THE AUDITORY PSYCHOBIOLOGY OF THE MOUSE

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Chapter 7

ANATOMY OF THE CENTRAL AUDITORY SYSTEM

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Introduction

THE use of the mouse in neuroanatomical investigations was advocated by Ramón y Cajal (1909, 1937), who found that neonatal and juvenile mice were well impregnated by Golgi methods, and that following individual neurons and their processes was much easier in small brains. In the larger brains of carnivores and primates, the great and tortuous distances covered by the processes of larger cells defied most efforts at analysis (Ramón y Cajal, 1937). It was argued that investigations should begin with the rodent, proceed to larger mammals, and finally undertake the problem of the human brain. Consequently, Ramón y Cajal (1909) and his student, Lorente de Nó (1933, 1976, 1979), used the mouse extensively in their now classic studies. More recently, the availability of strains of mice that carry specific

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genetic abnormalities affecting the central nervous system has prompted a renewed interest in mouse neuroanatomy (Ross, 1962, 1965; Taber-Pierce, 1967; Caviness, 1975; Yorke and Caviness, 1975; Ollo and Schwartz, 1979; Caviness and Frost, 1980; Frost and Caviness, 1980; Martin, 1981).

Our interest in the neuroanatomical organization of the mouse auditory nervous system arises from a desire to understand the role of the brain in hearing. Classically, the auditory system has been regarded as consisting of neurons grouped into nuclei, which have been shown to receive a majority of their input (either directly or via synaptic relays) from the auditory nerve. Anatomical investigations of the auditory system have been conducted along two basic lines: one strategy has been to examine the neurons that comprise specific auditory nuclei, while the other has been to study the pattern of connections between auditory nuclei. Both types of morphological data are needed in order to establish the sequence in which auditory information is processed at the cellular level.

The sheer number and variety of cells in the brain poses technical problems in studying the central nervous system in mammals. Consequently, we have sought conceptual frameworks for our descriptive work by classifying cells into various groups. The utility of such an approach is that it allows us to formulate and test hypotheses about tissue organization and tissue interactions among neuron sets. Defining cell types, however, is a difficult task. Within most regions of the brain, more than one neuronal type is found, and the characteristics used in defining neuronal types show graded rather than abrupt changes in distribution. The problem of gradation found within any group of neurons defined as constituting a single class is compounded by the gradation of characteristics across cell classes. Furthermore, it remains to be determined which anatomical features are most useful in cell classification. Therefore, our classification schemes are not meant as a final definition of cell groupings but rather as an hypothesis that the cell groupings being delineated fulfill distinct functional roles.

The purpose of this chapter is to review the major anatomical features of the mature mouse auditory system, drawing mainly from our observations on ICR albino mice that have been made

over the past several years. Our discussion of the central auditory system will follow an orderly progression through the brain, beginning at the cochlear nucleus and ending at the auditory cortex (Fig. 7-1). The anatomical descriptions of the auditory nuclei

