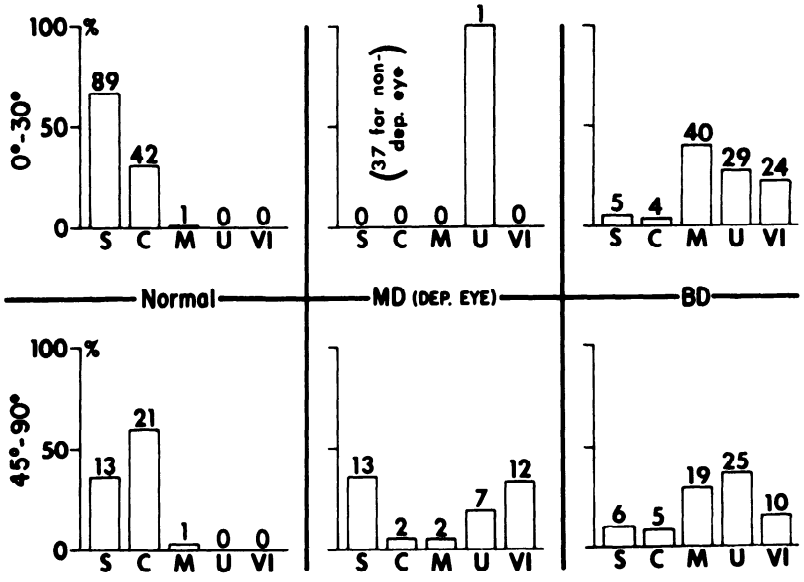

FIG. 9. Histograms of percentage of neuronal receptive-field types found in striate cortex. Histograms are separated into binocular segment (*upper row*, receptive fields within 30° of area centralis) and monocular segment (*lower row*, receptive fields beyond 45° from area centralis) for normal cats (*left column*), deprived eye of monocularly sutured cats (*middle column*), and binocularly sutured cats (*right column*). Five receptive-field types are distinguished: simple cells (S), complex cells (C), clearly responsive cells easily mapped but without normal orientation or direction selectivity (M), poorly responsive cells with diffuse receptive-field borders that are unmappable (U), and visually inexcitable cells (VI). Number above each bar is number of cells in each category. [From Watkins et al. (392).]

abnormal after monocular deprivation (Fig. 9). Wilson and Sherman (400) found that fewer cells than normal can be driven by the deprived eye (67% vs. 100%) and that about a third of the responsive cells have diffuse or nonspecific receptive fields. In addition the proportion of cells with complex receptive fields is abnormally low, although the proportion of simple cells is unaffected. Similar results are seen over a wide range of visual-field eccentricities across the deprived monocular segment. Therefore it can be concluded that monocular deprivation produces abnormalities in striate cortex that are independent of abnormal binocular competition.

2. *Geniculostriate afferent connectivity*

a) Morphological studies of connectivity. In view of the abnormalities in cortical area 17 produced by early monocular deprivation, it is of interest to consider the changes in the afferents and their terminations in striate cortex that underlie the cortical abnormalities. Because so few striate cortex cells respond to the deprived eye, it might be thought that the geniculo-

cortical inputs for the deprived eye are largely eliminated by monocular deprivation. However, it is now clear from anatomical studies that many deprived geniculate axons at least reach the visual cortex. Visual cortex lesions result in extensive retrograde degeneration of cells in the deprived laminae (336, 373), HRP injections in striate cortex result in retrograde labeling of many cells in the deprived laminae (85, 224; however, see 371), and anterograde tracing studies with autoradiography show that substantial inputs from the deprived eye to striate cortex persist (300). Thus some geniculostriate axons develop from deprived laminae despite the monocular suture.

Attempts have been made to determine the extent of the terminal distribution of these projections in layer IV of cortical area 17 with the use of anterograde tracing methods. After intraocular injections of tritiated amino acids, transneuronal autoradiographic studies suggest that the ocular-dominance bands in layer IV of striate cortex are 25–35% narrower than normal for the deprived eye and correspondingly wider for the nondeprived eye (299, 300). However, these results are difficult to interpret for a variety of reasons. The width of the ocular-dominance bands determined by these methods varies with the amount of amino acid uptake and transport, the angle at which the tissue is cut, the amount of time the autoradiographs are exposed and developed, and how the gradual borders of the ocular-dominance bands are defined. Since the width of the ocular-dominance bands was measured in only one normal cat and one monocularly deprived cat with the deprived eye injected (300), it is impossible to know if the differences seen are due to the deprivation or to variations caused by any of the factors just listed. Such quantitative assessments require a large sample of normal and monocularly deprived cats. Qualitatively, however, it seems clear from these studies that there is at least some reduction in terminal inputs from the deprived eye to striate cortex, but that substantial deprived inputs to layer IV remain.

The transneuronal autoradiographic studies also suggest that the terminal distribution of deprived lateral geniculate afferents differs in the upper and lower parts of layer IV. Specifically, deprived terminals in the lower part of layer IV appear more widespread than deprived terminals in the upper part of the layer, a difference not seen in normal animals (300, plate 2). This is of particular interest because Y-cell afferents seem to terminate predominantly in the upper part of layer IV, whereas X-cell afferents terminate predominantly in the lower part (see sect. II*B1d*). Thus the terminal distribution of deprived Y-cell afferents appears to be more reduced than is the distribution of deprived X-cell afferents.

Geniculocortical pathways from deprived laminae to layers other than layer IV (see sect. II) have not been assessed anatomically, primarily because these inputs are not adequately revealed by transneuronal autoradiographic methods in either normal or monocularly deprived cats (299, 300).

b) Physiological studies of connectivity. Neurophysiological experiments indicate a good correspondence between the location of geniculocortical in-

puts for each eye and the location of layer IV striate cortex cells that respond to each eye (300). Thus layer IV cells driven by the deprived eye generally are located within the autoradiographically identified, ocular-dominance bands for that eye, and likewise for cells driven by the nondeprived eye. Binocular cells and intermingling of monocular cells for each eye occur primarily at the borders of the ocular-dominance bands. Altogether about 30% of the cells sampled within layer IV give some response to the deprived eye, and about 19% respond exclusively to the deprived eye. By comparison, in normal cats studied in the same experiment, about 80% of the cells sampled within layer IV give some response to either eye and about 20% respond exclusively to one eye. Thus even in layer IV, where most geniculocortical afferents terminate, there is a substantial loss in the ability of the deprived eye to drive striate cortex cells. In addition many of the responsive layer IV cells have abnormal receptive fields for the deprived eye. In other cortical layers, cells driven by the deprived eye are rarely encountered.

Recent evoked-potential studies have provided further information about deprived geniculate afferents to cortical area 17. Jones and Berkley (172) recorded surface evoked potentials from monocularly deprived cats while separately stimulating each eye with a diffuse field that varied in temporal frequency (flicker rate). They found that, compared with cortical evoked potentials from the nondeprived eye, those from the deprived eye are of larger amplitude for low temporal frequencies and of smaller amplitude for high temporal frequencies. Jones (171) went on to determine the intensity modulation threshold of evoked potentials to stimuli that varied in temporal frequency. He found that cortical evoked potentials for the deprived eye have a normal intensity modulation threshold for stimuli of low temporal frequency. However, at high temporal frequencies the stimulus intensity needed to evoke a response increased markedly. Moreover at the highest temporal frequencies that can evoke a response from the nondeprived eye, no evoked potential could be elicited from the deprived eye in visual cortex.

Analogous experiments have been carried out by Snyder and Shapley (329) and Bonds et al. (26) using contrast-modulated grating stimuli that varied in spatial frequency. These investigators found that cortical potentials evoked from the deprived eye are abnormal in waveform and reduced in amplitude. However, the degree of reduction in evoked-potential amplitude depends on the spatial frequency of the grating stimulus. At lower spatial frequencies the amplitude for the deprived eye is much smaller than that for the nondeprived eye, and at higher spatial frequencies the amplitude difference between eyes is slight. Consequently plots of evoked-potential amplitude versus spatial frequency for the deprived eye are attenuated at the low-spatial-frequency end compared with normal cats or the nondeprived eye of monocularly deprived cats.

These abnormalities evoked by low spatial and high temporal frequencies are consistent with a reduction of Y-cell inputs to visual cortex, since Y-cells normally respond better to these stimuli than do X-cells. Current-

source density analysis of striate cortex potentials evoked by electrical stimulation of the deprived and nondeprived optic nerves provides further evidence of differential effects of monocular deprivation on the X- and Y-cell inputs to striate cortex (241). Such analysis indicates that the layer IV geniculocortical excitatory activity evoked from the deprived optic nerve is smaller in amplitude than that evoked from the nondeprived optic nerve. In addition the monosynaptic excitatory activity from the rapidly conducting (Y-cell) inputs is reduced much more than that from the slowly conducting (X-cell) inputs. This is consistent with the observation noted earlier in this section that deprived ocular-dominance columns are more shrunken dorsally, where Y-cell axons terminate, than they are ventrally, where X-cell axons distribute.

The results described thus far present an apparent paradox: substantial inputs to cortical area 17 remain for the deprived eye in monocularly deprived cats, but few striate cortex cells respond to visual stimulation of the deprived eye, even in layer IV. The obvious question is: What is the fate of the remaining deprived eye inputs? Recent neurophysiological experiments suggest that the remaining geniculostriate inputs for the deprived eye are functional, but that they are subthreshold for producing postsynaptic action potentials in response to visual stimulation. Three different types of experiments lead to this conclusion.

First, Kratz et al. (199) showed that if the nondeprived eye is enucleated in monocularly deprived cats, the percentage of striate cortex cells responding to visual stimulation of the deprived eye increases from 5% to over 30%. This increased response to the deprived eye was observed consistently in every animal studied after removal of the nondeprived eye. Furthermore the response to the deprived eye appears within hours of the enucleation and remains unchanged for periods of over 1 yr (199). The responsive cells are present in all layers of cortical area 17, but they occur in clusters that may be related to the ocular-dominance columns for the deprived eye. Most of the cells have very abnormal receptive-field properties and lack both direction and orientation selectivity. Therefore residual inputs from the deprived eye appear to form abnormal excitatory synaptic connections in striate cortex. These basic observations have since been repeated and extended by several investigators (116, 141, 328, 339, 388; however, see 21, 120). In addition recent experiments with reversible blockage of the nondeprived eye have shown that the appearance of a response to the deprived eye occurs within minutes of such blockage and that the response can be produced reversibly in the same cell (55).

The second type of experiment demonstrating residual cortical function related to the deprived eye has employed pharmacological manipulations. Duffy et al. (69) found that intravenous injection of bicuculline (an antagonist of the putative inhibitory neurotransmitter γ-aminobutyric acid) in monocularly deprived cats rapidly restores the ability of the deprived eye to drive striate cortex cells. Over 50% of the cells studied become responsive

to visual stimulation of the deprived eye after the injection, and the effect can be observed reversibly. More recently other studies have extended this observation by the use of iontophoretic application of bicuculline directly into the striate cortex (36, 320). These studies indicate that 29–42% of the cells become responsive to the deprived eye after bicuculline treatment. Control experiments suggest that the effect is due to release from tonic inhibition rather than to nonspecific increases in cortical excitability.

Third, experiments with electrical stimulation of the optic nerves also have provided evidence for a subthreshold geniculostriate input from the deprived eye in monocularly deprived cats (322, 379). These studies found that very few cells in the binocular segment of striate cortex give a short-latency discharge to electrical stimulation of the deprived optic nerve. This observation is consistent with the failure of these cells to respond to visual stimulation of the deprived eye. However, if continuous visual stimulation is applied to the nondeprived eye (i.e., visual conditioning) to lower the discharge threshold of the postsynaptic cortical cells, a large proportion of striate cortex cells respond to electrical stimulation of the deprived optic nerve (379). The latency of these responses suggests that they are mediated by X-cell lateral geniculate inputs for the deprived eye. In addition a normal proportion of cells in cortical area 17 respond to electrical stimulation of the deprived optic nerve with long-latency excitation (30–190 ms), even without visual conditioning of the nondeprived eye (322). Interestingly, intracellular recordings indicate that the same cells that receive these functional inputs from the deprived eye also receive short-latency excitation and long-latency (polysynaptic) inhibition from the nondeprived eye (322, 379).

Taken together these results make it clear that many (perhaps most) striate cortex cells do receive functional synaptic inputs from deprived laminae of the lateral geniculate nucleus, at least from X-cells. It has also been suggested that inputs from the deprived eye cannot drive striate cortex cells under standard recording conditions because they are inhibited by inputs from the nondeprived eye. Enucleation or application of bicuculline is thought to release the inhibition (36, 69, 199). This possibility is considered in more detail in section VII.

3. Intracortical connectivity

Little is known about excitatory intracortical connections related to the deprived eye. The failure of nearly all cells outside layer IV to respond to the deprived eye under standard recording conditions could be a result of abnormal intracortical excitation from those layer IV cells that are responsive to the deprived eye. However, many cells in these other layers also receive monosynaptic geniculocortical inputs in normal cats (see sect. II; 32). Therefore the failure of these neurons to respond after monocular deprivation could be a result of abnormalities in the geniculocortical connections.

Indeed, based on current-source density analysis, Mitzdorf and Singer (241) have recently argued that no deficits for the deprived eye exist in terms of excitatory intracortical circuitry, at least for the current sources and sinks they could identify. Note, however, that current-source density analysis does not reflect postsynaptic inhibitory activity (240).

Nearly all striate cortex neurons in normal cats produce inhibitory as well as excitatory responses to stimulation of the geniculostriate pathways, and this inhibition is thought to be produced by intracortical interneurons (54, 326, 376, 378). The latency of the inhibitory response (inhibitory postsynaptic potential or discharge suppression) suggests that it is mediated predominantly or entirely by the geniculocortical Y-cell pathway (326, 378). Several studies have investigated whether the inhibitory responsiveness of area 17 neurons is affected by monocular deprivation. Unfortunately the evidence is conflicting. Based on evoked-potential analysis and on extracellular and intracellular single-unit recordings, Singer (322) concluded that electrical stimulation of the deprived optic nerve produces fairly normal inhibition in area 17. Conversely, Tsumoto and Suda (379) found much less evidence of inhibition evoked in area 17 by stimulation of the deprived optic nerve compared with results of nondeprived nerve stimulation. In agreement with these latter results, Wilson and Sherman (400) found that none of the 16 cells tested had an inhibitory receptive field for the deprived eye, whereas nearly all monocularly excited cells in normal striate cortex have an inhibitory field for the nondominant eye (e.g., 125).

The reasons for these differences in results are not clear. One possibility is that Singer's (322) cats were reared in the dark for 4 wk prior to monocular lid suture and placement in a lighted environment for 10 wk (they were studied at 3 mo of age). Tsumoto and Suda (379) and Wilson and Sherman (400) studied cats with lids sutured at 1–3 wk of age, no initial dark rearing, and maintained in this fashion until 4–24 mo of age, when electrophysiological studies of striate cortex were performed. Thus it is possible that initial dark rearing allows some normal development of intracortical inhibitory circuits that are resistent to later monocular deprivation (see sect. V on effects of dark rearing) or that prolonged deprivation further reduces the intracortical inhibition.

If one accepts that monocular deprivation produces a reduction in intracortical inhibition (379, 400), this provides further evidence for a functional loss of Y-cell pathways, because these pathways mediate such inhibition in normal cats (326, 378). Indeed the loss of intracortical inhibition may simply reflect abnormal Y-cell afferents and not changes in intracortical circuitry.

D. Cortical Area 18

Area 18 is of particular interest for understanding the effects of monocular deprivation on the visual system because it receives direct inputs

through the lateral geniculate nucleus from the W- and Y-cell pathways but not from the X-cell pathways (91, 118, 362, 375, 377). Unfortunately there have been relatively few studies of the effects of monocular deprivation on area 18.

Anatomical studies indicate that projections from deprived laminae of the lateral geniculate nucleus to area 18 persist after monocular deprivation, just as they do in area 17 (85, 224, 300). Although quantitative estimates are not available, the pattern of labeling in area 18 with transneuronal orthograde tracers suggests that the extent of the inputs from the deprived eye is not greatly reduced (299, 300). These extensive inputs may represent projections from the W-cell pathway in addition to what remains of the Y-cell pathway.

In the only published study on recordings from single neurons in area 18 of monocularly deprived cats, Singer (323) recorded in the binocular segment of area 18 and assessed eye dominance principally on the basis of responsiveness to electrical stimulation of the deprived and nondeprived optic nerves. Recordings from two deprived cats in which both visual and electrical stimulation were used indicate that the two methods for assessing ocular dominance are in agreement (323). The results suggest a marked difference in the effects of monocular deprivation in the two hemispheres. In area 18 ipsilateral to the deprived eye, 6 of the 54 cells that gave any response to electrical stimulation responded to stimulation of the deprived optic nerve, whereas 35 of 58 cells in the contralateral area 18 responded to electrical stimulation of the deprived optic nerve. In marked contrast to these results from single-cell recordings, however, current-source density analysis of field potentials evoked in area 18 by electrical stimulation of the optic nerves reveals a massive effect of monocular deprivation that is similar in the two hemispheres (241). The synaptic activity evoked by the Y-cell pathway from the deprived optic nerve is severely reduced (compared with that from the nondeprived optic nerve) in both hemispheres.

