The Roles of Specificity and Competition in the Formation of a Laminated Colliculogeniculate Projection

J. Keith Sutton and Judy K. Brunso-Bechtold

Department of Anatomy, Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, North Carolina 27103

In the present study, we examined the colliculogeniculate projection in normal adult tree shrews and in adults that were bilaterally enucleated at birth. We injected lectin-conjugated HRP into superficial superior colliculus and then mapped the pattern of anterogradely transported enzyme in the ipsilateral dLGN. In normal adult tree shrews, the results confirm that the colliculogeniculate projection is laminated and terminates predominantly in small-celled layers 3 and 6 and in the interlaminar space between layers 4 and 5 (Fitzpatrick et al., 1980); we report an additional sparse projection to layer 4. In bilaterally enucleated animals, the colliculogeniculate projection is unlaminated and tends to terminate in the lateral two-thirds of the dLGN even though synaptic sites are vacated throughout the nucleus. We suggest that this preference may be due to a specificity of the colliculogeniculate fibers for the lateral two-thirds of the dLGN, which, in normal adult tree shrews, contains cells with similar physiological characteristics. We further suggest that the normal lamination of the colliculogeniculate projection in the lateral two-thirds of the dLGN may be due to competition with retinogeniculate fibers so that colliculogeniculate fibers terminate predominantly in layers containing small, W-like cells.

In adult tree shrews, the dorsal lateral geniculate nucleus (dLGN) contains 6 well-developed cell layers separated by cell-sparse interlaminar spaces and receives clearly laminated projections from 3 main sources of afferent input—the retina, visual cortex, and superior colliculus (for review, see Brunso-Bechtold and Casagrande, 1984; Casagrande and Brunso-Bechtold, 1985). In neonatal tree shrews, the anatomy of the dLGN is quite immature since the cell layers do not become distinct until during the second postnatal week (Brunso-Bechtold and Casagrande, 1981, 1982). Of the 3 main afferent projections, only the retinogeniculate projection terminates in a relatively mature pattern at birth (Brunso-Bechtold and Casagrande, 1982). At the same time, the corticogeniculate fibers have entered only the medial extreme of the nucleus (Brunso-Bechtold et al., 1982, 1983) and the colliculogeniculate fibers terminate in an unlaminated band throughout the mediolateral extent of the nucleus (Brunso-Bech-

told et al., 1982; J. K. Sutton and J. K. Brunso-Bechtold, unpublished observations).

If retinogeniculate fibers are removed at birth, cells in the dLGN do not segregate into distinct layers (Brunso-Bechtold and Casagrande, 1981; Guillery et al., 1985). Moreover, following bilateral enucleation at birth, the corticogeniculate projection no longer terminates most densely at the laminar borders as it does in normal adult tree shrews. Instead, the corticogeniculate projection terminates in an unlaminated band across the nucleus. These results have been interpreted to suggest that a competition with retinogeniculate fibers plays an important role in establishing a laminated corticogeniculate projection in normal animals (Brunso-Bechtold et al., 1983).

The question then arises of whether competition with retinogeniculate fibers also plays a role in determining the laminated colliculogeniculate projection pattern. This issue is of interest because the colliculogeniculate projection normally terminates in layers as well as in an interlaminar space. At birth, the projection extends entirely across the dLGN and thus coexists with retinogeniculate fibers in each presumptive cell layer (Brunso-Bechtold et al., 1982; J. K. Sutton and J. K. Brunso-Bechtold, unpublished observations). The colliculogeniculate fibers subsequently retract to the lateral two-thirds of the nucleus. The fibers further withdraw and terminate most densely in layers 3 and 6 and the interlaminar space between layers 4 and 5 (Fitzpatrick et al., 1980; Sutton and Brunso-Bechtold, 1985) with a somewhat less dense, intermittent termination in layer 4. This complex laminar and interlaminar projection pattern suggests that additional developmental mechanisms besides competition with retinogeniculate fibers may play a role in the establishment of the normal adult colliculogeniculate projection pattern.

In an effort to understand the mechanisms involved in the development of a laminated colliculogeniculate projection, we have removed the retinogeniculate fibers at birth and examined the colliculogeniculate projection pattern at maturity. We can then study which features of the normally laminated projection, if any, are retained and which features fail to develop. Our results will describe the colliculogeniculate projection in adult tree shrews that were bilaterally enucleated at birth in comparison with the projection pattern in normal adult animals. We will then discuss possible mechanisms that may be involved in the normal development of a laminated colliculogeniculate projection. Preliminary results were reported previously in abstract form (Sutton and Brunso-Bechtold, 1985).

Materials and Methods

We studied projections from superior colliculus to the dLGN in 3 normal adult tree shrews (*Tupaia belangeri*) and in 4 adult tree shrews that

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Correspondence should be addressed to Dr. Judy K. Brunso-Bechtold, Department of Anatomy, Bowman Gray School of Medicine, 300 S. Hawthorne Road, Winston-Salem, NC 27103.

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Figure 1. Schematic drawings of Nissl-stained, horizontal sections through the dLGN demonstrating the typical cellular distribution in a normal adult tree shrew (*A*) and in an adult tree shrew that was bilaterally enucleated at birth (*B*). *A*, In normal adults, 6 dLGN layers can be distinguished by the presence of relatively cell-free interlaminar spaces and also by cytological characteristics (Casagrande et al., 1978). For example, cells in layer 3 and 6 are smaller and stain lighter than those in the other layers. Additionally, cells in layer 6 are scattered in orientation when compared to the other layers in which cells are oriented perpendicular to the layers. *B*, Following bilateral enucleation at birth, interlaminar spaces do not form; however, laminar regions may still be distinguished on the basis of cytological characteristics (Brunso-Bechtold and Casagrande, 1982). For example, cells in layers 3 and 6 are small and stain lightly, while cells in layer 6 maintain their random orientation when compared to the other layers.

were bilaterally enucleated on the first postnatal day (P0). Since the projection from superior colliculus to the dLGN is entirely unilateral, each side of the brain can be used for a separate experiment. Thus, 6 colliculogeniculate projections were studied in 3 normal adult tree shrews and 6 colliculogeniculate projections were studied in 4 adult animals that were bilaterally enucleated at birth (for enucleation technique, see Brunso-Bechtold and Casagrande, 1981); the remaining 2 injections were unsuccessful. Each animal was anesthetized by intraperitoneal injection of sodium pentobarbital (55 mg/kg) and placed in a stereotaxic apparatus. A midsagittal incision was made through the scalp, and the skull was opened bilaterally over occipital cortex. The caudal poles of the occipital cortices were aspirated to reveal the superior colliculi.

Horse radish peroxidase conjugated with wheat germ agglutinin (WGA-HRP, Type VI; Sigma; St. Louis, MO; 1% in 0.9% PBS, pH 7.4) was injected (20–98 nl) into the superficial layers of the superior colliculi approximately 0.3 mm beneath the surface using a picospritzer (General Valve; Fairfield, NJ) and micropipettes having tip diameters in the range of 20–35 μ m. After the injections were made, saline-saturated pieces of Gelfoam were placed in the openings, and the incisions were closed with 6-0 silk suture.

After 21–28 hr, the animals were overdosed with sodium pentobarbital and transcardially perfused with 0.9% PBS followed by 1 liter of fixative (1.25% glutaraldehyde/1% paraformaldehyde, buffered at pH 7.4 with sodium phosphate, 4°C) at a flow rate of 2 liters/hr. The fixative was cleared by perfusion with a series of sucrose solutions at 4°C: 1 liter of 10% phosphate-buffered sucrose, followed by 250 ml 20% phosphate-buffered sucrose and 250 ml 30% phosphate-buffered sucrose (Gibson et al., 1984). Each brain then was removed from the skull and placed in 30% phosphate-buffered sucrose overnight at 4°C.

Frozen sections were cut at 40 μ m using a sliding microtome, and the tissue was processed according to Mesulam (1982). The only modification of this procedure was to use fresh solutions of 3,3',5,5'-tetramethylbenzidine (TMB; Sigma) and sodium nitroprusside (SNP; Fisher, Fairlawn, NJ) during enzymatic reaction with hydrogen peroxide. This modification reduced the formation of artifactual reaction product attributed to chemical contamination. Sections were mounted onto gelatin-coated glass slides, stained with neutral red (Fisher, 1% in 0.2 M acetate buffer, pH 3.3), and dehydrated in cold, acetate-buffered ethanols (Mesulam, 1982; Gibson et al., 1984). The slides were stored in sealed boxes containing silica gel desiccant at 4°C. The sections were then examined using both light- and dark-field optics on a Nikon Optiphot microscope equipped with a camera lucida attachment.