The reasons for the marked hemispheric difference seen in single-cell recordings, but not in current-source density recordings, are unclear. Anatomical studies with both retrograde (85, 224) and anterograde (299, 300) methods do not show differences in the extent of inputs from the deprived eye to the two hemispheres. However, the specific contribution of the W-cell projections to area 18 in monocularly deprived cats has not been investigated. One possible basis for the hemispheric differences seen in single-cell recordings is that the W-cell projections to area 18 primarily represent the contralateral eye, and these are unaffected by monocular deprivation (e.g., 133). They could then underlie the greater response to the deprived eye in the contralateral hemisphere compared with the ipsilateral hemisphere (323). Since the current-source density analysis was concerned only with the rapidly conducting (presumably Y-cell) pathways, a hemispheric difference attributable to the slowly conducting W-cell pathways would have been overlooked. Another possibility is that the hemispheric difference seen in

single-cell recordings is fortuitous, since they are based on recordings from a small sample of cells in a small number of cats.

As in area 17, recent current-source density experiments suggest that the excitatory intracortical activity in cortical area 18 is largely unaffected by monocular deprivation and that the abnormalities after monocular deprivation are due to abnormal thalamocortical inputs (241). The qualifications to this conclusion mentioned in section IV*C3* for cortical area 17 apply here as well.

E. Superior Colliculus

1. General physiological effects

Several studies have investigated the effects of monocular deprivation on the responses of neurons in the upper layers of the superior colliculus. In normal cats each eye is able to drive about 90% of these collicular cells in the binocular segment, although there is a slight dominance by the contralateral eye (12, 139, 285, 354). After monocular deprivation, the ability of the deprived eye to drive the collicular cells is reduced, but this reduction is not the same for both hemispheres (16, 144, 355, 395). In the hemisphere ipsilateral to the deprived eye, roughly 5–20% of the superior colliculus cells can be driven by the deprived eye, whereas in the contralateral hemisphere, roughly 25–60% can be driven by the deprived eye (16, 144, 395). The results for the contralateral hemisphere seem to vary from cat to cat. In most cats only about a third or less of the cells sampled in this hemisphere respond to the deprived eye. However, in some cats nearly all the sampled cells are driven by the contralateral deprived eye and many cells are driven exclusively by it (16, 144). There are two possible explanations. One is that in all monocularly deprived cats patches of cells in the superior colliculus are dominated by the contralateral deprived eye, and these patches were sampled in some cats and not in others. The other possibility is that there are overall differences in the effects of monocular deprivation among cats; that is, in some cats the contralateral deprived eye dominates most or all of the superior colliculus cells but in other cats it does not. These two explanations have very different implications for understanding the effects of monocular deprivation, and it is important to determine which is correct. Unfortunately the data are currently insufficient to do so.

Cells driven by the deprived eye in the binocular segment have abnormal receptive-field properties. Most of the cells lack direction selectivity and most respond better to stationary flashing stimuli than do cells in normal cats (16, 144, 395). Nonetheless the velocity sensitivity of cells driven by the deprived eye appears normal (144). Except for cats in which the deprived eye dominates the contralateral colliculus, the nondeprived eye is able to drive

nearly all superior colliculus cells in the binocular segment, and the visual receptive fields through the nondeprived eye are normal (16, 144, 395).

In contrast to the effects seen in the binocular segment, the deprived monocular segment of the superior colliculus appears normal (144). The deprived eye is able to drive the normal proportion of cells, and the incidence of direction selectivity among these cells is normal. These results indicate that binocular interactions are important in the effects of monocular deprivation in the superior colliculus. However, this analysis is based on a rather small sample of cats and neurons.

2. Role of retinotectal and corticotectal afferents

In monocularly deprived cats, two separate types of evidence indicate that the direct retinotectal connections for the contralateral deprived eye have actually developed normally and that all the effects of monocular deprivation seen in the superior colliculus are due to abnormal corticotectal inputs. First, electrical stimulation experiments indicate that the W-cell and Y-cell direct retinotectal pathways are normal for the contralateral deprived eye but that the indirect Y-cell corticotectal pathway is nonfunctional (144). It is not known if the corticotectal pathway for the deprived eye has actually been lost or if it is simply unable to influence superior colliculus cells because the cortical cells themselves do not respond to the deprived eye (see also sect. V*E2*). The indirect Y-cell corticotectal pathway for the ipsilateral experienced eye still is present, however, and may even be increased compared with normal cats (144).

The second type of evidence that the direct retinotectal connections for the contralateral deprived eye are normal comes from experiments with cortical lesions. If visual cortex (areas 17, 18, and 19) is removed in monocularly deprived cats, the receptive-field properties are the same as in normally reared cats after visual cortex lesions. That is, collicular neurons become dominated by the contralateral eye (whether deprived or nondeprived), their receptive fields lack direction selectivity, and the neurons respond better than normal to stationary flashing stimuli (16, 395). The increased response to the contralateral deprived eye occurs immediately after removal of the visual cortex (16). Therefore this phenomenon is unlikely to be due to a growth or sprouting of new connections from the deprived eye. Instead the corticotectal inputs for the ipsilateral, nondeprived eye apparently have a suppressive effect on the retinotectal inputs (including those from the contralateral deprived eye), and removal of the visual cortex produces a release from suppression (16). This phenomenon may also occur in normal cats; that is, the intact corticotectal pathway may normally suppress the retinotectal input.

These results suggest that, in the superior colliculus, the competition between the inputs for the two eyes also is a competition between inputs

from two different structures: visual cortex (ipsilateral nondeprived eye) and retina (contralateral deprived eye). The data also suggest that the patches (or animals) in which most superior colliculus cells are dominated by the contralateral deprived eye represent regions (or animals) in which the retinotectal inputs have won the binocular competition over the corticotectal inputs (16). Finally, these results explain why the superior colliculus cells that do respond to the contralateral deprived eye lack direction selectivity and respond better than normal to stationary flashing stimuli. These are the properties of normal retinotectal inputs in the absence of corticotectal inputs for that eye.

Figure 3*B* summarizes results concerning the pathways underlying the effects of monocular deprivation in the superior colliculus contralateral to the deprived eye. A comparable analysis of the nature of the input pathways ipsilateral to the deprived eye has not been done. However, the results in this hemisphere can be understood in similar terms. Because the superior colliculus neurons continue to respond to the contralateral nondeprived eye with normal receptive-field properties, the direct retinotectal and indirect corticotectal pathways for this eye appear to develop normally. On the other hand, since the response of superior colliculus cells to the ipsilateral eye depends primarily on corticotectal inputs, the indirect corticotectal pathway for the ipsilateral deprived eye appears to be nonfunctional (or lost).

F. Lateral Suprasylvian Cortex

The only cortical area outside of areas 17 and 18 studied in visually deprived animals is the lateral suprasylvian visual area [more specifically, the PMLS area described by Palmer et al. (271)]. This region is of particular interest because it provides an opportunity to study the effects of monocular deprivation on a brain region that receives inputs from the geniculostriate-corticocortical pathway, the tectothalamocortical pathway, and a retinogeniculocortical pathway (see sect. II*E2a* and Fig. 4). In addition the retinogeniculate pathway probably consists primarily (or exclusively) of W- and Y-cell projections.

1. General physiological effects

In normal cats most cells in the binocular segment of the lateral suprasylvian cortex are binocularly driven, although there is an overall dominance by the contralateral eye (155, 327, 333). Spear and Tong (341) found that, after monocular deprivation, only about 10% of the binocular segment cells respond to the deprived eye. Furthermore the receptive fields of neurons driven by the deprived eye are abnormal. They generally lack direction selectivity, have abnormally large receptive-field-activating regions, and lack internal or surround receptive-field inhibition.

Monocular deprivation also produces abnormalities in the monocular segment of lateral suprasylvian cortex (341). There is a decrease in the percentage of responsive cells (54.5%) compared with normal cats (85.3%) and with the nondeprived monocular segment of monocularly deprived cats (77.6%). Also the receptive-field properties of cells in the deprived monocular segment are very abnormal. There is a loss of direction selectivity, an increase in receptive-field size, and a loss of internal or surround receptive-field inhibition. Nevertheless the monocular segment is much less severely affected by monocular deprivation than is the binocular segment, since the proportion of cells driven by the deprived eye is roughly 5 times greater in the deprived monocular segment than in the binocular segment.

These results indicate that abnormal binocular interactions play an important role in the effects of monocular deprivation on neurons in the binocular segment of the lateral suprasylvian cortex. In addition the presence of abnormalities in the deprived monocular segment suggests that mechanisms other than binocular competition also affect the inputs from the deprived eye to this area of the cortex.

2. Role of thalamic and visual cortical afferents

Tong and Spear (373) investigated whether the effects of monocular deprivation on lateral suprasylvian cortex neurons are caused by abnormal inputs from visual cortex (areas 17, 18, and 19), as is the case in the superior colliculus, or whether they are caused by functional changes in the lateral suprasylvian cortex and its thalamic inputs that are independent of visual cortex. To answer this question, the response properties of lateral suprasylvian cortex neurons were studied in monocularly deprived cats that had the inputs from the visual cortex removed as adults.

Ipsilateral to the deprived eye, a lesion in the visual cortex has no effect on lateral suprasylvian cortex ocular dominance: cells are driven by the contralateral nondeprived eye through the remaining thalamic inputs, just as in normal cats (see sect. II*E2b*). The receptive-field properties formed by these thalamic inputs also are the same as in normal cats. The situation is more complex in the lateral suprasylvian cortex contralateral to the deprived eye. The ocular-dominance distribution becomes bimodal in this hemisphere after removal of the visual cortex. Approximately equal numbers of cells are driven by the contralateral deprived eye and by the ipsilateral nondeprived eye. This represents a marked increase in the ability of the contralateral deprived eye to drive neurons in the lateral suprasylvian cortex compared with monocularly deprived cats with intact visual cortex. Therefore many inputs for the contralateral deprived eye from thalamus to the lateral suprasylvian cortex are present in these animals; however, they appear to be suppressed by the visual cortex inputs and can be demonstrated only after

removal of the visual cortex. Nonetheless fewer cells in lateral suprasylvian cortex can be driven by the contralateral deprived eye via the thalamic inputs (after removal of visual cortex) than can be driven by the contralateral eye in normally reared cats lacking the visual cortex. Therefore the remaining (suppressed) thalamocortical inputs to the lateral suprasylvian area for the contralateral deprived eye are reduced in number and/or effectiveness.

The ability of the ipsilateral, nondeprived eye to drive many lateral suprasylvian cortex cells via the thalamic inputs (after removal of visual cortex) in monocularly deprived cats represents a marked increase compared with normally reared cats. It is not known if this is due to an abnormally large terminal spread of these thalamocortical inputs for the ipsilateral eye or if it is due to inputs from neurons that normally do not project to this area. Interestingly the receptive-field properties formed by these inputs are similar to those found in normally reared cats lacking visual cortex, since they generally lack direction selectivity.

Figure 5*B* presents a schematic representation of the changes in the thalamic and visual cortex inputs that underlie the effects of monocular deprivation in the lateral suprasylvian cortex. Contralateral to the deprived eye, monocular deprivation produces a number of abnormalities in the thalamic inputs to the lateral suprasylvian cortex: *1*) the thalamic inputs for the deprived eye are reduced, *2*) nevertheless many inputs for the deprived eye remain and apparently are suppressed by visual cortex inputs, and *3*) thalamic inputs for the nondeprived eye are increased. In the hemisphere ipsilateral to the deprived eye, the thalamic inputs to the lateral suprasylvian cortex continue to provide information for the contralateral nondeprived eye, just as in normal cats. Finally, in both hemispheres the visual cortex inputs for the nondeprived eye function normally, but those for the deprived eye are nonfunctional. It is not known if the visual cortex afferents for the deprived eye actually are lost or if they fail to influence the lateral suprasylvian cortex simply because they do not respond to the deprived eye.

V. BINOCULARLY DEPRIVED CATS

In these experiments cats are raised from birth until adulthood with both eyes deprived of normal visual input. The two preparations most commonly used are considered here: *1*) cats raised with binocular lid suture but otherwise housed in a normally lighted colony and *2*) cats raised in total darkness. Binocular lid suture and dark rearing obviously differ in important ways, and these must be considered when evaluating the effects of each method. Dark rearing eliminates all photic stimulation, but binocular lid suture does not. Rather, lid suture severely reduces (or eliminates) spatial and temporal patterns at the retina and reduces the intensity of retinal illumination for a given light source. Direct measurements of lid transmis-

sion indicate that, at 4–5 wk of age, the eyelids reduce retinal illumination by about 2 log units. This increases to an attenuation of 3–4 log units by 12–14 wk of age and through adulthood (52, 225, 396). The attenuation by 2 log units is potentially overcome by enlarged pupils, so that the actual photic deprivation of these cats may be minimal (225).

Recent experiments indicate that diffuse light stimulation through the closed eyelids can influence the discharges of visual system neurons. Recordings in striate cortex of 4- to 5-wk-old binocularly sutured kittens show that many cells respond to changes in overall illumination through the closed eyelids (343). In fact changes in illumination caused by the movement of large contours in the visual field excite many area 17 neurons. Moreover the stimulus intensities that produce a response are within the range of intensities present in the typical rearing colony. Other experiments have shown that adult cats reared with binocular lid suture can learn brightness discriminations through the closed eyelids and that the brightness-discrimination thresholds are reduced by only 1–3 log units (depending on light-adaptation levels) as a result of the closed eyelids (225).

Since effective light stimulation is present through the closed eyelids, the nature of the visual deprivation for the visual system clearly is very different from that in dark rearing. The effects of binocular lid suture and dark rearing on the visual pathways thus may be very different. Unfortunately very few direct comparisons between the two rearing conditions are available from the same laboratory. In the discussion that follows we distinguish between the two methods of binocular deprivation and point out any likely differences in their effects.

A. Retina

Only one rather limited study has been published concerning the status of retinal ganglion cells in these cats, and this was further limited to binocular lid suture (310). Not surprisingly these results are essentially identical to those reported for the sutured eye of monocularly deprived cats. That is, the retinal ganglion cells have normal soma sizes, and their response properties seem grossly normal with a normal population of W-, X-, and Y-cells. However, Sherman and Stone (310) did not perform detailed tests of spatiotemporal properties for these cells, and subtle abnormalities cannot be ruled out.

B. Lateral Geniculate Nucleus

Data available from the lateral geniculate nucleus of binocularly deprived cats are also rather limited. These data are further restricted to laminae A and A1.

1. Binocular suture

a) Soma sizes. Wiesel and Hubel (398) reported that geniculate somata are as abnormally small after binocular suture as they are in deprived laminae after monocular suture (i.e., only about ⅔ normal size). More recently, however, Guillery (107) and Hickey et al. (135) have found much smaller effects on the size distribution of geniculate cells after binocular suture (Fig. 7). These latter authors suggest that such suture retards geniculate soma growth by roughly 5–10%. The cause of this discrepancy is not completely clear, but normal variation in soma sizes among brains (due to genuine biological variability, vagaries in tissue processing, etc.) makes such inter-animal comparisons difficult. Another potential cause of the discrepancy is the possibility that Wiesel and Hubel (398) compared material from binocularly sutured cats with that from nondeprived laminae of monocularly deprived cats (398, p. 1036, lines 21–22). The hypertrophy of these latter cells (see above; 135) could create the false impression of abnormally small cells in the binocularly deprived tissue. Guillery (107) and Hickey et al. (135) explicitly stated that they used material from normal cats as a control.

Hickey et al. (135) also found no difference in the pattern of soma sizes between binocular and monocular segments. That is, the small abnormality in the cell size distribution that does develop occurs equally in the two segments. Of particular interest is the comparison between the deprived monocular segments (of lamina A) after monocular and binocular suture (135). The somata tend to be smaller after binocular suture, although the differences are not statistically significant. This point is considered again below.

b) X- and Y-cells. Sherman et al. (308) reported a functional abnormality for binocularly sutured cats (see Fig. 8). As with monocular suture, fewer Y-cells could be found electrophysiologically in geniculate laminae of the binocularly sutured cats. Again, geniculate X-cells after binocular suture were found in roughly the normal rate per millimeter electrode traverse and with fairly normal response properties, although neither contrast sensitivity nor spatial or temporal resolution has yet been measured for these cells.

An interesting and somewhat puzzling comparison can be made between the Y-cell deficit in monocularly and binocularly sutured cats (see Fig. 8). In the binocular segment, the deficit is more severe for monocular than for binocular suture, as expected from a mechanism of binocular competition (see sect. III*B2*). In contrast the deprived monocular segment is more severely affected after binocular suture than after monocular suture. This pattern matches the trend in soma growth described by Hickey et al. (135). The different effects in the monocular segments for these two rearing conditions are surprising, because the deprivation is the same in these segments. This suggests that different mechanisms operate during monocular and binocular suture (cf. 303, 306), a possibility considered more fully in section VII.

2. Dark rearing

Few published studies have concentrated on the lateral geniculate nucleus in dark-reared cats.

First, Kalil (176) reported that the geniculate cell size distribution in dark-reared cats is not significantly different from that in normal cats.

Second, Kalil and Worden (180) reported that roughly twice the normal population of cells with cytoplasmic laminated bodies could be found in the A laminae of these cats. If these cells with laminar bodies represent X-cells, as LeVay and Ferster (211) have suggested (sect. II*C2*), then many Y-cells are physically absent in dark-reared cats. Kalil and Worden (180) further suggested the possibility that neurons that normally would develop as Y-cells become X-cells during dark rearing. Even if cytoplasmic laminated bodies mark X-cells in normal cats, however, it is not at all clear that they continue to do so in visually deprived cats.

Third, Kratz et al. (197) reported that very few geniculate Y-cells could be found in either the binocular or monocular segments of these cats (see Fig. 8). In fact the recorded geniculate Y-cell percentage is considerably lower after dark rearing than after binocular lid suture and is as low or lower than that seen in the deprived binocular segment after monocular suture. A normal geniculate soma size distribution was observed in these same cats (197). In addition, as with binocular suture, the abnormalities after dark rearing are equivalent in the binocular and monocular segments (at least in terms of geniculate Y-cell development).