Results

The purpose of the present study was to examine the effects of the postnatal absence of retinogeniculate input from birth on the laminar organization of the colliculogeniculate projection in adult tree shrews. We therefore compared the distribution of WGA-HRP that was transported anterogradely from superficial layers of the superior colliculus to the dLGN in normal adult tree shrews with that in adult tree shrews that were bilaterally enucleated at birth.

Figure 1*A* shows a schematic drawing of the cytoarchitectural and cytological characteristics of the dLGN in a normal adult tree shrew. Six cell layers can be distinguished based upon the presence of interlaminar spaces and upon the cytological characteristics of individual layers (Casagrande et al., 1978; Brunso-Bechtold and Casagrande, 1982). For example, cells in layers 1, 2, 4, and 5 are larger and tend to stain darker than cells in layers 3 and 6. In addition, cells in layer 6 tend to be randomly oriented rather than arranged perpendicular to the layers as they are in the other cell layers.

The effects of bilateral enucleation on the appearance of the tree shrew dLGN have been reported previously (Brunso-Bechtold and Casagrande, 1981) and are illustrated schematically in Figure 1*B*. In the complete absence of retinal input, the dLGN is smaller and interlaminar spaces do not form. Nevertheless, presumptive laminar regions can be distinguished based on neuronal size, staining intensity, and orientation. For example, layers 3 and 6 can be delineated by the presence of small cells that do not stain heavily. Outside these 2 layers are larger, more darkly staining cells that compose unseparated layers 4 and 5, as well as unseparated layers 1 and 2. Determination of individual layers within these 2 bands of large cells is based on their location medial or lateral to an imaginary line that bisects these cell groups along their longitudinal axes.

Colliculogeniculate projection in normal adult tree shrews

A dark-field photomicrograph demonstrating the laminar pattern of reaction product in the dLGN of a normal adult tree shrew following a small injection of WGA-HRP into the ipsilateral superior colliculus is shown in Figure 2*A*. The dLGN cell layers (cf. Fig. 1*A*) can be seen in a light-field view of the same section (Fig. 2*B*), in which small arrows indicate the interlaminar spaces. The 3 most consistent sites of dense label are in-

Figure 2. Horizontal sections through the dLGN of a normal adult tree shrew (*A* and *B*) and through the dLGN of an adult tree shrew that was bilaterally enucleated at birth (*C* and *D*). Both animals received injections of WGA-HRP into the ipsilateral superior colliculus approximately 24 hr prior to sacrifice. *A*, Dark-field photomicrograph of the laminated colliculogeniculate projection in a normal adult tree shrew (TS 85-26 L). *Open arrows* indicate label found in layers 6 (*upper arrow*) and 3 (*lower arrow*); *solid arrow* indicates label found in the interlaminar space between layers 4 and 5. In this case, less dense label is also found between the *solid arrow* and the *lower open arrow*, i.e., in layer 4. *B*, Light-field view of the same section in *A* showing the nuclear boundaries and indicating individual layers. The *small arrows* indicate the interlaminar spaces. *C*, Dark-field photomicrograph demonstrating the unlaminated colliculogeniculate projection pattern in an adult tree shrew (TS 84-63 R) that was bilaterally enucleated at birth. *D*, Light-field view of the same section in *C* showing the nuclear boundaries. Comparison between *C* and *D* shows that the densest colliculogeniculate projection in bilaterally enucleated animals is to the lateral two-thirds of the nucleus. Note that in both *A* and *C*, label is infrequent in the medial one-third of the nucleus regardless of the presence or absence of retinal input. In each plate, medial is toward the *bottom* and caudal is toward the *right*. OT, optic tract. Scale bar, 0.5 mm.