Finally, two recent reports (195, 256) state that dark rearing does not interfere with the development of spatial resolution in geniculate X-cells.

C. Cortical Area 17

1. General physiological effects

a) Binocular segment. Both binocular lid suture and dark rearing result in a striate cortex less responsive than normal to visual stimulation. In the binocular segment, the percentage of cells encountered that give any response at all to light is reduced. Estimates of the percentage of responsive cells vary from about 33% (325) to about 80% (23, 29, 79, 392). These estimates probably vary because of differences among studies in the age of the animals, in criteria for judging a cell responsive, in cortical layers sampled, and even in anesthesia. For example, Singer and Tretter (325) regarded as unresponsive any cell with too sluggish or variable a response to plot reliably. Other investigators probably regarded these as responsive, if abnormal (see discussion in 392). If these cells are regarded as responsive, this explains the low value of responsive neurons reported by Singer and Tretter (325) and suggests that the actual value is closer to 80%. Even with this higher es-

timate, both dark-reared and binocularly sutured cats still contain abnormally few responsive cells. In addition cells that do respond to light in these animals often have lower peak response rates and greater variability than normal (218, 392).

The receptive-field properties of the responsive cells also are very abnormal in both dark-reared and lid-sutured cats. There is general agreement that an abnormally large proportion of responsive cells in the binocular segment have nonspecific receptive fields. That is, they respond to stimuli of any orientation and moving in any direction. Again estimates of the proportion of responsive cells with nonspecific receptive fields vary substantially, from about 30% (24, 198, 273, 398) to about 90% (29, 57, 79, 167, 392). The remaining responsive cells maintain some specificity for response to direction of stimulus movement. However, there has been much disagreement concerning whether any of these cells are also orientation selective. This disagreement appears to stem largely from whether tests are used to distinguish between direction selectivity and orientation selectivity (e.g., 126, 127, 273). For example, if a cell is tested with only moving, elongated slits, selectivity of response may lead to the conclusion that the cell is orientation selective when in fact it is simply direction selective. Nevertheless it seems clear from studies that have carefully distinguished between direction and orientation selectivity that about 10–20% of the responsive cells maintain orientation selectivity in both dark-reared and lid-sutured cats (23, 29, 57, 79, 198, 218, 273, 392). Sherk and Stryker (302) reported a much higher percentage of orientation-selective cells in lid-sutured kittens; however, their animals were only 3–4 wk old at the time of recording, and possibly more prolonged deprivation would have resulted in a lower percentage of orientation-selective cells, as found by others. Finally, in lid-sutured cats, the receptive-field inhibitory side bands are weak or absent for an abnormally large proportion of cells, and, perhaps as a result, many cells have large receptive fields with borders more diffuse than normal (325, 392). In contrast, studies of dark-reared cats suggest that receptive-field size is normal in these animals (57, 218). It is not known if this represents a difference between rearing conditions or between laboratories, since there has never been a systematic comparison of the effects of the two rearing conditions on striate cortex.

The gross potentials evoked by contrast-modulated gratings are also abnormal in binocularly sutured cats (329). Although evoked-potential amplitude and latency vary with spatial frequency of the stimulus in an approximately normal fashion, the waveforms of these potentials are quite abnormal, and these abnormalities are greater for stimuli with lower spatial frequencies. Jones and Berkley (172) found no abnormalities in potentials evoked by temporally modulated stimuli, although only one binocularly sutured cat was studied.

In addition to their abnormal receptive-field properties, responsive cells in binocularly deprived cats have abnormal binocular interactions. This is indicated by two findings. First, cells in area 17 of binocularly deprived cats

display poor disparity tuning. In normal cats many of these cells are binocularly acivated, with extreme sensitivity to retinal disparity. That is, small misalignments between the stimuli on each retina can lead to inhibition of the cell's response (8, 19, 174, 276). In cats reared with binocular lid suture, however, binocularly driven cells are insensitive to changes in retinal disparity. They show either no change in binocular response or diffuse, weak inhibition over a wide range of disparities (276). Second, there are fewer binocularly driven cells than normal in the binocular segment of area 17 (see Fig. 2*C*). In every study of cats reared with binocular lid suture that has reported ocular-dominance results, the proportion of binocularly driven cells is lower than normal (23, 198, 392, 398). However, the percentage of binocularly driven cells reported to be present varies widely among studies. Some studies report that the ocular-dominance distribution is fairly flat in binocularly sutured cats (see Fig. 2*C*; 23, 398), whereas others find a distinctly bimodal ocular-dominance distribution (198, 392). A decrease in the percentage of binocularly driven cells also has been observed in dark-reared cats (57, 218), although some studies report normal ocular dominance among responsive cells after dark rearing (29, 79, 167). These differences in the degree to which binocularly driven cells are lost may be due partly to differences in the area of visual-field representation (i.e., eccentricity) that was studied in striate cortex [for discussion of this question, see Kratz and Spear (198)]. It may also be due to differences in the extent to which certain cell types or cortical layers were sampled.

Several studies have reported an interesting interaction between ocular dominance and receptive-field properties in binocularly deprived cats. Cells with nonspecific receptive fields tend to be binocularly driven, whereas orientation-selective cells tend to be monocularly driven (23, 198, 218, 392). This interaction has been found in both lid-sutured and dark-reared cats. In addition Leventhal and Hirsch (218) reported that the monocularly driven, orientation-selective neurons in dark-reared cats tend to prefer either horizontal or vertical, but not oblique, stimulus orientations.

b) Monocular segment. Effects of binocular deprivation on the monocular segment of area 17 have been studied only in lid-sutured cats. The results are essentially identical to those in the binocular segment (392). This is summarized in Figure 9. Fewer cells than normal respond to visual stimulation, and those that respond generally have nonspecific receptive fields. In addition the receptive fields have more diffuse borders than normal and generally lack side-band inhibition. Only about 18% of the responsive cells have normal orientation-selective receptive fields. Thus the monocular segment of striate cortex is severely affected by rearing with binocular lid suture.

Binocular suture appears to affect development of the monocular segment of striate cortex more severely than does monocular lid suture (see Fig. 9). The most striking difference is that nearly 50% of the responsive cells in the monocular segment have normal orientation-selective receptive

fields in monocularly deprived cats, whereas only about 18% have normal receptive fields in binocularly deprived cats.

2. *Geniculostriate afferent connectivity*

a) Morphology. There is no direct anatomical information available concerning the fate of geniculocortical projections to area 17 of binocularly deprived cats. For example, studies of the percentage of lateral geniculate cells that project to striate cortex or of the terminal distribution of geniculostriate afferent fibers (such as those studies conducted in monocularly deprived cats) have not been carried out in binocularly deprived animals. Although electron-microscopic studies of synaptic connectivity have been performed in area 17 of both dark-reared and lid-sutured cats (50, 87), these experiments cannot bear directly on the question of afferent connectivity. This is because geniculostriate terminals account for a relatively small proportion of the synapses in striate cortex [5–30% in layer IV (90, 213) and about 10% in layer VI (213)], and their contribution to the changes described in these studies cannot be assessed.

b) Electrophysiology. Electrophysiological experiments suggest that effects of binocular deprivation on afferent connectivity are relatively slight in striate cortex. Singer and Tretter (325) reported that electrical stimulation of the optic chiasm drives 39% fewer striate cortex cells in lid-sutured cats than in normal cats, but when the retinogeniculate contact is bypassed by stimulating the optic radiations directly, there is only a 20% loss of responsiveness in striate cortex. Thus much of the loss of visual responsiveness among striate cortex cells in lid-sutured cats appears due to transmission failure in the lateral geniculate nucleus. It is not known if this reduced response to stimulation of the optic radiations is caused by an additional transmission failure at the geniculostriate contact, an anatomical loss of geniculostriate synaptic connections, or other factors.

Comparison of the response latencies to stimulation of the optic chiasm and radiations suggests that the responsive striate cortex cells continue to receive inputs from both the X-cell and Y-cell pathways (325). In fact there is a relative increase in the proportion of cells responding via the Y-cell pathway, which suggests a relative loss of X-cell inputs. This conclusion should be viewed with caution, however, because the nature of the input pathways could be tested for only 36 striate cortex neurons (22% of the total sample) in this study (325).

Clearly much remains to be learned about geniculostriate connectivity in binocularly deprived cats. Nevertheless many area 17 cells in lid-sutured cats apparently continue to receive functional inputs from X-cells and remaining Y-cells in the lateral geniculate nucleus, and the overall loss of functional connections seems small compared with the loss of ability to respond to visual stimulation. The relative extent to which X-cell or Y-cell

geniculostriate connections are affected remains to be determined conclusively.

3. Intracortical connectivity

Electron-microscopic studies have been directed at the synaptic connectivity of striate cortex in both dark-reared and lid-sutured cats. Cragg (50) reported a number of morphological changes in the striate cortex of kittens reared with binocular lid suture to 45 days of age, at which time the cortex of normally reared kittens has an adult appearance. These changes are summarized in Figure 10. Although lid suture decreases neuron size by only 5.6%, it increases neuron density by 28.7%. This suggests that the neuropil has decreased in these animals. Direct counts of synaptic density reveal a decrease of only 10.1% overall. This decrease is largest (and statistically reliable) at depths corresponding to layers IV and V. The overall number of synapses per neuron is also decreased by 29.6%, although the *length of the synaptic profiles is unchanged by lid suture. In a related study,* LeVay (210) reported that ribosomes in spiny stellate cells of layer IV fail to aggregate in cats reared with binocular lid suture. He suggested that this effect may be related to deficits in protein synthesis and axonal transport in these neurons and that this could contribute to the decreased number of cortical synapses observed by Cragg (50). LeVay (210) found that other intracellular organelles are normal in the deprived cats and that other cell types in layer IV, as well as cells in other cortical layers, have normal ribosome aggregation.

The only morphological study of striate cortex connectivity in dark-reared cats concentrated on measures of synaptic vesicle density in layers III and IV (87). The experimental animals were 4–5 wk old at the time of study. Dark rearing reduces the density of synaptic vesicles in small synaptic terminals ($<0.4\ \mu m^2$ in cross-sectional area) of layer III and in both small and large synaptic terminals of layer IV. In each case the reduction in vesicle density is between 40 and 45%. Synaptic terminal size itself is not affected, however, in agreement with the results in lid-sutured kittens just described. These differences in synaptic vesicle density could be demonstrated between stimulated and unstimulated hemispheres of the same cat by use of a clever procedure for providing visual stimulation to only one hemifield. Presumably these changes in synaptic vesicle density reflect changes in synaptic function; however, it is not known if they are permanent changes or transient reflections of synaptic activity.

Taken together these morphological studies indicate that binocular deprivation does produce changes in synaptic connectivity of striate cortex. However, the more significant finding may be that much of the synaptic connectivity remains intact: the largest changes represent a 30% reduction

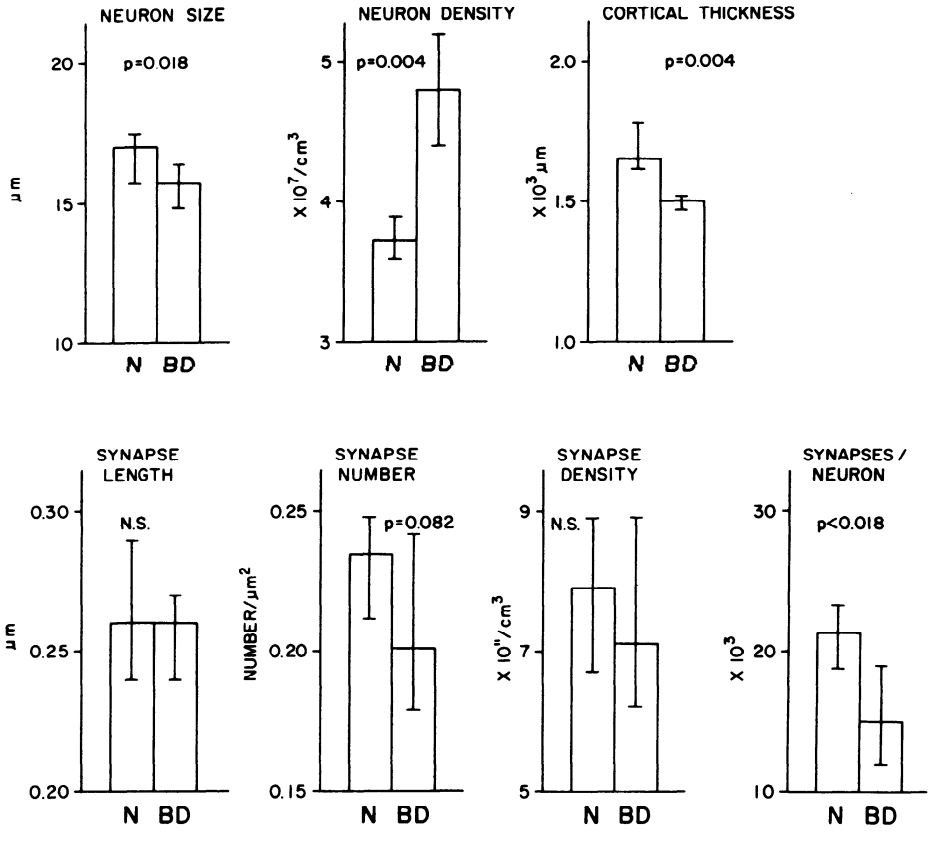

FIG. 10. Size and density of neurons and synaptic profiles in striate cortex of 6 normal (N) and 5 binocularly deprived (BD) kittens. Deprived kittens had binocular lid suture during 1st wk of life and were usually deprived until studied at 45 days of age. For each cat, samples of neurons and synapses were studied across all layers of cortex, and mean was determined for each measure in each cat. *Bars*, mean of means for individual cats; *brackets*, total range for all cats. For each measure, statistical comparisons were made between the 2 groups by a Mann-Whitney *U* test; all probability values are two-tailed. NS, no significant difference between the 2 groups ($P > 0.1$). [Data redrawn from Cragg (50, Table I).]

in the number of synapses per neuron and a 40–45% reduction in the density of vesicles per synapse. Neurophysiological studies suggest that much of the intracortical connectivity does in fact remain functional in lid-sutured cats (325). Polysynaptic responses to electrical stimulation of the optic radiations remain, and they are even increased compared with monosynaptic afferent responses. In addition, multiple discharge responses to optic radiation stimulation, responses that are due to intracortical polysynaptic connectivity (326), occur in the normal proportion of cells in striate cortex of lid-sutured cats (325).

D. Cortical Area 18

Singer and Tretter (325) have performed the only detailed receptive-field study of area 18 neurons in binocularly deprived cats. The deficits generally seem quite similar to those reported in the same study for area 17 of binocularly sutured cats. In area 18 the percentage of cells responding to light is reduced from 78% in normal cats to 44% in lid-sutured cats. In addition the percentage of responsive cells with direction-selective and orientation-selective receptive fields is markedly reduced. Many of the receptive fields are abnormally large, have diffuse boundaries, and lack side-band inhibition. The only response property that seems unaffected by the deprivation is the characteristic response of area 18 cells to high stimulus velocities. Similar effects are seen in all layers of area 18 (325). Unfortunately no information is available concerning the ocular-dominance distribution of area 18 cells in binocularly deprived cats.

Experiments with electrical stimulation of the afferent pathways indicate that many area 18 cells that fail to respond to light nevertheless continue to receive functional afferent connections from the lateral geniculate nucleus (325). Thus the proportion of cells that respond to light or electrical stimulation of the optic chiasm is 40–44% less than normal, whereas the proportion of cells that respond to electrical stimulation of the optic radiations is only 19% less than normal. Cells that continue to respond to electrical stimulation of the afferent pathways are driven by rapidly conducting (presumably Y-cell) afferents, just as in normal cats. Thus the failure of most area 18 cells to respond to light appears due to a conduction failure in the lateral geniculate nucleus, plus a conduction failure and/or loss of some geniculocortical inputs. Intracortical connectivity in area 18 also appears to be only slightly affected by binocular lid suture. In fact, polysynaptic excitatory responses to electrical stimulation of the afferents appear to be increased in these cats (325). Intracortical postsynaptic inhibition also is still present, though its magnitude seems somewhat less than normal (325). This slightly reduced magnitude of inhibition may be the cause of the increased polysynaptic excitation.

E. Superior Colliculus

1. General physiological effects

The effects of both dark rearing and binocular lid suture on responses of superior colliculus neurons appear to be very similar. Studies have concentrated on the upper three collicular layers that receive both retinal and visual cortex inputs.

After both binocular lid suture (145) and dark rearing (73), abnormally few superior colliculus neurons respond to light. In normal cats all superior

colliculus cells sampled respond to light, whereas 69–83% do so after binocular deprivation. In addition the percentage of responsive cells that are direction selective is dramatically reduced, from 60% or more in normal cats to about 15% in binocularly deprived cats (56, 73, 74, 145, 355). There is also a slight, but statistically significant, effect of binocular lid suture on preferred stimulus velocity in that more cells prefer slower stimuli in the deprived cats (145). Finally, both dark rearing and lid suture alter the ocular dominance of superior colliculus neurons. From about 50 to 75% of the cells are driven exclusively by the contralateral eye, and most of the binocular cells are dominated by the contralateral eye (74, 145, 355). Stated differently, binocular deprivation reduces the ability of collicular cells to respond to the ipsilateral eye. Most of these effects of binocular deprivation are similar to the effects of visual cortex removal in normally reared cats (see sect. II*E1b*), a point to which we return later.

Very little information is available concerning the effects of binocular deprivation on cells in the monocular segment of superior colliculus. In one study of lid-sutured cats, 10 monocular segment cells were recorded, and their receptive-field properties were found to be similar to those of binocular segment cells (145). Thus there is tentative evidence that binocular lid suture produces abnormalities in the monocular segment comparable to those in the binocular segment of superior colliculus. If so, then binocular suture creates more serious abnormalities in the monocular segment of the superior colliculus than does monocular suture. An analogous point was raised for the monocular segments of the lateral geniculate nucleus (sect. IV*B1*) and area 17 (sect. IV*C1b*).