Figure 3. Camera lucida drawings illustrating the termination of the colliculogeniculate projection in representative horizontal sections from 2 cases with WGA-HRP injections into the ipsilateral superior colliculus of normal adult tree shrews. The densest projection is to layers 3 and 6 and to the interlaminar space between layers 4 and 5; there is a less dense projection to layer 4. Label is never present in layer 1 and rarely in layer 2; fibers of passage are sometimes labeled in layer 5. Sections with the lowest numbers are the most dorsal. *Inset*, Drawing of a horizontal section through the superior colliculi indicating the location and extent of the injection site. *A*, Same case as in Figure 2, *A* and *B*. *B*, Similar, representative case from another normal animal. *OT*, optic tract; *SC*, superior colliculus; *c*, caudal; *l*, lateral; *m*, medial; *r*, rostral.

indicated by white arrows in Figure 2*A*. By comparison with Figure 2*B*, the upper open arrow indicates WGA-HRP reaction product in layer 6, along the optic tract; the lower open arrow indicates label in layer 3. The solid arrow indicates label in the interlaminar space between layers 4 and 5. The label between the solid arrow and the lower open arrow is in layer 4. Although label in layer 4 is quite apparent in this case, it is intermittent or absent in other cases.

Camera lucida drawings of the injection site and distribution of reaction product in individual dLGN sections from the case in Figure 2*A* are shown in Figure 3*A*; the injection site and sections from another representative normal case are shown in Figure 3*B*. As illustrated in the photomicrograph (Fig. 2*A*), in each normal adult animal, the termination of the colliculogeniculate projection is clearly laminated, with the densest label consistently present in layers 3 and 6 and in the interlaminar space between layers 4 and 5. Label is never seen in layer 1 or in the interlaminar space between layers 1 and 2, although very sparse label can be seen at the lateral edge of layer 2 in one case.

In layer 5, reaction product is rare; however, when present, it is distributed in a pattern resembling fibers of passage. In layer 4, labeled fibers of passage are also present along with intermittent, scattered terminals.

Colliculogeniculate projection in adult tree shrews that were bilaterally enucleated at birth

A dark-field photomicrograph of the distribution of label in the dLGN following a WGA-HRP injection into the superior colliculus of an adult tree shrew that was bilaterally enucleated at birth is shown in Figure 2*C*. As in the dLGN of a normal adult tree shrew (Fig. 2*A*), the WGA-HRP label in this dLGN extends across approximately the lateral two-thirds of the nucleus. In contrast to the laminated pattern of label seen in the dLGN of normal adult animals, the distribution of WGA-HRP label in bilaterally enucleated tree shrews is unlaminated within the termination area. Figure 2*D* is a light-field view of the same section as Figure 2*C* and demonstrates the absence of cellular segregation into layers following bilateral enucleation (cf. Fig. 1*B*).

Figure 4. Camera lucida drawings illustrating the termination of the colliculogeniculate projection in representative horizontal sections from 2 cases with WGA-HRP injections into the ipsilateral superior colliculus of adult tree shrews that were bilaterally enucleated at birth. Note that the projection is unlaminated and that even in the absence of retinal input, the colliculogeniculate projection does not extend to the medial border of the dLGN. Label is occasionally seen in the region of layer 2. In *A*, an isolated patch of label can be seen near the medial edge of the nucleus (i.e., section 22); however, cell orientation and serial reconstruction show that this label is not in the region of layer 1. Sections with the lowest numbers are the most dorsal. *Inset*, Drawing of a horizontal section through the superior colliculi indicating the location and extent of the injection site. *A*, Same case as in Figure 2, *C* and *D*. *B*, Similar, representative case from another bilaterally enucleated animal. SC, superior colliculus; c, caudal; l, lateral; m, medial; r, rostral.

Camera lucida drawings of individual sections from the case in Figure 2*C* are shown in Figure 4*A*; those from another representative enucleation case are shown in Figure 4*B*. In each bilaterally enucleated animal, label is present in an unlaminated band. In no case is there a concentration of labeled terminals in either the region of layer 3 (small, oriented cells in the middle of the nucleus), the region of layer 6 (small, scattered cells at the lateral edge of the nucleus), or the region of the border between layers 4 and 5 (middle of the group of large cells between layers 3 and 6). Label is found occasionally in the region of layer 2 (lateral half of the group of large cells medial to layer 3) and is shown in Figure 4*A* (e.g., sections 22, 27, 38). Serial reconstruction in this and similar cases, however, demonstrates that the label does not extend to the medial border of the nucleus. Thus, the colliculogeniculate projection in bilaterally enucleated tree shrews, as in normal adult animals, terminates predominantly in the lateral two-thirds of the dLGN. In contrast to

normal adult animals, the colliculogeniculate projection in bilaterally enucleated tree shrews is unlaminated and is somewhat more likely to terminate in the region of layer 2.