2. Role of retinotectal and corticotectal inputs

Effects of binocular lid suture on the direct W-cell and Y-cell retinotectal inputs and the indirect Y-cell inputs through the geniculocorticotectal pathway have been examined by electrical stimulation of the afferent pathways (145). These experiments show that the direct W-cell retinotectal connections are normal in lid-sutured animals. However, the direct Y-cell retinotectal connections appear to be slightly reduced: 9% of superior colliculus cells sampled receive direct Y-cell inputs in normal cats, whereas only 2% do so in lid-sutured cats. Because the proportion of retinal Y-cells is normal in lid-sutured cats (310), the reduced response to direct Y-cell inputs must be due to a retinotectal transmission failure.

The indirect Y-cell corticotectal pathway seems completely nonfunctional after binocular lid suture: not a single colliculus cell appeared to receive an indirect Y-cell input via the lateral geniculate nucleus and visual cortex (145). Nevertheless electrical stimulation of visual cortex drives the normal proportion of superior colliculus cells in these animals (145), and Singer and Tretter (325) were able to stimulate many visual cortex neurons

antidromically from the superior colliculus in binocularly sutured cats. Therefore the loss of the indirect Y-cell pathway must be due to a functional loss in the inputs to the corticotectal efferents. Figure 3*C* summarizes the changes in connectivity that underlie the effects of binocular lid suture in the superior colliculus.

Considered in the light of the role of retinotectal and corticotectal afferents in normally reared cats, these results provide some insight into the causes of the changes in receptive field and ocular dominance among collicular cells in lid-sutured cats. The loss of direction selectivity and loss of responses to the ipsilateral eye in binocularly deprived cats are similar to the effects of removal of the visual cortex in normally reared cats (12–14, 242, 285, 347, 394). Thus these effects in deprived cats are probably due to the functional loss of the indirect Y-cell pathway through visual cortex. However, the alteration in velocity preference occurring among superior colliculus cells in lid-sutured cats is not mimicked by removal of the visual cortex in normally reared cats (13, 145, 242). Therefore this effect is probably due to the abnormal retinotectal connections from the direct Y-cell pathway.

F. Lateral Suprasylvian Cortex

1. General physiological effects

No studies of lateral suprasylvian cortex in dark-reared cats have yet been published. However, the effects of early binocular lid suture on this cortex are quite dramatic.

a) Binocular segment. In the binocular segment only 21% of the cells encountered respond to light in lid-sutured cats compared with 88% in normal cats (374). About 50% of the responsive cells have large receptive fields with ill-defined borders or respond only to whole-eye illumination. Cells with well-defined receptive fields tend to respond maximally to stationary flashing stimuli, and none of the responsive cells are direction selective; in normal cats 80% of responsive cells are direction selective. Internal or surround receptive-field inhibition, which serves to limit optimal stimulus size for about 40% of the cells in normal cats, is present for only 3% of the responsive cells in lid-sutured cats. Thus nearly all the responsive cells in the lateral suprasylvian cortex of lid-sutured cats respond best to the onset and offset of diffuse light flashes. This is precisely the type of stimulus delivered through the closed eyelids during development.

Eye dominance of neurons in lateral suprasylvian cortex is also altered by rearing with binocular lid suture. This is due to a disproportionate loss of response to the ipsilateral eye. As a result 48% of the responsive cells can be driven by the ipsilateral eye in lid-sutured cats compared with 70% of the cells in normal cats (374).

b) Monocular segment. The responsiveness and receptive-field properties of neurons in the monocular segment are similar to those in the binocular segment in these cats (374). Thus binocular lid suture produces comparable abnormalities in the monocular and binocular segments of the lateral suprasylvian cortex. Interestingly the abnormalities in the monocular segment of binocularly sutured cats are more severe than those in the monocular segment of monocularly sutured cats studied in the same laboratory (341, 374). For example, this segment has fewer responsive cells, including a lower proportion with well-defined receptive fields, after binocular suture than after monocular suture. Again the same type of difference was noted above for the superior colliculus, area 17, and the lateral geniculate nucleus.

2. Role of thalamic and visual cortical afferents

Visual cortex (areas 17 and 18) exerts a powerful influence over the receptive-field properties and ocular dominance of lateral suprasylvian cells in normally reared cats (334). Yet independent of visual cortex, thalamic inputs provide a variety of receptive-field properties to lateral suprasylvian cortex neurons. Tong et al. (374) assessed the separate contribution of the visual cortical and thalamic pathways to deficits in binocularly sutured cats by studying lateral suprasylvian cortex neurons after removal of the visual cortex when the cats were adults.

Cortical removal in binocularly sutured cats further reduces the proportion of lateral suprasylvian cortex cells in the binocular segment that respond to the ipsilateral eye (from 48 to 25%). However, unlike the situation in normal cats (see sect. II*E2b*), the visual cortex lesion does not alter the receptive-field properties or overall responsiveness of lateral suprasylvian cortex cells in lid-sutured cats. These results indicate that some ipsilateral eye inputs reach the lateral suprasylvian cortex from visual cortex in binocularly sutured cats. However, visual cortex inputs do not develop the normal influence on receptive-field properties of lateral suprasylvian cortex cells during binocular suture.

A comparison of the responses of lateral suprasylvian cortex cells after removal of the visual cortex in normally reared and lid-sutured cats also provides information about the status of the remaining thalamocortical inputs. After removal of the visual cortex, the lid-sutured cats have a much smaller percentage of responsive cells via the thalamic inputs than do normally reared cats. In addition fewer of the responsive cells have well-defined receptive fields and fewer have internal or surround receptive-field inhibition than in normal cats. Thus the influence of the thalamic pathways on lateral suprasylvian cortex cells is severely affected by binocular lid suture. The nature of the cortical and thalamic inputs to lateral suprasylvian cortex in binocularly lid-sutured cats is summarized in Figure 5*D*.

VI. DEVELOPMENT OF VISUAL PATHWAYS

Although studies of adult cats raised normally or with visual deprivation can provide many insights into mechanisms of visual development, a complete understanding of these processes requires a description of both the starting point and the dynamic sequence of developmental events. In other words, one must understand the status of the visual pathways in neonatal kittens as well as the changes in these pathways during normal development and visual deprivation. Studies of these vital areas of research have not yet produced a sufficiently complete description of developmental events. This shortcoming reflects insufficient data and a frustrating lack of agreement among a number of studies. So far, limited developmental data are available for the retina, the lateral geniculate nucleus, cortical area 17, and the superior colliculus. Ironically most confusion seems to center on the development of area 17, despite the fact that this has been the most intensively studied visual area.

Because many receptive-field properties of immature neurons seem abnormal and the optics of neonatal kittens are rather unclear, one must consider the possibility that optics, not functional pathways or their central connections, limit the response properties of immature pathways. Accordingly we consider development of physiological optics in kittens before describing development of the visual pathways.

A. Optical Development

A casual ophthalmological inspection of an eye of a kitten younger than about 3–4 wk reveals little about fundus detail because of a number of optical aberrations and impediments in the eye. The optics appear to clear during the ensuing few weeks, and the appearance of the normal adult fundus gradually develops.

Bonds and Freeman (25) described the postnatal development of the kitten's physiological optics in terms of optical modulation transfer functions. They found considerable postnatal improvement in the optics, by roughly a factor of 2 between the 1st and 5th wk after birth. A more gradual and slight improvement occurs thereafter. Nonetheless the optics in neonatal kittens are better than one might have imagined. Bonds and Freeman (25) point out that standard ophthalmoscopic examinations often are limited by the light intensity of the fundal image, and for such an examination the light must pass through the poor optics twice, whereas the light must pass through only once to excite retinal elements. Thus ophthalmoscopy of young kittens would often exaggerate the optical defects due to light scatter and attenuation. In fact a comparison between the data of Bonds and Freeman (25) and those from behavioral assessments (238) and receptive-field studies (164) of such young kittens (see also below) suggests that optics do not limit visual performance.

A number of features probably limit optical quality in the young kitten's eye, but the most serious seem to be deformations in the cornea and a vascular network covering the posterior and anterior surfaces of the lens (76, 77, 370). This network exists at birth and begins to dissolve during the 3rd wk after birth. Its gradual clearing during subsequent weeks coincides with the improvement in optical quality.

The other major feature of optical development in kittens is the physical growth of the eye, with most ocular dimensions roughly doubling in size from birth to adulthood (265, 370). Because the focal length of the eye increases after birth, the size of the image on the retina of a visual object likewise increases. This is significant for the development of certain receptive-field properties, such as receptive-field size and spatial acuity.

B. Retina

1. Anatomy

Donovan (62) offered a rather sketchy, but widely quoted, description of postnatal development of the kitten retina. She stated that this development occurs along a gradient such that cells closer to the area centralis mature earlier than more peripheral neurons. One might assume that this developmental gradient applies specifically to retinal ganglion cells, but little is mentioned of these cells. Retinal ganglion cells appear small at birth and "gradually assume a more mature appearance, until at about 2½ weeks of age they appear fully developed" (62, p. 251). In a combined light- and electron-microscopic analysis, Vogel (390) concluded that retinal ganglion cells are essentially mature by the end of the 2nd wk.

Tucker (380) recently challenged these conclusions. She argued that ganglion cells in the area centralis attain adult size later than those in more peripheral retina and that the adult cell size pattern still is not present at 8 wk.

Yet another view has been offered by Rusoff and Dubin (290) in a study of Golgi-impregnated ganglion cells in 3-wk-old kittens and adult cats. Their study was limited to β-cells (see sect. II*C1*; 28), since other cell types were rarely impregnated sufficiently. Within 5 mm of the area centralis on a retinal whole mount, Rusoff and Dubin (290) found little difference in the size of β-cell dendritic fields between the kittens and adults, but farther than 5 mm peripherally the kitten cells were smaller. Consequently dendritic growth apparently is nearly complete at this early age and develops more rapidly nearer the area centralis, at least for β-cells.

Moore et al. (245) studied the development of myelination of optic nerve and tract in normal and dark-reared cats. Only 3% of the axons have myelin at birth. This increases gradually to 23% by the end of the 2nd week, more rapidly to 80% by the end of the 4th wk, and utimately reaches 100%, as

in the adult, by the end of the 7th wk. Dark rearing has no effect on myelin development for these axons. Finally, Anker and Cragg (6, 7) showed that the retinogeniculate and retinotectal pathways are present prenatally.

2. Physiology

Physiological studies of neonatal kittens are notoriously difficult because of the fragility of the experimental preparation; consequently such studies are fairly rare. We focus here on single-cell, receptive-field studies.

Rusoff and Dubin (289) studied receptive-field properties of retinal ganglion cells in kittens 3–7 wk old. They used a transscleral electrode approach to record activity within the ganglion cell layer, thus sampling from somata. In 3-wk-old kittens, most cells have large, diffuse fields and poor responses, but after 4 wk of age, more and more cells exhibit well-defined receptive fields with brisk responses. Many of these cells in 4-wk-old kittens could be classified as W-, X-, or Y-cells. These adultlike cells are often found next to poorly responsive neurons, which seems to rule out optical artifacts for the presence of rather immature cells after 4 wk of age. The adultlike cells at 4 wk of age have two obvious abnormalities that may be related. *1*) Their center sizes are somewhat larger than normal and *2*) their surround responses are generally poor or absent. By 7 wk many of these cells have normal center sizes and adultlike center responses, but the surrounds remain weak and abnormally large. Rusoff and Dubin (289) felt that they could identify these as W-, X-, or Y-cells on the basis of center response alone. Interestingly they found that the decline for W-, X-, or Y-cells in field center size from 4 wk to adulthood could be explained entirely by the growth of the eye and increase in focal length. That is, although after 4 wk of age the mean center size expressed in degrees of visual angle decreased, this mean size expressed in millimeters on the retina remained constant. To the extent that the diameter of the dendritic field corresponds to that of the receptive field, this is consistent with the observation that kitten β-cells are nearly fully developed 3 wk after birth (288, 290).

In an analogous study of optic tract fibers, Hamasaki and Flynn (112) emphasized that, although many properties of ganglion cells are immature at 21–24 days of age, the basic center/surround organization is already present. This seems to contradict the conclusions of Rusoff and Dubin (289), although possibly only the most mature cells (with the largest and best-developed axons) can be sampled from the optic tract. A major point of agreement is the suggestion by Hamasaki and Flynn (112) that the receptive fields of cells decrease in size after 3 wk of age only if measured in degrees of visual angle; if measured in millimeters of retinal extent, they remain constant during development. These authors also noted that the mean temporal resolution of neurons in the 3-wk-old kitten is roughly half the adult value.

Hamasaki and Sutija (114) recently added a description of retinal X- and Y-cell development. They recorded from optic tract fibers in kittens 3–12 wk of age and found many Y-cells but few X-cells until 5–6 wk of age, at which time the ratios of X-cells to Y-cells approached adult values of 2:1. This might reflect a sampling bias among immature or abnormally small axons favoring Y-cell axons over X-cell axons, although Hamasaki and Sutija (114) provide other explanations. They also note several signs of immaturity in response properties of these cells until 12 wk of age, by which time the retinal ganglion cells appear fully mature in their responses.

All the above-mentioned studies were performed on normal kittens. To date there have been no published studies directed at the development of retinal ganglion cells in visually deprived animals. Such studies are important, because although available evidence suggests that these cells achieve normal development during deprivation, their developmental rate might be abnormal. Such a potential abnormality might well contribute to defects found more centrally.

C. Lateral Geniculate Nucleus

1. Anatomy

Kalil (177) and Hickey (133) gave similar detailed descriptions of the growth of geniculate somata in the A laminae of normal and monocularly sutured cats. Their results are in substantial agreement. Normally, rapid growth is observed during the first 4 wk, by which time the soma size distribution is practically normal, although slight growth may occur during the next 4 wk. The growth of nondeprived somata in monocularly sutured cats closely resembles that of somata in normal cats. In contrast, deprived somata grow somewhat more slowly than normal during the first 4 wk. After this a gradual and slight atrophy occurs. By 8 wk of age the adult monocularly deprived pattern of soma sizes is essentially present, although Kalil (177) described minor progressive changes until 16 wk of age. Interestingly, Kalil (177) reported no mediolateral gradient in the rate of soma growth in normal kittens that might correspond to evidence of an area centralis/periphery gradient for retinal ganglion cells (62, 240, 380).

Kalil (176) also studied the growth of geniculate somata during dark rearing. Compared with normal growth, deprived neurons grow at a slower rate during the first 2 mo and then atrophy somewhat during the 3rd mo. However, another period of growth occurs during the 4th mo, so that by 16 wk of age and thereafter the geniculate soma sizes of dark-reared and normal cats are similar.

Winfield et al. (404–406) performed ultrastructural studies of development in the kitten's lateral geniculate nucleus. They reported relatively little synaptic development during the first 3 wk after birth. The most rapid syn-

aptic development occurred during the 7th and 8th wk, after which the ultrastructural features of the nucleus seemed mature. Neither monocular nor binocular eyelid suture had any observable effect on the features of synaptic development studied by these authors.

2. *Physiology*

a) Normal development. The few studies of response properties of geniculate neurons in kittens have been directed at X- and Y-cells and suggest that the former mature before the latter. Norman et al. (262) reported that only about one-third of the cells could be identified as X or Y by 3 wk of age, and this proportion gradually increased to adult values over the ensuing 3 wk. After identifying a neuron as an X- or Y-cell, they measured its response latency to optic chiasm shock. Responses to visual and electrical stimuli were generally variable and unreliable, but many X-cells seemed to mature during the 3rd wk after birth, before any Y-cells with mature responses were seen.

Daniels et al. (59) amplified these observations with a more complete receptive-field description of these cells in kittens 1–6 wk old. Before the 3rd wk, neuronal responsiveness was poor and cells were hard to identify, although a few relatively mature X-cells were found. Many more X-cells with fairly mature receptive fields appeared during the 3rd–5th wk, but only after this period did reasonably normal Y-cells begin to emerge. For both cell types, surround responses seemed to develop later than center responses, and surrounds matured earlier in X-cells than they did in Y-cells. At the oldest ages studied (6 wk), many immature cells were still observed. Despite the robust early responsiveness of X-cells, Ikeda and Tremain (164) noted that not until about 12 wk of age do these cells develop adult spatial resolution. It is presently unclear how much this improved spatial resolution reflects the improvement in optics and increase in axial length of the eye (cf. 265).

Daniels et al. (59) made two further points. First, even at the youngest ages tested, some adultlike cells with small receptive fields and brisk responses were found among immature cells with large, diffuse fields and poor responses. Thus optics are unlikely to be responsi le for poor responsiveness in these immature cells. Second, several unit pairs, which included an optic tract afferent and presumed postsynaptic geniculate cell, were recorded simultaneously. In each case the optic tract responses were mature and the geniculate responses were immature. Daniels et al. (59) thus suggested that geniculate development is not limited by optic tract input. However, they described neither how many such pairs were studied nor at what age each was found.