Topography of projection columns

The position of dLGN labeling varies systematically with the position of the superior colliculus injections in bilaterally enucleated as well as in normal adult tree shrews, suggesting that the topography of the colliculogeniculate projection seen in normal adult animals (Lane et al., 1971) is maintained following bilateral enucleation. This topographic relationship is summarized for the present results in Figure 5, which illustrates representative cases from 3 normal adult and 3 bilaterally enucleated tree shrews. In both sets of cases, rostromedial superior colliculus injections result in projections to caudal portions of the dLGN, and, conversely, more caudolateral superior colliculus injections result in projections to rostral portions of the

Figure 5. Schematic illustrations of representative superior colliculus and dLGN sections in normal adult (*A*) and bilaterally enucleated (*B*) tree shrews. The location and extent of WGA-HRP injections in the superior colliculus are shown on the *left*, while the location and extent of the densest distributions of anterograde labeling in the dLGN are shown on the *right*. *A*, The colliculogeniculate projection in normal adult tree shrews is topographic with rostromedial superior colliculus projecting to caudal dLGN and caudolateral superior colliculus projecting to rostral dLGN; this projection pattern is consistent with data from electrophysiological studies (Lane et al., 1971). *B*, The basic topographic organization of the colliculogeniculate projection is unchanged following the removal of retinogeniculate fibers. OT, optic tract; SC, superior colliculus; c, caudal; l, lateral; m, medial; r, rostral.

dLGN. No injections were made in the caudolateral extreme of the superior colliculus in order to avoid projections limited to the monocular segment of the dLGN (Lane et al., 1971).

Discussion

Distribution of the colliculogeniculate projection

Retrograde transport studies in several species have shown that the colliculogeniculate projection originates primarily in the upper division of stratum griseum superficiale (e.g., Robson and Hall, 1976; Albano et al., 1979; Graham and Casagrande, 1980; Kawamura et al., 1980; Harrell et al., 1982; for review, see also Huerta and Harting, 1984a, b). In adult tree shrews, as well as in several other species with laminated dLGNs such as squirrel monkeys (Harting et al., 1978), rhesus monkeys (Harting et al., 1980), and *Galago* (Fitzpatrick et al., 1980; Harting et al., 1986), anterograde tracing techniques demonstrate that the colliculogeniculate projection terminates in a laminated pattern in specific cell layers and interlaminar spaces.

Fitzpatrick et al. (1980) have reported that the colliculogeniculate projection in normal adult tree shrews terminates most densely in layers 3 and 6 and in the interlaminar space between layers 4 and 5. The results of the present study confirm this colliculogeniculate projection pattern and also suggest a smaller projection to layer 4 (confirmed by David Fitzpatrick, personal communication). In tree shrews, the primary colliculogeniculate targets, layers 3 and 6, both contain small cells (Casagrande et al., 1978) and receive input from small retinal ganglion cells (E. J. DeBruyn, J. T. Weber, and V. A. Casagrande, personal communication). Small retinal ganglion cells also project to superficial layers of the superior colliculus from which the colliculogeniculate projection originates (E. J. DeBruyn, J. T. Weber, and V. A. Casagrande, personal communication).

Small retinal ganglion cells in cats are classified as W-cells, having sluggish responses to visual stimuli and slow conduction velocities (Hoffmann, 1973; Boycott and Wässle, 1974; Fukuda and Stone, 1974; Stone and Fukuda, 1974). These small ganglion cells project heavily to the superficial layers of superior colliculus in cats and *Galago* (Fukuda and Stone, 1974; Itoh et al., 1981, 1982; see also Huerta and Harting, 1984b). In cats, fibers from these superficial collicular layers project to the lateralmost C layers of the dLGN (Graham, 1977; Torrealba et al., 1981) that contain small, W-cells (Wilson and Stone, 1975; Wilson et al., 1976; Stanford et al., 1983) and that also receive input from small retinal ganglion cells (Itoh et al., 1981). Similarly, colliculogeniculate fibers in *Galago* terminate in interlaminar zones and in small-cell layers in the dLGN (Fitzpatrick et al., 1980; Harting et al., 1986), both of which are reported to contain W-like cells (Norton and Casagrande, 1982; Irvin et al., 1986). In both tree shrews (Carey et al., 1979; Conley et al., 1984) and *Galago* (Carey et al., 1979; see also Casagrande and DeBruyn, 1982), the small-cell layers in which colliculogeniculate fibers terminate are unique since only these layers project to layers I and III of primary visual cortex. Thus, in several species, the visual pathway passing through the small-cell layers of the dLGN, both directly via small retinal ganglion cells and indirectly through superficial layers of superior colliculus, appears to be composed of small, W-like cells.