Mangel (233), in a study of monocularly sutured kittens from 6 wk of age through adulthood, arrived at conclusions complementary to those of Daniels et al. (59). In nondeprived laminae, X-cells seem generally adultlike at the youngest age (6 wk), although a slight and gradual increase in spatial

resolution occurs after that, and normal adult values are attained by the 12th wk after birth (see also 164). However, many Y-cells at 6–12 wk of age have incomplete development of their nonlinear responses to visual stimuli. These nonlinear responses are unreliable for many individual Y-cells, often waxing and waning in contradistinction to the clear and stable linear responses from these same cells. Such properties are not seen for normal Y-cells of older animals. This may coincide with the later development of surround responses, because Hochstein and Shapley (138) showed that stimuli limited to the center of normal Y-cells often fail to evoke detectable responses from nonlinear components of the receptive field.

b) Development during monocular suture. In the only developmental study of geniculate neuronal response properties available in lid-sutured cats, Mangel (233) described several differences between X- and Y-cells. An effect of monocular suture on recorded Y-cell percentages was first detected between 8 and 12 wk of age. That is, from 8 wk onward the Y-cell percentage in nondeprived laminae gradually increases from roughly 20% to the adult value of 40%–50%. In deprived laminae the Y-cell percentage stays constant or drops slightly to approximately 15%. At 12 wk many deprived cells have unusual response properties, and these are probably Y-cells, because of their short response latencies to optic chiasm stimulation. Such abnormal Y-cells become fairly rare by 6 mo of age.

Deprivation effects on X-cells [i.e., lower spatial resolution (146, 208)] occur much later and more gradually. Not until 6 mo of age is an X-cell difference between deprived and nondeprived laminae seen, and this occurs only for deprived lamina A1. Effects for X-cells in deprived lamina A are not found until the next age studied (>1 yr old). This probably explains why Lehmkuhle et al. (208) reported an equal effect on X-cell spatial resolution for deprived laminae A and A1, whereas Hoffmann and Sireteanu (146) noted the effect only in lamina A1. Lehmkhule et al. (208) studied cats 1–2 yr of age, whereas the cats in the study of Hoffmann and Sireteanu (146) were 5–7 mo old. Although Mangel (233) supports the conclusion that lid suture ultimately affects spatial resolution of X-cells, we repeat that Shapley and So (298) have challenged this conclusion.

D. Cortical Area 17

1. Anatomy

a) Geniculate afferents. Geniculate afferents reach area 17 by embryonic day 48, which is approximately 12 days before birth (6). These geniculostriate inputs are initially more widely distributed in the embryonic or neonatal animal than they are in adults. For example, during the 1st wk after birth, the geniculate inputs project more heavily to the upper cortical layers (especially layer I) than is the case in adult cats (6, 7, 205, 214). An abnormally dense projection to layer V has also been reported in the neonate (214). The

adult laminar distribution of afferents, with the highest density of inputs to layer IV, appears by the end of the 3rd wk after birth (205, 214). Transneuronal autoradiographic studies also suggest that the layer IV (and probably layer VI) ocular-dominance bands for the two eyes overlap extensively during the 1st wk of life and gradually segregate, attaining their adult appearance by about 6 wk of age (214). Unfortunately no direct information is available concerning the relative time of development of the X-, Y-, and W-cell geniculostriate afferents. In addition the time at which the geniculostriate afferents form synapses has not been studied with the electron microscope.

b) Intracortical connectivity. Intrinsic striate cortex connectivity and cellular morphology also undergo marked developmental changes during the first 4–6 wk of postnatal life. Long horizontal fibers intrinsic to area 17 are present at birth, but they are not fully developed (6). The age at which these connections reach maturity is unknown. Axonal myelination in striate cortex first appears between 19 and 23 days of age (51).

Neuronal density in striate cortex is very high at birth, declines rapidly during the first 10 days of life, and then slowly reaches adult levels by the end of the 4th wk (51). These density changes occur first in the upper cortical layers and then in the lower layers (51). Dendritic spines on intracortical neurons first appear between 7 and 10 days of age (1). Nevertheless ultrastructural studies show that some synapses are present in area 17 at birth and that they are the same size as synapses in adult cats. Cragg (51) reported that synaptic density remains very low during the 1st wk of life and then rapidly increases to adult values by about 4 wk. Synaptic density increases first in the lower cortical layers and then in the upper layers. In terms of the number of synapses per neuron, the kitten's striate cortex has only about 1% of the adult synapses at the end of the 1st wk of life. The number of synapses per neuron then rapidly increases, reaching a peak value between 4 and 6 wk of age. After this, there is a slight decline to adult values (51).

Many of the intrinsic morphological characteristics that show marked developmental changes during the first 4–6 wk of life are the same characteristics that are abnormal in binocularly deprived cats (see sect. V*C3*). Consequently these abnormalities could represent a failure to develop rather than an alteration of preexisting properties. Nevertheless the values observed in binocularly deprived cats are all greater than those present at birth or at the time of normal eye opening (~1 wk of age), which suggests that significant, if incomplete, morphological development of area 17 clearly proceeds in the absence of normal visual stimulation.

2. Physiology

a) Normal development. Electrical stimulation of the optic nerves produces evoked potentials in area 17 of newborn kittens (235, 236). However,

single-cell responses to light stimulation cannot be recorded until 4–6 days of age (163). Estimates of the proportion of cells that respond to light in 8- to 9-day-old kittens vary from 10% (29, 79) to nearly 85% (23, 163). These differences may be due to factors such as the anesthesia used, the state of the animal, the criterion for judging a cell responsive, and the ability to identify spontaneously active but nonresponsive cells. Despite these differences in estimates of the proportion of nonresponsive cells, all investigators report that responsive striate cortex cells in 8- to 14-day-old kittens are sluggish and fatigue rapidly (29, 79, 153, 163, 214).

There has been much discussion and controversy in the literature about whether or not striate cortex cells in young kittens respond selectively to stimulus orientation. Is orientation selectivity an innate property or does it require a patterned visual environment to develop? Much of the apparent disagreement appears to stem from two factors. First, some investigators have assumed that binocularly deprived kittens are comparable to normal kittens and have based their assertions about neonatal kittens on data actually obtained from deprived animals (153, 302). However, young binocularly sutured kittens may be quite different than young experienced kittens, even at 3–4 wk of age. Second, many investigators have failed to distinguish between direction-selective and orientation-selective response properties (24, 153, 302), and these investigators may have concluded that a cell was orientation selective when it was simply direction selective (see 126, 127, 273).

Nevertheless several physiological studies of normally reared, neonatal kittens have carefully distinguished between direction-selective and orientation-selective responses. These studies generally report few or no orientation-selective striate cortex cells in kittens between 8 and 14 days of age (29, 78, 79, 273), although one study reported 20% of the cells are orientation selective in a 9-day-old kitten (23). In addition no more than 20% of the cells respond selectively to the direction of stimulus movement (23, 24, 29, 78, 79, 273). Most striate cortex cells are thus nonselective prior to 2 wk of age: they respond to any stimulus moving in any direction through the receptive field. The receptive fields of these cells are abnormally large, with diffuse and ill-defined borders (78, 79, 273). Control experiments indicate that these immature response properties are not due to the poorly developed optics (24).

Between 2 and 6 wk of age, the responsiveness and receptive-field properties of kitten striate cortex cells progressively mature. The percentage of responsive cells increases and the responses become more brisk and consistent. In addition the proportion of nonselective cells decreases while the proportion of cells with both direction and orientation selectivity increases (23, 24, 29, 78, 79, 273). The orientation tuning of selective cells also becomes narrower and attains adult levels by 5–6 wk of age (24). Finally, peak contrast sensitivity to grating stimuli, optimum spatial frequency, and spatial resolution of striate cortex cells increase and spatial frequency bandwidth decreases between 2 and 6 wk of age (60). Despite these changes, the responsiveness and receptive-field properties of striate cortex cells do not appear

to be fully mature at 6 wk of age. Both the overall proportion of responsive cells and the proportion of responsive cells with orientation selectivity are lower than in adults (273; see also 24, 29, 79). These differences between 6-wk-old kittens and adults are slight, and any changes after 6 wk of age are minor compared with the enormous changes between 2 and 6 wk of age.

There is general agreement that both eyes have inputs to area 17 prior to 2 wk of age and that the contralateral eye dominates a larger proportion of these cells than it does in adult cats (23, 79, 153, 214). Most studies also report that the large majority of these cells are binocularly driven. In fact LeVay et al. (214) reported that a larger proportion of cells are binocularly driven in 10- to 17-day-old kittens than in adult cats, in correspondence with the high degree of overlap of the anatomically defined ocular inputs at this age. However, Fregnac and Imbert (79) reported that most striate cortex cells are monocularly driven prior to 3 wk of age, whereas most are binocularly driven in kittens older than 4 wk. The reason for this discrepancy is not clear.

Although many cells in area 17 are binocularly driven in young kittens, certain aspects of their binocular interactions are immature. In kittens younger than 4 wk of age, none of the binocularly driven cells are sensitive to the disparity between the two retinal images of a single stimulus (273). By 5–6 wk of age, about 35% of the cells are disparity sensitive, compared with 63% in adults (273). Thus binocular disparity sensitivity continues to develop for many of these cells after 6 wk of age, although the age at which striate cortex becomes fully mature for this property is unknown.

Finally, there is evidence that the relationship between the ocular dominance and the receptive-field characteristics of striate cortex cells changes with age in normally reared kittens. Fregnac and Imbert (79) have reported that, in kittens younger than 3 wk, cells with nonspecific receptive fields tend to be binocularly driven, whereas orientation cells tend to be monocularly driven. In addition the monocularly driven orientation-selective cells tend to have horizontal or vertical preferred orientations. This is remarkably similar to the relationship reported for adult cats reared in darkness (218). Fregnac and Imbert (79) found that the correlation between ocular dominance and orientation selectivity disappears after 4 wk of age in normally reared kittens. That is, both monocular and binocular cells are orientation selective, and they include oblique as well as horizontal and vertical preferred orientations. Presumably the nonresponsive cells and cells with nonspecific receptive fields develop these properties as the kittens grow older.

b) Monocular lid suture. Since all studies of normal neonatal kittens show that both eyes can drive striate cortex cells prior to 2 wk of age (23, 79, 153, 214), there must be a progressive loss of responsiveness to the deprived eye of monocularly deprived cats during development. This loss occurs very rapidly, because the results in kittens deprived to 4–5 wk of age are nearly identical to those in animals deprived for months or years (22, 156, 253, 339).

Recent experiments have shown that the mechanisms underlying the loss of response to the deprived eye at 4–5 wk of age are very different from those at later ages. As discussed earlier, removal of inputs from the nondeprived eye results in a rapid increase in the ability of some striate cortex cells to respond to the deprived eye in monocularly deprived cats (sect. IV*C2b*). Spear et al. (339) used this phenomenon to assess the nature of inputs from the deprived eye to striate cortex during development with monocular suture. They found that, after removal of the nondeprived eye at 4–5 wk of age, the deprived eye can drive a nearly normal percentage of striate cortex cells (65%), although most of the cells that now respond to the deprived eye have abnormal receptive fields. Among the responsive cells, only about 50% are direction selective and fewer than 10% are orientation selective. Control experiments with enucleation of one eye in a normal adult cat indicate that the abnormal response properties are not a by-product of the eye removal. Rather, they reflect the nature of the remaining connections for the deprived eye. These receptive-field properties are similar to those in 2- to 3-wk-old, normally reared kittens. Therefore these results indicate that a nearly normal percentage of striate cortex cells continues to receive functional connections from the deprived eye at 4–5 wk of age and that response specificity has either failed to develop or developed only minimally. Activity from the nondeprived eye must be removed, however, to reveal these inputs.

After more prolonged rearing with monocular deprivation, the percentage of striate cortex cells responding to the deprived eye after removal of the nondeprived eye decreases dramatically. This decrease is evident by 9–10 wk of age, when only 14% of the cells respond to the deprived eye after the nondeprived eye is removed. There is subsequently an increase in older cats, and about 30% of the cells respond to the deprived eye after removal of the nondeprived eye in animals deprived until 19–92 wk of age. At all ages studied, the receptive fields remain abnormal (e.g., about 10% are orientation selective) for cells that respond to the deprived eye. Thus with continued monocular deprivation the proportion of cells responding to the deprived eye decreases, even when inputs from the nondeprived eye have been removed. Nevertheless the proportion of responsive cells is still much greater (30%) when the experienced eye is removed than when it is intact (5%).

Together these results indicate that the loss of response to the deprived eye in 4- to 5-wk-old monocularly deprived kittens is due almost entirely to an interaction (presumably suppressive) with inputs from the nondeprived eye. There is no evidence of a loss of inputs or even of a direct change in synaptic efficacy at this age. By 9–10 wk of age, however, the synaptic efficacy and/or connections from the deprived eye have deteriorated. Nevertheless many functional connections remain well into adulthood.

c) Dark rearing. Several studies have directly compared the development of response properties for area 17 neurons in dark-reared and normally reared kittens. Fregnac and Imbert (79; see also 29, 78) found that these neurons follow a similar course of development in dark-reared and normally

reared kittens up to 3–4 wk of age, although development in dark-reared kittens appears to be slightly slower than normal. These investigators thus reported that both responsiveness and orientation selectivity develop to some extent in the absence of any visual stimulation. After 4 wk of age, however, the sequence reverses. By 6 wk of age, only 4% of the responsive cells are orientation selective, whereas 90% have nonselective (i.e., lack both direction and orientation selectivity) receptive fields in dark-reared kittens. Responsiveness also decreases to some extent (29, 78, 79).

In contrast to receptive-field properties, however, Fregnac and Imbert (79) found that ocular dominance develops normally in dark-reared kittens. Prior to 3 wk of age, most cells are monocular and dominated by the contralateral eye, and orientation-selective cells with horizontal or vertical preferred orientations tend to be monocular. After 4 wk of age, most cells are binocular, just as in normal kittens. The results of Fregnac and Imbert (79) thus indicate that certain response properties of striate cortex cells (or certain classes of cells) are innately determined and begin to develop normally without visual stimulation. After 3–4 wk of dark rearing, these properties deteriorate rapidly.

Bonds (24), however, recently reported results of a similar study leading to very different conclusions. He found that the proportion of cells with axis direction selectivity (response to movement in one direction along an axis through the receptive field and no response to movement in the opposite direction) remains constant between 2 and 6 wk of age in dark-reared kittens, whereas the proportion of such cells increases during this period in normally reared kittens. Bonds (24) also reported that the proportion of orientation-selective and orientation-bias cells remains constant with dark rearing, although this must be qualified because tests to distinguish between orientation and direction selectivity were not employed. The directional and/or orientational tuning of striate cortex cells remains broad in dark-reared cats but becomes narrower during the first 6 wk of normal rearing. In a related study, Derrington (60) found that the spatial frequency selectivity and sensitivity of striate cortex cells remain constant between 3 and 6 wk of age in dark-reared kittens, whereas both measures increase between these ages in normal kittens. Taken together the results of Bonds (24) and Derrington (60) indicate that, although certain response properties of striate cortex cells are innately determined (albeit crudely), there is no subsequent deterioration with dark rearing. Instead striate cortex cells simply fail to develop specificity beyond that present at 2–3 wk of age.

Even different conclusions were suggested by Leventhal and Hirsch (218), who found that, after long-term dark rearing, there is a higher proportion of monocularly driven striate cortex cells than is found in normal cats (see also 57) and that orientation-selective cells tend to be monocular (and to prefer horizontal or vertical orientations) and nonselective cells tend to be binocular. This is comparable to the results of Fregnac and Imbert (79) in both normal and dark-reared kittens less than 3 wk old. This com-

parison leads to the conclusion that the monocular, orientation-selective cells are innately specified and develop normally without visual stimulation, whereas binocular, nonselective cells simply fail to develop. Conversely, if most cells in neonatal kittens are binocular, as observed by some investigators (23, 153, 214), then the results of Leventhal and Hirsch (218) would suggest that at least some binocular cells are lost during dark rearing.

Thus, depending on the comparisons one makes, it is possible to conclude that the abnormalities present in striate cortex of dark-reared cats are due to *1*) a simple failure to develop, *2*) normal (but somewhat slow) initial development followed by deterioration, *3*) normal development of some properties (or classes of cells) and a failure of others to develop, or *4*) normal development of some properties (or classes of cells) and a deterioration of others. At present there is no simple resolution of these conflicting results and conclusions. By judicious selection of the literature, one can find support for virtually every hypothesis concerning development in dark-reared kittens. Finally, note again that it is not clear to what extent development of the optics and axial length of the eye contributes to the data on spatial acuity in normal and dark-reared kittens (265).

d) Binocular lid suture. There is similar uncertainty about the changes (or lack of them) that occur during development with binocular lid suture. Pettigrew (273) compared the development of orientation selectivity, direction selectivity, and disparity sensitivity of area 17 neurons in normal and lid-sutured kittens from 1 to 6 wk of age. He found that no cells are orientation selective or disparity sensitive and few are direction selective in 1- to 2-wk-old normal kittens. This situation changes little during the first 6 wk of development with binocular lid suture, although about 10% of the responsive cells are orientation selective after 5–6 wk of deprivation. Normal kittens at this age already have many responsive and selective neurons. Also Derrington (60) found that there is little change between 3 and 6 wk of age in sensitivity and selectivity of area 17 neurons to spatial frequency during binocular suture but that these properties improve considerably during normal rearing. These results of Pettigrew (273) and Derrington (60) suggest that striate cortex fails to develop (or develops only minimally) during rearing with binocular lid suture.

However, other conclusions can be drawn from studies assessing ocular dominance in lid-sutured cats. As already noted (sect. V*C1a*), these studies find that the proportion of binocularly driven cells is lower than normal in lid-sutured cats and that the orientation-selective cells tend to be monocularly driven, whereas cells with nonspecific receptive fields tend to be binocularly driven (23, 198, 392, 398). The conclusions drawn from these studies depend on which results are considered to be the starting point in neonatal kittens. If neonatal striate cortex cells are predominantly monocular and the orientation-selective cells tend to be monocular (79), then one would conclude that binocular lid suture simply leads to a failure to develop beyond a certain point. However, if neonatal striate cortex cells are predominantly

binocular with no correlation between ocular dominance and orientation selectivity (23, 159, 214), then one would conclude that binocular lid suture leads to a loss of binocularly driven cells. Again there is currently no simple resolution of these possibilities.

E. Superior Colliculus

1. Anatomy

Retinal afferents grow into the superior colliculus between embryonic days 30 and 37. By embryonic day 37, afferents from both eyes are present, although, as in normal adults, those from the contralateral eye are denser than are those from the ipsilateral eye (6). Corticotectal afferents from areas 17 and 18 reach the superior colliculus by embryonic day 48 (7, 349). Because there have been no electron-microscopic studies of the developing superior colliculus in the cat, it is not known when these afferents form synaptic connections.

2. Physiology

The development of response properties of cells in the upper three collicular layers has been described by Stein et al. (350, 351) and Norton (263), and their results are in close agreement. During the 1st wk of life (and prenatally as well), spontaneously active neurons are encountered in these collicular layers. These cells do not respond to light, although cells in the lower layers of the superior colliculus do respond to somatic stimulation before birth (350). The first visually responsive cells appear at 7 days of age, but their responses rapidly fatigue and are weaker than those of adult neurons. In addition the responses to visual stimulation are of extremely long latency (351). By 3 wk of age the responses become as brisk and consistent as in adults (263), and by 4–6 wk of age they have adult latencies to visual stimulation (351).

The receptive fields of the first responsive cells are similar in size to those in adult cats. The percentage of cells with inhibitory receptive-field surrounds is slightly lower than in adults, however, and for those cells with inhibitory surrounds the strength of the inhibition is less than seen in adults. Other receptive-field properties are very abnormal in 1- to 2-wk-old kittens. The cells respond better to stationary flashing stimuli than to moving stimuli, those cells that respond to movement prefer abnormally slow velocities, and most are driven exclusively or nearly so by the contralateral eye. All these properties show progressive changes over the next few weeks, and by 4–6 wk of age the response properties are similar to those in adult cats. For

example, most cells respond best to moving stimuli (including high velocities), are direction selective, and are driven about equally by both eyes in 4- to 6-wk-old kittens (263, 350).

The response properties of these superior colliculus neurons in 1- to 2-wk-old kittens generally resemble those in adult cats with cortical areas 17 and 18 removed. This suggests that much of the normal development of neuronal response properties in the superior colliculus is due to a functional maturation of the corticotectal pathway between 2 and 6 wk of age. The responses of collicular neurons in neonatal kittens also resemble those in binocularly sutured and dark-reared cats. Therefore the abnormalities after binocular deprivation may simply represent a failure of the corticotectal pathway to mature functionally. In the absence of studies of the development of the superior colliculus in binocularly deprived kittens, however, one cannot rule out the possibility of an initial period of normal development followed by a loss of selectivity.

VII. CONCLUSIONS AND HYPOTHESES

Despite the large body of research on animals raised with monocular or binocular deprivation, we can neither provide a unified description of the effects of such deprivation on development of the central visual pathways nor explain the mechanisms by which visual deprivation affects neural development. Nonetheless certain general principles have emerged, and in this section we attempt to provide a theoretical framework for much of the research reviewed here. This framework, however, is necessarily somewhat speculative and incomplete.

A. General Mechanisms of Development

As suggested in section III, mechanisms by which the visual environment can influence the developing brain can be placed into one of two broad categories: competitive and noncompetitive. A yawning gap in our understanding of these mechanisms exists, because experiments have been designed to analyze only the presence or absence of binocularly competitive mechanisms. We can barely begin to speculate on the existence of numerous other possible competitive mechanisms, such as X-cell versus Y-cell, on-center cell versus off-center cell, area 17 versus area 18, and many others. Our comments consequently must focus on competitive and noncompetitive mechanisms as they relate to binocular interactions. However, we stress that a deprivation-induced deficit attributable to a binocularly noncompetitive mechanism might result from other types of competitive mechanisms (e.g., X-cell vs. Y-cell).

1. Binocularly competitive and noncompetitive mechanisms

Two separate lines of evidence suggest the presence of binocularly competitive and/or noncompetitive mechanisms: comparisons between the natural or artificial monocular and binocular segments in monocularly sutured cats and comparisons between monocularly and binocularly sutured cats. For brevity we refer to the former as the between-segment comparison and the latter as the between-animal comparison. (In sect. III*B*, we explain the rationale behind these approaches.) Results from the between-segment comparison are somewhat at variance with those from the between-animal comparison, and this difference provides some insights into the nature of the underlying developmental mechanisms.

a) Monocular and binocular segments. Much of the evidence regarding the role of binocular interactions in visual development derives from comparisons between deprived monocular and binocular segments of the central visual pathways in monocularly sutured cats. Briefly the rationale for this approach is that abnormalities due to a binocularly noncompetitive component of deprivation can be isolated in the monocular segment, because binocular interactions cannot occur there. The competitive component of deprivation can then be elucidated on the basis of more serious abnormalities found in the binocular than in the monocular segment.

In the lateral geniculate nucleus, evidence exists for both binocularly competitive and noncompetitive mechanisms. Soma size, at least for the A laminae, is affected much more in the binocular than in the monocular segment. The slight effects reported for the deprived monocular segment, however, do suggest a moderate noncompetitive component.

The distribution and response properties of recorded geniculate Y-cells can be completely accounted for by a mechanism of binocular competition, because these neurons are rarely found in the deprived binocular segment but occur in normal numbers and with normal response properties in the deprived monocular segment. Development of X-cells, on the other hand, seems to be controlled by a binocularly noncompetitive mechanism. These neurons are found in normal numbers in both segments, but they do not exhibit the sensitivity to high spatial frequencies normally seen. This acuity loss is equal in both monocular and binocular segments.

The relationship between the soma size pattern and X-cell and Y-cell development in deprived laminae is not clear, but the analysis of LeVay and Ferster (211) suggests a fairly straightforward correlation. These authors conclude that, in the deprived binocular segment of monocularly sutured cats, the growth of Y-cell somata is more affected than that of X-cell somata (see also 85, 224). If true, then perhaps Y-cell somata are smaller only in the binocular segment, whereas X-cell somata are equally affected in both segments. This would produce a relatively mild effect of deprivation on mean soma size in the monocular segment and a much larger effect in the binocular segment.

An analogous pattern also has been described for the striate and lateral suprasylvian cortices in monocularly sutured cats. In both areas the deprived eye activates very few neurons in the binocular segment but many more in the monocular segment. Neural responsiveness is not, however, normal in the monocular segment of either cortical area. In area 17, for instance, simple cells seem to develop fairly normally in the deprived monocular segment, but complex cells do not. Consequently both binocularly competitive and noncompetitive mechanisms are indicated in these areas.

Finally, limited data from the superior colliculus suggest that the monocular segment receives relatively normal input from the deprived eye, whereas the binocular segment does not. These observations implicate binocular competition alone. This may not be surprising, because the abnormalities seem to be a product mostly of a loss of the Y-cell indirect pathway (i.e., retinogeniculocorticotectal), which in turn might result from the abnormalities described for geniculate Y-cells. These geniculate abnormalities are limited to the binocular segment.

b) Monocular and binocular suture. An analogous strategy has been employed to elucidate binocular interactions by comparing development after monocular (i.e., unbalanced) and binocular (i.e., balanced) deprivation by lid suture. The rationale behind this strategy is that there is little or no binocular competition during binocular deprivation, so that any resultant abnormalities reflect a noncompetitive component of development. Any added abnormalities for the deprived eye after monocular suture reflect the added competitive component. However, the conclusions drawn from this strategy are not always equivalent to those reached from the between-segment comparison.

Although there is not complete agreement concerning geniculate soma sizes in binocularly sutured cats (see sect. V*B1a*), most of the evidence suggests that these somata are only slightly below normal size, in contrast to the much smaller somata seen in deprived laminae after monocular suture. Abnormally few geniculate Y-cells are recorded after binocular suture, but the number of these neurons is reduced more in deprived laminae of monocularly sutured cats than it is in binocularly sutured cats. These data consequently support the notion that both binocularly competitive and noncompetitive mechanisms control soma size and Y-cell development.

Analogous comparisons for striate cortex also seem to support the concept of binocularly competitive and noncompetitive mechanisms of development. After monocular suture, less than 10% of these cells are influenced by the deprived eye, whereas most can be activated by one or the other eye after binocular suture. However, very few cells of any class have normal receptive-field specificity in the binocularly deprived cats. This comparison suggests that visual responsiveness of these cortical neurons develops by way of both binocularly competitive and noncompetitive mechanisms but that only a binocularly noncompetitive process controls development of receptive-field specificity.

The between-animal comparison for lateral suprasylvian cortex suggests that binocular competition plays little or no role in the development of abnormalities during lid suture. The deprived eye excites few neurons here after either monocular or binocular deprivation (10% and 20%, respectively), and practically none of these have normal receptive fields. If binocular suture indeed establishes the noncompetitive component of deprivation, then on the basis of the between-animal comparison the monocular deprivation of lateral suprasylvian cortex can be explained with reference to rather limited binocular competition.

Finally, the between-animal analysis for the superior colliculus suggests some binocular competition during development, although few relevant comparisons have been made for collicular cells. Since the deprived eye influences many more collicular cells after binocular than after monocular suture, especially in the contralateral colliculus, a competitive mechanism is suggested. Normal responsiveness is not seen among collicular neurons after binocular suture, however, which suggests a significant noncompetitive component.

c) Differences in between-segment and between-animal comparisons. Obviously conclusions concerning the role of binocular interactions are not always identical for the between-segment and between-animal comparisons. This lack of agreement stems from different determinations of the noncompetitive component of development as deduced from the two comparisons. That is, often fewer abnormalities are seen in the deprived monocular segment after monocular suture than are found in the central visual pathways after binocular suture.

Both types of comparison lead to the conclusion that the noncompetitive component of geniculate soma growth is small but clearly present. However, the between-segment comparison suggests no noncompetitive component for geniculate Y-cell development, although a substantial component for this is indicated by the between-animal comparison. In striate cortex, the between-segment comparison suggests no noncompetitive component for simple cell development, but the between-animal comparison implicates such a component. For lateral suprasylvian cortex, the between-segment comparison indicates that the noncompetitive component permits slightly over half of the neurons to be influenced by visual stimulation, but the between-animal comparison suggests that only about one-fifth of the neurons develop visual responses through this mechanism. Finally, although the data are limited, studies of the superior colliculus indicate no noncompetitive component based on the between-segment comparison and a large component based on the between-animal comparison.

It seems clear that the central visual pathways of binocularly sutured cats and the deprived monocular segment of monocularly sutured cats do not develop by the same binocularly noncompetitive process. Neurons of the former consistently have more serious abnormalities than those of the latter. An extra factor apparently contributes to the deficits seen after binocular suture, and there are at least two possible explanations for this.

First, all of the data from binocularly sutured cats considered above for the between-animal comparisons derived from the binocular segment. A general assumption is that abnormal binocular competition does not occur during binocular deprivation, because each eye is equally deprived, and the competitive balance is preserved. The possibility has been raised that this assumption may be invalid (198, 343). That is, despite balanced binocular deprivation, some deleterious binocular interactions could occur that might add to the deficits. For example, differential activity from the two eyes (or geniculate laminae), either spontaneous or in response to visual stimuli delivered through the closed lids, could lead to abnormal binocular interactions in these animals. There is little direct evidence for this possibility (cf. 198), but it cannot be ruled out.

Second, the additional deficits seen in the binocularly deprived cats compared with the deprived monocular segment of the monocularly deprived cat could result from additional or different and more serious noncompetitive effects of binocular deprivation. Evidence for this is provided by a comparison between the deprived monocular segments after binocular and monocular suture. Here binocular interactions can be ruled out, and all deficits can be attributed to binocularly noncompetitive processes. Such a comparison suggests roughly equal deficits only for responsiveness of complex cells in area 17. Otherwise, more serious deficits are seen after binocular suture (cf. Figs. 7–9). Geniculate soma sizes, geniculate Y-cells, simple cells in area 17, superior colliculus neurons, and neurons in lateral suprasylvian cortex all seem to suffer more serious consequences in the deprived monocular segment after binocular suture than after monocular suture. That is, the deprived monocular segment seems to develop less normally in a completely deprived visual system (i.e., binocular deprivation) than in a partially deprived one (i.e., monocular deprivation).

This analysis suggests two rather different explanations. First, complete (binocular) deprivation may lead to an additional set of deficits due to an additional or more severe noncompetitive process than occurs during partial (monocular) deprivation. Second, the two different deprivation conditions may induce qualitatively different mechanisms of noncompetitive development. These two possibilities suggest very different developmental mechanisms. For the sake of clarity and illustration only, a speculative example is offered for each possibility.

First, perhaps neurons in the monocular segment have two afferent inputs through which activity is important for development. One represents the retinotopically faithful or serial projections from other structures (e.g., geniculocortical input for a cortical neuron). The other represents lateral interconnections between neurons that are not in retinotopic register. Such lateral pathways have been described for striate cortex (53, 95, 222).

A noncompetitive mechanism of development based on activity over these two routes (i.e., serial and lateral pathways) might affect monocular segment neurons during monocular and binocular suture in the following

manner. During monocular suture, these neurons would receive functional input via lateral interconnections from the binocular segment because of the development here of functionally normal cells related to the nondeprived eye. During binocular suture, few normal cells develop in the binocular segment and thus little normal input arrives from these cells via lateral interconnections to neurons in the monocular segment. Consequently the noncompetitive effects of deprivation would be more severe in the monocular segment of binocularly deprived cats because both the serial and the lateral inputs are deprived. In the monocular segment of monocularly deprived cats, the retinotopically faithful inputs are deprived while lateral interconnections from the binocular segment are stimulated by the nondeprived eye. Functional inputs from the binocular segment may be sufficient for the normal development of some properties in the monocular segment but not of others.

This example illustrates the possibility that the noncompetitive effects of complete (binocular) deprivation can logically be viewed as the sum of noncompetitive effects during partial (monocular) deprivation plus further effects that develop only during more complete deprivation. Such an explanation has been previously suggested (110, 306, 307, 337).

Second, perhaps complete (binocular) deprivation prevents many (but not all) normal developmental mechanisms from operating, as if they must be switched on by some normal visual input present during partial (monocular) deprivation. For one example, Kasamatsu and Pettigrew (183, 274) suggested that global, diffuse noradrenergic projections into the visual system (and indeed the rest of the brain) from the locus coeruleus (247) control development during the critical period. These inputs hypothetically could switch on normal developmental mechanisms only if some normal vision is possible. This might happen during partial (monocular) but not complete (binocular) deprivation. Interestingly a number (but certainly not all) of the deficits seen after binocular deprivation are reminiscent of properties seen in normal neonatal kittens (see sect. V and VI).

This example illustrates the possibility that development during binocular and monocular suture might share few if any mechanisms. If so, comparisons between binocularly and monocularly sutured cats to elucidate binocularly competitive and noncompetitive mechanisms would be inappropriate until we understand the nature of mechanisms controlling development during binocular deprivation (cf. 303). Nonetheless only by these between-animal comparisons can it be determined if different or additional developmental mechanisms exist for the different deprivation conditions.

d) Conclusions. Two very different hypotheses have been generated to explain differences seen in the central visual pathways of monocularly and binocularly sutured cats. One suggests that development during both deprivation conditions shares many common mechanisms; the other suggests qualitatively different mechanisms. We emphasize again that the specific examples described above are almost entirely speculative and are offered

only to clarify the two hypotheses. In fact the available evidence does not permit favoring one of these general hypotheses over the other.

2. *Loss of inputs versus suppression of inputs*

The actual synaptic mechanisms underlying any of these competitive or noncompetitive processes are unclear and can be discussed only at the level of hypothetical proposals (e.g., 353). At this point it is not possible to consider synaptic mechanisms at any specific level. However, two general classes of such synaptic modification are worth mentioning.

a) Loss of inputs. Some synaptic populations related to the deprived eye fail to develop normal strength and/or numbers. For instance, anatomical evidence from transneuronal autoradiographic pathway tracing suggests that fewer geniculostriate projections develop from the deprived laminae than from the nondeprived laminae. This general form of synaptic modification is probably quite common in visually deprived cats.

b) Suppression of inputs. Abnormal suppression of one pathway by another is the second synaptic modification. For instance, the observation that the deprived eye can drive many striate cortex cells after removal of inputs from the nondeprived eye or after bicuculline administration suggests active suppression of deprived eye inputs by those of the nondeprived eye through inhibitory circuits. There also seems to be suppression of deprived retinotectal pathways by the corticotectal pathways in monocularly deprived cats. Likewise, deprived pathways from thalamus to the lateral suprasylvian cortex appear to be suppressed by inputs from areas 17 and 18. Suppression in these cases is indicated by an increase in the ability of the deprived eye to drive neurons in superior colliculus and lateral suprasylvian cortex after removal of areas 17 and 18. Both examples may also represent interocular suppression, with inputs from the deprived and nondeprived eyes arriving by way of different structures (e.g., 373).

In contrast to these examples, the reduction of Y-cells encountered in deprived lateral geniculate laminae of monocularly deprived cats does not appear to be a result of suppressive mechanisms. Removal of the nondeprived eye (while leaving the deprived eye closed), which results in a renewed response to the deprived eye in striate cortex, does not produce a reappearance of Y-cells in the lateral geniculate nucleus (92). In addition, acute removal of corticogeniculate inputs from areas 17 and 18 does not increase responses of Y-cells to the deprived eye (408). Thus, although suppression of inputs is important in the effects of monocular deprivation in some structures, there seem to be exceptions.

These mechanisms of suppression of some pathways by others may occur normally in the cat's central visual pathways. For example, recent evidence indicates that inhibitory interactions contribute to ocular dominance of

striate cortex cells in normal cats (321). Therefore these interactions may simply be increased or altered by binocular competition during monocular suture, rather than appearing de novo. Unfortunately such mechanisms are poorly understood.