In normal adult tree shrews, the colliculogeniculate projection has 2 different target areas in that it terminates in selected cell layers and in an interlaminar space. In contrast, the mature corticogeniculate projection terminates predominantly in the interlaminar spaces (Brunso-Bechtold et al., 1983). Following

bilateral enucleation at birth, it has been shown that the corticogeniculate projection spreads homogeneously across all layers of the dLGN and does not terminate more densely at the presumptive laminar borders as might be expected in the absence of interlaminar spaces (Brunso-Bechtold et al., 1983). Perhaps, it is not surprising, then, that the colliculogeniculate projection does not terminate more densely at the laminar border between layers 4 and 5 following bilateral enucleation. However, it is noteworthy that the projection remains concentrated in the lateral two-thirds of the nucleus and that within that portion of the nucleus, the small-cell regions of layers 3 and 6 do not receive a denser projection than do the other presumptive layers.

Roles of specificity and competition in the establishment of the colliculogeniculate projection pattern

The normal, postnatal withdrawal of colliculogeniculate fibers from layers 1, 2, 4, and 5 to terminate in layers 3 and 6 could be due to one of 2 major factors, or a combination of both. First, this projection pattern could result from an inherent specificity of the colliculogeniculate fibers for a distinct population of cells as has been reported for regenerating retinotectal fibers in amphibians (Attardi and Sperry, 1963; Sperry, 1963; Fujisawa et al., 1981; see also Gaze, 1974). Alternately, the projection pattern could result from competition with other afferent fibers.

The present data demonstrate that in bilaterally enucleated tree shrews, as in normal adult animals, the vast majority of the colliculogeniculate projection remains concentrated in the lateral two-thirds of the nucleus. Thus, in the postnatal absence of competition with retinogeniculate fibers, the colliculogeniculate fibers do not project to the region of layer 1 at the medial extreme of the nucleus and project only intermittently to the region of layer 2, despite the presence of vacant retinogeniculate synaptic spaces *throughout* the nucleus. Presumably, those vacated synaptic spaces are the object of a competition between both of the dLGN afferent systems that remain after bilateral enucleation—the colliculogeniculate and corticogeniculate fibers. However, a competition between those 2 sets of fibers cannot explain the concentration of colliculogeniculate fibers in the lateral two-thirds of the nucleus since the corticogeniculate projection in bilaterally enucleated animals terminates homogeneously across the entire mediolateral dimension of the nucleus.

This line of reasoning leads to the conclusion that at least some degree of specificity may play a role in the establishment of the laminated colliculogeniculate projection in normal tree shrews and may result in the concentration of the projection in the lateral two-thirds of the nucleus in bilaterally enucleated animals. However, because the projection tends to extend somewhat more medially in the enucleated animals, there may be a "hierarchy of specificities" similar to that proposed by Hollyday et al. (1977) for neuromuscular innervation in chick embryos. According to this schema, the preferred termination of the colliculogeniculate fibers would be in the lateral two-thirds of the nucleus with any extension of the projection outside of that terminal area into the region of layer 2.