3. Failure to develop versus atrophy

From sections IV and V it is clear that cats raised with monocular or binocular deprivation have central visual pathways that are very different from those of normally reared cats. Whether these differences result from lack of development of normal properties or from the loss of normal properties already present is not so clear. To distinguish between these possibilities requires detailed knowledge of the status of the neonatal visual pathways before the critical period begins and a description of the dynamic changes occurring during the critical period. Unfortunately, as noted in section VI, unambiguous data generally are not available to make this distinction, and the available data are generally limited to the geniculostriate pathways and superior colliculus.

a) Geniculostriate pathways. The effect of monocular suture on geniculate soma growth is mainly one of arrested development for deprived laminae, although some slight atrophy might also occur later in the critical period. The same seems generally true for Y-cell development, because relatively few can be recorded at any age in deprived laminae of monocularly deprived cats. However, the effect of monocular suture on geniculate X-cell spatial acuity seems to be degenerative. These deprived X-cells develop and maintain normal acuity until about 6 mo of age, and only after this time are deficits seen.

The results in striate cortex relevant to this issue, particularly with regard to receptive-field development during binocular deprivation, are the most confused of any body of data considered in this review. There are so many contradictory claims (sect. VI*D2*) that every possibility, ranging from lack of development to degeneration of neonatally functional pathways, can be supported by some studies as an explanation for the physiological effects of binocular deprivation. Anatomical studies clearly indicate considerable maturation of striate cortex during binocular deprivation. Studies of monocularly sutured cats employing removal of the nondeprived eye suggest that deprivation effects result from a two-step process. First, the deprived eye's inputs are suppressed, and later there is a loss of some inputs with continued suppression of others.

b) Superior colliculus. The superior colliculus at birth is clearly immature, and the last properties to develop normally seem to reflect the corticotectal input. The corticotectal input (via the Y-cell indirect pathway) is selectively affected by monocular or binocular suture. Therefore it seems parsimonious to suggest that this reflects a failure of the Y-cell indirect

pathway to develop during lid suture. So far, however, there are no data comparing collicular neurons in normally reared and visually deprived cats at different ages during the critical period.

B. Differential Abnormalities Among W-, X-, and Y-Cell Pathways

Because W-, X-, and Y-cells in the retina represent the beginnings of three parallel, independent visual pathways, it is of considerable interest to determine the extent to which visual deprivation differentially affects the development of these pathways. Our understanding of developmental mechanisms depends largely on conclusions concerning differential effects of deprivation on these pathways, so we deal with this in some detail. Because there is no clear evidence that retinal ganglion cells are affected by lid suture or total darkness, deprivation effects on these pathways must be analyzed more centrally.

1. Is there a functional loss of geniculate Y-cells?

The strongest evidence for a relatively selective effect of visual deprivation on Y-cells derives from studies of the lateral geniculate nucleus and geniculocortical pathways. Least is known about deprived geniculate W-cells, but soma measurements in the C laminae suggest little or no effect of lid suture on these cells. Visual deprivation seems not to affect responses of geniculate X-cells to most visual stimuli, and only the subtle deficit of reduced spatial acuity has been reported for these cells. Normal Y-cells in deprived laminae, however, are difficult to record.

Although this inability to record deprived geniculate Y-cells has been observed in numerous studies (e.g., 71, 92, 141, 142, 197, 201, 233, 256, 308, 312, 313, 408), the interpretation of these physiological data is far from clear. Two major explanations have been proposed. The first is that the results are due to electrode sampling biases (e.g., 71, 298, 308). Implicit in this hypothesis is the notion that electrode sampling probability is directly related to soma volume (cf. 162). The implication is that in normal cats the recorded proportion of Y-cells in the A laminae (~40–50%) exaggerates their actual proportion by a factor of 5–10 due to the larger somata of Y-cells compared with those of X-cells. Lid suture presumably reduces soma growth more for Y-cells than for X-cells, and thus fewer Y-cells are recorded. If so, this differential lack of growth for X- and Y-cells is presumably without functional significance. The second explanation is that the loss of recorded Y-cells truly reflects a severe functional deficit and cannot be completely explained by electrode sampling characteristics.

Although most anatomical and physiological evidence apparently supports the latter interpretation, we emphasize that a definitive understanding of these phenomena is presently not possible. Also the interpretation of

virtually all electrophysiological studies, including those discussed in this review, are subject to the possibility of electrode sampling artifacts. Below we review briefly and critically some of the evidence for the loss of recorded Y-cells from deprived geniculate laminae.

a) Evidence for sampling artifacts. The evidence for sampling biases comes from two studies of cats reared with monocular lid suture. In one, Eysel et al. (71) compared the relative frequency of X-cell versus Y-cell axons recorded in the optic radiations with the relative frequency of these cells recorded among somata in the lateral geniculate nucleus. Their soma recordings confirm the observations of Sherman et al. (308), since few Y-cells were found in deprived laminae. In the optic radiations, however, an equal ratio of X-cells to Y-cells was noted for the deprived and nondeprived eyes. Eysel et al. (71) suggested that geniculate Y-cells might be physiologically quite normal with normal axons projecting to cortex, but that these cells are difficult to record in the lateral geniculate nucleus either because of their retarded growth or other factors.

However, Eysel et al. (71) note an important proviso to this interpretation: although their optic radiation recordings revealed a normal relative frequency of X-cells to Y-cells among deprived axons, this resulted not from a normal frequency of deprived Y-cell axons but rather from a reduced frequency of deprived X-cell axons as well. This could imply additional abnormalities or perhaps thinner axons among deprived X-cells. Alternatively these results might simply reflect the enormous sampling problems among a fiber population, particularly with the metal microelectrodes used and small overall sample (12 deprived axons with receptive-field identification plus an additional 79 deprived axons identified on the basis of response latency to optic tract stimulation) obtained by Eysel et al. (71).

In the other study, Shapley and So (298) also argue that the loss of recorded Y-cells is merely an electrode sampling artifact based on retarded soma growth. Previously they reported that in normal cats metal microelectrodes are strongly biased for larger (presumably Y-cell) somata among geniculate neurons, but "fine" micropipettes isolate a much smaller proportion of Y-cells (330). The proportion obtained with micropipettes was roughly 15%, which approximates the expected value from retinal estimates (i.e., without considering retinal W-cells). These authors then used the micropipettes in monocularly deprived cats and found equally low percentages of Y-cells in deprived and nondeprived laminae (298). The basic difference between these data and those of other investigators is in the ratio of Y-cells in nondeprived laminae: few (<20%) were found in the Shapley and So (298) study, whereas more (35–50%) were found by other investigators. In any case, Shapley and So (298) suggested that their micropipettes are free from gross sampling biases. That is, these electrodes can isolate the abnormally small Y-cells as easily as normal Y-cells, whereas the electrodes used in other studies were unable to isolate the deprived Y-cells. Shapley and So (298) therefore concluded that, despite lack of growth in deprived geniculate (Y-cell) somata, these cells are quite normal functionally.

For several reasons, however, the report by Shapley and So (298) is difficult to evaluate. First, they describe percentages rather than actual numbers of recorded cells, and neither sample size nor statistical reliability is described. (For instance, does the normal percentage of deprived Y-cells result from normal or equally reduced numbers of X- and Y-cells?) Second, the "fine" microelectrodes described by So and Shapley (330) seem to be relatively coarse, because they were filled with physiological saline and had resistance values of 5–15 MΩ. If such an electrode were filled with the more common and more conductive solution of 3–4 M NaCl, its resistance would drop to roughly 1 MΩ or less (see 81). In any case, Sherman et al. (308) used apparently finer micropipettes (5–15 MΩ filled with 4 M NaCl), and thus their failure to record small somata because of coarser electrodes seems unlikely. Third, if major sampling biases do occur and are related strongly to soma size, it is not clear why even the finest electrodes would not suffer from this bias. Presumably smaller (Y-cell) somata result in smaller volumes of extracellular tissue in which an electrode can isolate action potentials from background noise (for details see 162). If this were the explanation for the failure to record deprived Y-cells, why did not the electrodes of Shapley and So (298) also fail to record deprived Y-cells? Finally, note that both LeVay and Ferster (211) and Friedlander et al. (81) concluded on anatomical grounds that normal geniculate Y-cell proportions were larger than those estimated by So and Shapley (330). In conclusion, Shapley and So (298) describe data that actually do not support their basic hypothesis concerning an electrode sampling bias, although their data also offer no support for a selective deprivation effect on Y-cells.

A general difficulty with the approach of Eysel et al. (71) and Shapley and So (298) is that it may not be practical to demonstrate an electrode sampling bias in one study by using a variation of the same electrophysiological techniques in a subsequent study. Any such single-unit recording experiment, by definition, may be prey to uncontrolled electrode sampling biases that render any data difficult to interpret. Although the studies of Eysel et al. (71) and Shapley and So (298) also may suffer from this general problem, they nonetheless provide some positive evidence that such biases may well explain the original observations of Sherman et al. (308).

One final point may be made about these interpretations of the data. Even if the failure to record Y-cells is largely an electrode sampling artifact due to soma size, this nonetheless supports the notion of a selective effect of deprivation on Y-cells. The selective effect is at least one of soma growth, although the data of Shapley and So (298) do not even support such a growth phenomenon. It seems reasonable to assume that any such soma growth is related to functional properties of the neuron in question. For instance, although geniculate Y-cells in deprived laminae could conceivably have normal electrophysiological properties, their smaller somata might relate to reduced axonal terminal arbors in cortex (106, 215, 300), which in turn implies reduced geniculocortical transmission. By this reasoning, a selective deprivation effect on the Y-cell pathway still occurs. The debate about electrode

sampling factors consequently reduces to the less interesting question of whether the effect is seen in the lateral geniculate nucleus or visual cortex instead of the more interesting question of whether a selective effect of deprivation on the Y-cell pathway occurs at all.

b) *Evidence against sampling artifacts.* Scattered through sections IV, V, and VI are descriptions of experimental results that together provide a powerful argument that electrode sampling based on soma size alone cannot account for the loss of recorded Y-cells from deprived laminae. Although other bases of electrode sampling biases cannot be eliminated (and this proviso can apply to most electrophysiological studies), these experiments suggest that functional properties of geniculate Y-cells are relatively selectively affected by early visual deprivation. These results are only briefly reiterated and discussed here. At least six relevant sets of data can be considered.

1) Friedlander et al. (81) found little evidence for electrode sampling based on soma size for normal geniculate neurons. They also concluded that more than one-third of the A laminae neurons are normally Y-cells, which supports an earlier suggestion by LeVay and Ferster (211). LeVay and Ferster (211) also extended their analysis to geniculate neurons in deprived laminae and concluded that although the growth of deprived Y-cells is more retarded than that of X-cells, deprived Y-cell somata nonetheless grow larger than deprived X-cell somata. That these relatively large and numerous Y-cells are only rarely recorded electrophysiologically is thus probably due to either their lack of responsiveness or change in properties rather than a consequence of electrode sampling failure. There are, however, two major qualifications to this interpretation. First, it is not clear that the same principles for anatomical identification of X- and Y-cells apply to monocularly sutured cats. Second, LeVay and Ferster (211) performed their analysis on a single monocularly sutured cat.

2) Under certain conditions there seems to be a dissociation between soma sizes and recorded Y-cell proportions. A remarkable variety of experimental preparations has been described in which the geniculate soma size distribution is practically normal but few Y-cells can be recorded. This is true for binocularly sutured cats (107, 135, 308) and for cats raised in total darkness (176, 197). This also is true for cats raised with monocular suture followed by enucleation of the open eye and continued closure of the deprived eye during adulthood (92). Finally, in a developmental study of monocularly sutured kittens, Mangel (233) found few Y-cells in deprived or nondeprived laminae of 8-wk-old kittens, despite the pratically adult soma size pattern for these laminae at this age.

The opposite relationship between soma size and recorded Y-cell frequency has also been reported. Hoffmann and Hollander (142) described a condition (rearing with one eye sutured, then opening this eye and suturing the other in adulthood) in which normal numbers of Y-cells can be recorded in laminae with severely shrunken somata. Sherman and Wilson (312) and

Geisert et al. (92), however, failed to find a return of recorded Y-cells (i.e., a normal proportion of Y-cells) in this preparation.

These studies undermine the notion that the probability of recording a neuron electrophysiologically is closely related to its soma size. The qualification for these results is that a measurement of the geniculate soma size distribution does not provide separate X- and Y-cell distributions. However unlikely the possibility, the few Y-cells found in laminae with a normal soma size distribution could result from abnormally small Y-cells matched by abnormally large X-cells. The available evidence (i.e., 82, 211) contradicts this possibility, and the converse is also possible.

3) Studies of visually and electrically evoked field potentials recorded in the visual pathways of monocularly sutured cats are consistent with a fairly selective effect of lid suture on geniculate Y-cells (26, 171, 172, 239, 241, 329). These data are described more fully in section IV. Although they are clearly consistent with the notion that development of the Y-cell pathway is affected more by lid suture than is the X-cell pathway, an important proviso must be emphasized here. Studies of gross evoked potentials are free from microelectrode sampling characteristics involving single neurons, but it is not entirely clear what neuronal properties are reflected in these potentials nor is it obvious that other sampling artifacts are not contributing to the results.

4) In some select cases it has been possible in visually deprived cats to record activity from neurons identified as normal target cells for geniculate X- and/or Y-cells, and these data are consistent with the hypothesis that deprivation affects Y-cells more seriously than it does X-cells. Hoffmann and Sherman (144, 145) found that corticotectal cells, which normally receive input from geniculate Y-cells, do not develop functional input from the deprived eye. Although this study points to a rather specific deficit in the Y-cell pathway, it cannot address the question of whether analogous changes are seen in the X-cell pathway. The overall lack of cortical cells responsive to the deprived eye suggests that this may not be an abnormality limited to the Y-cell pathway. Mooney et al. (244) studied the effects of early monocular suture on inputs to perigeniculate neurons, each of which normally receives binocular input from both X- and Y-cells. This input derives from collaterals of the main axons as they pass through toward the cortex (81). As a result of monocular deprivation these perigeniculate neurons develop binocular X-cell input, but the Y-cell input develops only from the nondeprived eye. Finally, Tsumoto and Suda (379) found many subthreshold inputs from deprived geniculate laminae to striate cortical neurons in monocularly deprived cats and concluded that such deprived inputs are largely from X-cells.

These experiments have none of the problems of electrode sampling artifacts in deprived geniculate laminae, and they provide data consistent with the hypothesis that geniculate Y-cells are affected more than are X-cells by early visual deprivation. However, these results cover only select,

small neuronal samples from which generalizations about X- and Y-cell pathways are risky. These experiments also can only provide indirect data about the status of deprived geniculate neurons, and many interpretations other than that considered here may be possible.

5) Anatomical studies of geniculocortical projections have also provided some support for the special sensitivity to visual deprivation of Y-cell development. Orthograde, autoradiographic demonstrations of ocular-dominance columns in layer IV of cat striate cortex have shown that early monocular suture seems to enlarge columns related to the nondeprived eye at the expense of deprived columns. Close inspection of the data further suggests that reduction of deprived column size is greater in the dorsal part of layer IV, in which Y-cell axons terminate, than in the ventral part, in which X-cell axons terminate.

The use of HRP in retrograde studies of geniculocortical projections from laminae A and A1 in monocularly deprived cats has produced analogous results. The A laminae cell population projecting to area 18 (i.e., Y-cells) seems more affected by monocular suture than does the population projecting to area 17 (i.e., X- and Y-cells). Compared with their nondeprived counterparts, the cell population projecting to area 18 shows less soma growth and fewer numbers than does the population projecting to area 17.

These anatomical data have the virtue of being entirely free of electrode sampling biases, and they certainly suggest that geniculate Y-cells are more affected by lid suture than are geniculate X-cells. However, all the usual qualifications apply when anatomical data like these are interpreted in a physiological perspective. For example, it is not clear how a reduced extent of orthogradely transported amino acid or retrogradely transported HRP should be interpreted functionally.

6) Finally, there are preliminary, very limited data from intracellular staining and morphological analysis of deprived geniculate X- and Y-cells that suggest much more than a shift in electrode sampling biases is needed to explain the loss of recorded Y-cells. Friedlander et al. (82) have found that, although some deprived X- and Y-cells have fairly normal structure-function relationships, except perhaps for small somata, other deprived geniculate neurons have unusual features. Some deprived Y-cells have abnormalities in response properties as well as morphology, and some deprived cells with Y-cell structure seem to develop as functional X-cells. Neurons with X-cell physiology and Y-cell morphology are consistent with the earlier suggestion (180) that some deprived geniculate cells that normally would develop as Y-cells become X-cells instead. These data are too preliminary and sparse to evaluate properly, but they certainly suggest that processes other than electrode sampling must be considered to explain the electrophysiological data from visually deprived cats.

c) Conclusions. Obviously there is less than a complete picture of the potentially differential effects of visual deprivation on development of the W-, X-, and Y-cell pathways. Too few data are available for W-cells. Although

most attention has been focused on X- and Y-cells and considerable data have been generated, no single experiment convincingly demonstrates functional effects of deprivation selective to one of these pathways. The subtle effects of deprivation on the X-cell pathway are considered again in section VII*C1b*. Most of the data, albeit indirect, strongly support the notions that development of the Y-cell pathway is much more strongly affected by deprivation than is development of the W- and X-cell pathways, that these effects occur central to the optic tract, and that the Y-cell pathway is affected at the level of the lateral geniculate nucleus. In addition the overall inability of the deprived eye to drive cortical neurons suggests serious abnormalities in the W- and X-cell pathways as well, at least at the level of the striate cortex.

2. Mechanisms of X- and Y-cell development

We argue above that the effects of lid suture can be broken down into a binocularly competitive process and at least two noncompetitive processes that involve serial and lateral connections. Several possibilities can be suggested as to why geniculocortical Y-cells seem to be so differently affected by visual deprivation than are X-cells.

a) Binocular competition. The process of binocular competition requires that pathways from the two eyes interact and compete with one another during development. Interestingly, geniculate Y-cells in the normal adult show two different anatomical substrates for the occurrence of binocular interactions during development; X-cells share neither of these substrates.

The first substrate was suggested by Ferster and LeVay (72). They described the morphology of the individual geniculocortical axons tentatively identified as emanating from X- or Y-cells (see also 32, 95). The presumed X-cell axons have confined terminal arbors in cortex small enough to be limited to single ocular-dominance columns. Y-cell terminal arbors, in contrast, are much more extensive and must innervate several ocular-dominance columns related to one eye. This leads to the possibility that during early development, when the ocular-dominance columns are segregating (214), Y-cell axons from each lamina overlap and binocular interactions take place, whereas X-cell axons develop largely within a single ocular-dominance domain in which binocular interactions cannot occur. Perhaps geniculate Y-cells from one eye compete for cortical synaptic sites with Y-cells from the other eye, and this does not occur for geniculate X-cells. In monocularly sutured cats, the (nondeprived) Y-cells that emerge victorious develop normally, whereas the (deprived) losers do not. During binocular suture, a separate noncompetitive mechanism appears to control geniculate Y-cell development (see sect. VII*A1*).

The second potential morphological substrate for binocular interactions among geniculate Y-cells was found by Friedlander et al. (81) in normal

adult cats. These authors observed that every relay Y-cell has some dendrites that cross laminar borders. Y-cells thus have dendritic arborizations extending into domains related to each eye. X-cell dendrites, in contrast, are limited to a single geniculate lamina.

b) Delayed Y-cell development. Another factor that might contribute to the Y-cell susceptibility to early visual deprivation is the developmental time course of geniculate neurons. Geniculate X-cells begin to develop excellent responsiveness to visual stimulation fairly early and before the critical period begins, whereas Y-cell development lags behind to the point that these neurons are still quite immature as the critical period begins. Relatively mature neurons (X-cells) are possibly less likely to be affected by an abnormal sensory environment than are the more actively developing, immature neurons (Y-cells). In particular this late development of Y-cells could be a contributing factor in their susceptibility to binocular competition and/or to competition for appropriate (X- or Y-cell) retinal inputs.

Even the subtle effect of deprivation on geniculate X-cell development through a binocularly noncompetitive process could be related to this developmental time course. Although these X-cells normally develop visual responsiveness early, their development of spatial acuity is a slower process that extends through the first 4 mo after birth (164, 233). Continued development or maintenance of spatial acuity during the critical period might depend on normal afferent activity. Again this suggests that the last properties to develop are the most susceptible to lid suture.

C. Sites of Deprivation-Induced Abnormalities

A complete understanding of the consequences of visual deprivation on development of the central visual pathways requires the identification of which deprivation-induced abnormalities are primary and which are not. This is not trivial, and relevant data generally are lacking. An initial strategy for this identification might be to study the final pattern of neural deficits seen in adult cats raised with visual deprivation and consider a neuron's abnormality to be primary if it cannot be accounted for by abnormalities in the inputs to that neuron. For instance, abnormal geniculate neurons in the presence of normal retinal ganglion cells would suggest a primary abnormality in the retinogeniculate synapse, and at least some cortical deficits might be secondary to that. Thus the most peripheral sites at which further deficits are seen suggest that these represent primary abnormalities.

There are, however, serious flaws in this logic. For instance, abnormally slow development in a peripheral structure that ultimately achieves normal status could be the primary cause for deficits that develop more centrally. Also a primary deficit located centrally could cause secondary, later changes at more peripheral sites. For example, a retinogeniculate defect might itself occur later than and secondary to a primary geniculocortical deficit. Thus

one must know not only the pattern of abnormalities seen as a final consequence of early visual deprivation but also the temporal sequence by which this pattern develops. Because data from monocularly sutured cats are so much more extensive than those from binocularly deprived animals, our discussion below concentrates on monocular suture, and data from binocularly deprived cats are considered where available.

With these cautions in mind, there are several general and qualified conclusions that can be inferred from the final pattern of neural abnormalities seen in cats raised with monocular or binocular deprivation. First, no obvious deficits are found among the retinal ganglion cells of these cats, so primary deficits probably occur central to the optic tract. Second, studies of abnormalities among collicular neurons suggest that they result secondarily from abnormal corticotectal input and that the retinotectal input is essentially unaffected by the deprivation. Third, many of the deprivation-induced abnormalities seen in lateral suprasylvian cortex are secondary to deficits in areas 17 and/or 18. Some additional primary deficits occur in the thalamocortical pathway to this cortex, and these may be related to abnormal geniculocortical inputs to the lateral suprasylvian cortex. Therefore the retinogeniculocortical pathways (including geniculate pathways to lateral suprasylvian cortex) can be regarded as a major locus of primary deficits. We do not wish to imply that other deficits found and not covered in detail in this review (e.g., in corpus callosum projections, nucleus of the optic tract neurons) have their origins in geniculocortical abnormalities (e.g., 140, 168, 228). However, the evidence just discussed indicates that the lateral geniculate nucleus and striate cortex are fruitful structures in which to assess primary sites of deprivation-induced abnormalities at a synaptic level.

1. Primary deficits within the lateral geniculate nucleus?

The lateral geniculate nucleus represents the most peripheral site at which dramatic functional effects of early visual deprivation seem to occur. We have already discussed the problems with interpretation of these results, problems due mainly to vagaries of electrode sampling characteristics. Nonetheless we feel that the bulk of the evidence indicates both a serious deficit among Y-cells and a more subtle one among X-cells in deprived laminae. There is no concurrent physical loss of deprived neurons seen histologically, and the optic tract seems to include a normal population of axons with normal properties for both X- and Y-cells. Therefore the geniculate deficits are best explained by abnormalities among retinogeniculate synapses.

a) Y-cells. There are at least two types of retinogeniculate abnormalities, singly or in combination, that could be invoked to explain the loss of deprived Y-cells. First, the Y-cell retinogeniculate synapses could be nonfunctional, either because of deficiencies in the presynaptic terminals or because of postsynaptic (e.g., dendritic) pathology. In their ultrastructural studies of

the lateral geniculate nucleus in monocularly sutured cats, Winfield et al. (404–406) found no evidence of abnormalities among deprived optic tract synapses. However, Friedlander et al. (82) reported preliminary evidence of postsynaptic pathology that is not inconsistent with the presence of apparently normal optic tract terminals. The second and less straightforward possibility involves an abnormality by which X-cell axons from optic tract form synapses on presumptive Y-cells at the expense of Y-cell synapses. Such a change might not be evident at the ultrastructural level, since it is not clear how, if at all, terminals of optic tract X-cells differ from those of Y-cells.

b) X-cells. It is somewhat more difficult to imagine synaptic abnormalities that could explain the pattern of X-cell deficits involving a loss of spatial resolution. Two speculative possibilities can be suggested. First, the normal spatial resolution in deprived retina suggests that X-cells there that develop the highest spatial resolution may fail to generate stable retinogeniculate synapses. Since spatial resolution for these geniculate X-cells normally improves during the first 4 mo of a cat's life (164), visual deprivation might arrest the process at some point by prohibiting the formation of retinogeniculate synapses conveying higher-resolution information.

A second possibility is that the effects seen in the X-cell pathway represent a retrograde transneuronal process cascading down from the visual cortex. Support for this idea comes from recent studies showing a loss of retinal ganglion cells in cats raised with lesions of the visual cortex (178, 272; see also 393). X-cells are particularly susceptible to such a process (342). Perhaps the neurons most sensitive to such degenerative changes are the last X-cells to mature, which could also represent the cells with highest acuity. Mangel (233) reported that the loss of geniculate X-cell acuity does indeed seem to be a late-occurring degenerative process found in cats 6 mo of age or older, whereas younger cats show no X-cell abnormality. Perhaps this retrograde process stops at the retinogeniculate synapse in deprived animals. Alternatively, perhaps at the ages at which cats commonly are studied, the geniculate X-cells have degenerated and the retinal X-cells have had insufficient time to follow course. This can be investigated by studying cats raised for at least several years with visual deprivation.

Note that these possible explanations for the X-cell deficits suggest that abnormally few geniculate X-cells should exist in deprived laminae. No reports of a reduction in deprived X-cells exist, but most studies of lid-sutured cats are not designed to compare X-cell percentages in deprived and nondeprived laminae. Furthermore the preliminary results of Friedlander et al. (82) suggest that some neurons that would normally develop as Y-cells develop in deprived laminae as X-cells instead, and this process might counterbalance any expected reduction in deprived X-cell numbers.

c) Conclusions. Although the evidence clearly suggests the presence of retinogeniculate deficits in adult cats raised with visual deprivation, this does not necessarily imply that these are primary deficits. We have already

indicated the real possibility that deficits among geniculate X-cells are retrograde and secondary to primary cortical abnormalities. The same possibility exists for Y-cells. For example, one potential site of binocular competition among Y-cells is the binocular overlap among the immature geniculocortical axons of these cells (see discussion in sect. VII*B2a*). If Y-cells in deprived laminae fail to develop because they cannot establish functional geniculocortical synapses, then this geniculate abnormality should also be regarded as a secondary, retrograde consequence of a primary deficit occurring in the cortex. Indeed these retinogeniculate deficits also could be secondary, orthograde consequences of cortical abnormalities. That is, a massive corticogeniculate projection is well documented, and conceivably abnormal corticogeniculate input leads to the further development of geniculate deficits. Although Zetlan et al. (408) showed, for instance, that the Y-cell deficit in monocularly deprived cats is unaffected by cortical removal in adulthood, abnormal corticogeniculate input during the critical period might nonetheless cause the loss of recorded Y-cells. Therefore presently available data simply do not permit conclusions about whether these most peripherally occurring deficits among retinogeniculate synapses are primary or secondary to cortical pathology.

2. Primary deficits within the visual cortex?

Neurons of visual cortex undoubtedly develop abnormal functional properties during visual deprivation. A fundamental issue is the extent to which these abnormalities reflect secondary consequences of deficient geniculocortical input versus primary abnormalities at the cortical level. Both possibilities are explored below. Because most of these data are from the striate cortex, our discussion focuses on this area. Also most relevant data derive from monocularly sutured cats.

a) Primary cortical deficits. Significant primary deficits probably occur in striate cortex. Perhaps the strongest support for this idea comes from experiments in monocularly deprived cats, in which many geniculate neurons (X-cells) respond well to stimulation of the deprived eye but practically no cortical neurons outside of layer IV do so. Also, in the deprived monocular segment, all geniculate X- and Y-cells respond normally to most visual stimuli, but the cortical complex cells fail to develop normal response properties.

A major site of these abnormalities appears to be at the input synapses from deprived geniculate laminae to striate cortex neurons. Anatomical studies indicate that monocular deprivation leads to a reduced spread of geniculostriate terminals serving the deprived eye and an increased spread of terminals serving the nondeprived eye. In addition, current-source density analysis of potentials evoked in striate cortex by electrical stimulation of the afferent pathways shows that the monosynaptic excitatory activity for the deprived eye is reduced relative to that for the nondeprived eye. These

and other data suggest that excitatory geniculocortical synaptic connections for the deprived eye are reduced.

An additional cortical abnormality appears to involve inhibition of remaining inputs for the deprived eye by inputs for the nondeprived eye. Several types of evidence suggest this notion. Removal of the nondeprived eye produces a rapid increase in response of cortical neurons to the deprived eye. Although changes in the lateral geniculate nucleus (reappearance of Y-cells) also can be seen after enucleation, they take longer and require visual experience through the deprived eye (92). Therefore the primary site of the interocular inhibition and its reversal by enucleation probably lies in the cortex. The appearance of responses to the deprived eye after local iontophoresis of bicuculline also suggests a cortical site of inhibition of deprived eye activity. Finally, intracellular recordings show that stimulation of the nondeprived eye produces inhibitory postsynaptic potentials within the same cortical cells that receive subthreshold excitatory inputs from the deprived eye. Taken together these results suggest that the response of striate cortex cells to remaining inputs from deprived geniculate laminae is inhibited by nondeprived eye inputs within the striate cortex. One intracortical site of these interactions may be the borders of the layer IV ocular-dominance columns, where cells driven by the two eyes are intermingled in monocularly deprived cats. A second site of the interocular inhibition might be at the intracortical contacts between layer IV cells and cells in the upper and lower cortical layers. Evidence favoring these sites has been discussed elsewhere (339).

b) Nonprimary cortical deficits. Although many of the deprivation-induced abnormalities clearly occur within the striate cortex, their primary cause may lie outside the cortex. For example, the loss of excitatory connections for the deprived eye may simply reflect a loss of geniculate Y-cells and their inputs to cortex. Even the inability of remaining geniculate X-cells to drive many cortical neurons could, to some extent, be due to the loss of geniculate Y-cells. That is, normal Y-cell input to cortex may be needed at some time during development for X-cells to develop or maintain suprathreshold activation of cortical cells. Similar factors also could affect the development of abnormal intracortical inhibition in monocularly deprived cats.

c) Conclusions. When we consider the pattern of deficits developing in the lateral geniculate nucleus and striate cortex due to monocular or binocular deprivation, we find it impossible to determine unambiguously which are the primary deficits and which are nonprimary. This represents an embarrassing gap in our knowledge about the system. What is clearly needed is a detailed study of the dynamics of these patterns as they develop. There are too few such studies to address this issue definitively.

Nevertheless it is possible to outline what appear to be the best two candidates for primary sites of deprivation-induced changes. One is the Y-

cell retinogeniculate synapse, although the clear possibility exists that these abnormalities are retrograde consequences of the failure of geniculate Y-cells to develop cortical connections. The second candidate is at the cortical level, particularly with regard to input from X-cells. Indeed independent primary deficits could occur at both geniculate and cortical levels, and several primary deficits might occur within the complicated circuitry of the visual cortex. To go beyond such speculation requires a better understanding of the functional interrelationships among the various geniculate and cortical neurons in normal cats.

VIII. SUMMARY

In this review we have considered how early eyelid suture and dark rearing affects the development of the cat's central visual pathways. In particular we have focused on the neural sites at which the visual environment can interact with the developing visual system and on the mechanisms by which these interactions can occur. Although in most cases the data are insufficient to form definitive conclusions, we have been able to generate certain conclusions and useful working hypotheses.

A. Neural Sites of Abnormalities

Determinations of the primary and nonprimary (i.e., secondary, tertiary, etc.) sites at which visual deprivation causes developmental disorders are still largely speculative. We suggest from the available evidence that many of the primary deficits develop in the geniculocortical pathways and that many of the abnormalities in the superior colliculus and lateral syprasylvian cortex are thus secondary to the geniculocortical deficits. Contrary to the widely held view that deprivation-induced deficits are not seen peripheral to visual cortex (cf. 256, 298, 396), the evidence overwhelmingly supports the conclusion that functional deficits in lid-sutured and dark-reared cats exist at the level of the lateral geniculate nucleus (but not in the retina). Of course cortical deficits also exist in these cats, and it is not at all clear which geniculate or cortical deficits are primary and which are not. Primary deficits may develop independently at both sites during visual deprivation.

Within the geniculocortical pathways, we have separately considered evidence for deprivation-induced deficits in the W-, X-, and Y-cell pathways. Least is known about the W-cell pathway in normal or visually deprived cats. The very limited data suggest little or no effect of deprivation on this pathway, although we emphasize that future data could significantly alter this conclusion. Development of the X-cell pathway is affected moderately by visual deprivation. Geniculate X-cells in deprived laminae display only a subtle loss of spatial resolution, and even this deficit has not been uni-

versally replicated. These X-cells innervate striate cortex, but so few cortical cells can be driven from the deprived eye that the deprived X-cell pathway presumably exhibits more serious deficits at the cortical than at the geniculate level. Finally, the Y-cell pathway is most seriously affected, and significant deficits in this pathway are apparent in the lateral geniculate nucleus.

B. Developmental Mechanisms

We have defined two general forms of developmental mechanisms, competitive and noncompetitive, that can lead to neural abnormalities in visually deprived cats. Most of the relevant data are limited to binocularly competitive or noncompetitive mechanisms.

During monocular deprivation, both developmental processes evidently operate. For instance, binocular competition dominates development of geniculate Y-cells, but a noncompetitive process controls X-cell development. It is possible that competitive interactions occur between the earlier developing geniculate X-cells and later developing Y-cells, but relevant data are limited.

Mechanisms during binocular deprivation are more difficult to assess. It is not clear whether abnormal binocular competition operates during binocular deprivation. However, there is good evidence that the noncompetitive processes cause more serious deficits in these cats than in monocularly sutured cats. This means that either additional (or more severe) noncompetitive processes operate during binocular suture or the noncompetitive processes are qualitatively different and more deleterious during binocular than during monocular suture. The latter possibility suggests that comparisons between monocularly and binocularly sutured cats must be made with caution.

Finally, although we can identify certain competitive or noncompetitive processes, we can barely speculate about the synaptic events underlying these processes. There is limited evidence that visual deprivation can cause some synaptic circuitry to degenerate, some to arrest its further development, and some to develop but to be abnormally suppressed by other circuitry. For instance, recording of area 17 neurons in monocularly sutured cats with the nondeprived eye enucleated at various ages has provided evidence of all three synaptic processes. Much more data relevant to synaptic processes are needed. At present it seems that many different synaptic mechanisms combine to subserve the developmental mechanisms discussed in this review.

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