One possible basis for a specificity of the colliculogeniculate projection may lie in the cell type found in the lateral two-thirds of the nucleus. That portion of the nucleus clearly does not contain a morphologically homogeneous population since layers 3 and 6 contain small, presumably W-like cells and layers 4 and 5 contain large cells. The lateral two-thirds of the nucleus is, however, the only portion of the normal tree shrew dLGN in which OFF-center cells are found. Of cells that display center-

surround receptive field properties, Conway and Schiller (1983) report that layers 1 and 2 contain exclusively ON-center cells; that layers 3–5 contain 97% OFF-center cells; and that layer 6 contains a mixed population of ON-, OFF-, and ON-OFF-center cells. These physiological classifications are obviously meaningless in bilaterally enucleated animals; however, it is not unreasonable that there may be other cellular characteristics that co-vary with that physiological type and that remain following enucleation. Regardless of the basis for a specificity, the colliculogeniculate fibers do exhibit an apparent affinity for termination predominantly in the lateral two-thirds of the dLGN.

We cannot, of course, rule out the possibility that the developing fibers exhaust their capacity to expand before they have filled the nucleus. For example, the failure of the uncrossed retinogeniculate projection to fill the dLGN in monocular mice (Godement et al., 1980) could be explained by such an inability to expand. However, specificity for particular regions of the dLGN has also been included as one possible explanation of similar results in golden hamsters (So et al., 1984). Moreover, the extension of the colliculogeniculate fibers throughout the mediolateral extent of the nucleus at birth (Brunso-Bechtold et al., 1982; J. K. Sutton and J. K. Brunso-Bechtold, unpublished observations) suggests that, at least, in neonatal animals, these fibers do not lack the ability to extend to the medial border.

Within the lateral two-thirds of the nucleus, the colliculogeniculate projection normally becomes further restricted, predominantly to layers 3 and 6 and to the interlaminar space between layers 4 and 5. The fact that such a restriction does not take place in the absence of the retinogeniculate projection suggests that a competition between these 2 fiber systems may be essential for the establishment of the normal, laminated colliculogeniculate projection. Consistent with this hypothesis is the observation that the retinogeniculate and colliculogeniculate fibers overlap extensively at birth (Brunso-Bechtold et al., 1982; J. K. Sutton and J. K. Brunso-Bechtold, unpublished observations). Furthermore, retinogeniculate fibers project less densely to layer 3 (Glickstein, 1967; Conley et al., 1984). Therefore, one might argue that retinogeniculate cells in normal animals appear to display a higher affinity for non-W-like cells. However, the fact remains that in the absence of retinogeniculate fibers, the colliculogeniculate fibers do not display a preference for the small-cell regions. Finally, competition has already been shown to play a role in the development of a laminar pattern of corticogeniculate termination (Brunso-Bechtold et al., 1983).

Competition at the target is known to play an important role in determining connections in the developing nervous system (for review, see Purves, 1980; Purves and Lichtman, 1980, 1985; Oppenheim, 1981, 1985; Cunningham, 1982; Hamburger and Oppenheim, 1982; Cowan et al., 1984; Shatz and Sretavan, 1986). Competitive interactions in development may occur on 3 different levels. The first level is between cells in a single population, for example, between lateral motor column cells (Hamburger, 1975; Chu-Wang and Oppenheim, 1978a, b), ciliary ganglion cells (Landmesser and Pilar, 1978; Pilar et al., 1980), or retinal ganglion cells in the same eye for synaptic spaces at the target (Sretavan and Shatz, 1986b). A second level of competitive interactions is between fibers that differ in laterality, as in visual fibers driven by the right and left eyes (Hubel and Wiesel, 1962, 1965; Guillery, 1972; Rakic, 1976, 1977, 1981; Hubel et al., 1977; Constantine-Paton, 1982; Rakic and Riley, 1983; Shatz, 1983; Sretavan and Shatz, 1986a; for review, see also Shatz and Sretavan, 1986). Finally, competitive inter-

actions may occur between fibers from different populations that project to the same area and form separate terminal zones. An example of such a competition is that between the retinal, cortical, and collicular inputs converging on the dLGN (Brunso-Bechtold et al., 1983; present results). Accordingly, competition may result in the elimination of excess cells and the establishment of restricted terminal zones, as well as the appropriate termination of different afferent fiber systems within a target structure.

In summary, in both normal adult tree shrews and in adults that were bilaterally enucleated at birth, it appears that there is a greater specificity of the colliculogeniculate fibers for the lateral two-thirds of the dLGN, perhaps based on a general preference for the cell type found in layers 3–6. Within these layers, competition with retinogeniculate fibers appears to play a role in further restricting the colliculogeniculate projection to layers that contain small, W-like cells.

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