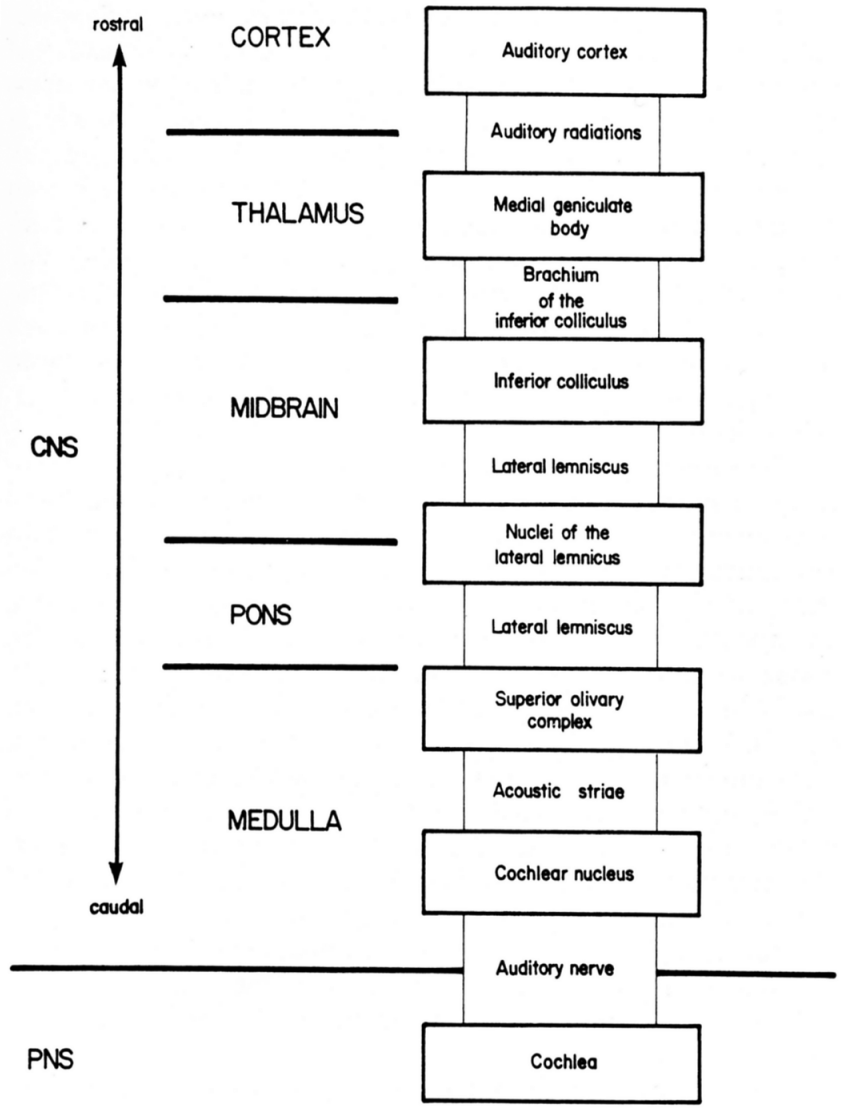


Figure 7-1. A simplified diagram illustrating the central auditory structures (thick lines) and their interconnecting pathways (thin lines) in relation to the major divisions of the mouse brain.

and their constituent cells are based on Nissl, protargol, and Golgi-stained material; the connections between auditory nuclei have been determined by anterograde degeneration methods and the retrograde transport of horseradish peroxidase (HRP). It is important to note that each of these techniques reveals only selected aspects of the neurons. Golgi methods have been particularly useful in revealing the overall form of individual neurons, but obscure the cytological details. On the other hand, Nissl stains and electron microscopy provide cytological detail but rarely, if ever, demonstrate individual neurons in their entirety. Only by piecing together data from many methods can we derive an anatomical concept of the neuron.

All descriptions and figures pertain to the mature mouse unless otherwise indicated. In a few instances, we presented data from the rat since nothing was available from the mouse. An atlas illustrating the histological appearance and spatial relationships of the various auditory nuclei is included as an appendix.

The Cochlear Nucleus

All of the known auditory input to the brain enters through the auditory nerve and terminates in the cochlear nucleus (Ramón y Cajal, 1909). The cochlear nucleus of the mouse is located on the lateral surface of the brain at the pontine-medullary junction. Its division into a dorsal and ventral part is visible externally, marked by a slight depression along its lateral surface (Fig. 7-2). In histological preparations, these two divisions are separated by a zone of granule cells and are quite distinct in their anatomical appearance (Figs. 7-37, 38). The auditory branch of the VIIIth cranial nerve enters the cochlear nucleus from the ventral surface. Each auditory nerve fiber bifurcates so that one branch proceeds rostrally (the ascending branch) and the other passes caudally (the descending branch).

Together, the two branches of each auditory nerve fiber innervate virtually the entire extent of the cochlear nucleus (Lorente de Nó, 1933). Axon collaterals can be seen to arise from these main branches throughout their trajectory. Two basic types of terminal endings are found: large, axosomatic endings called

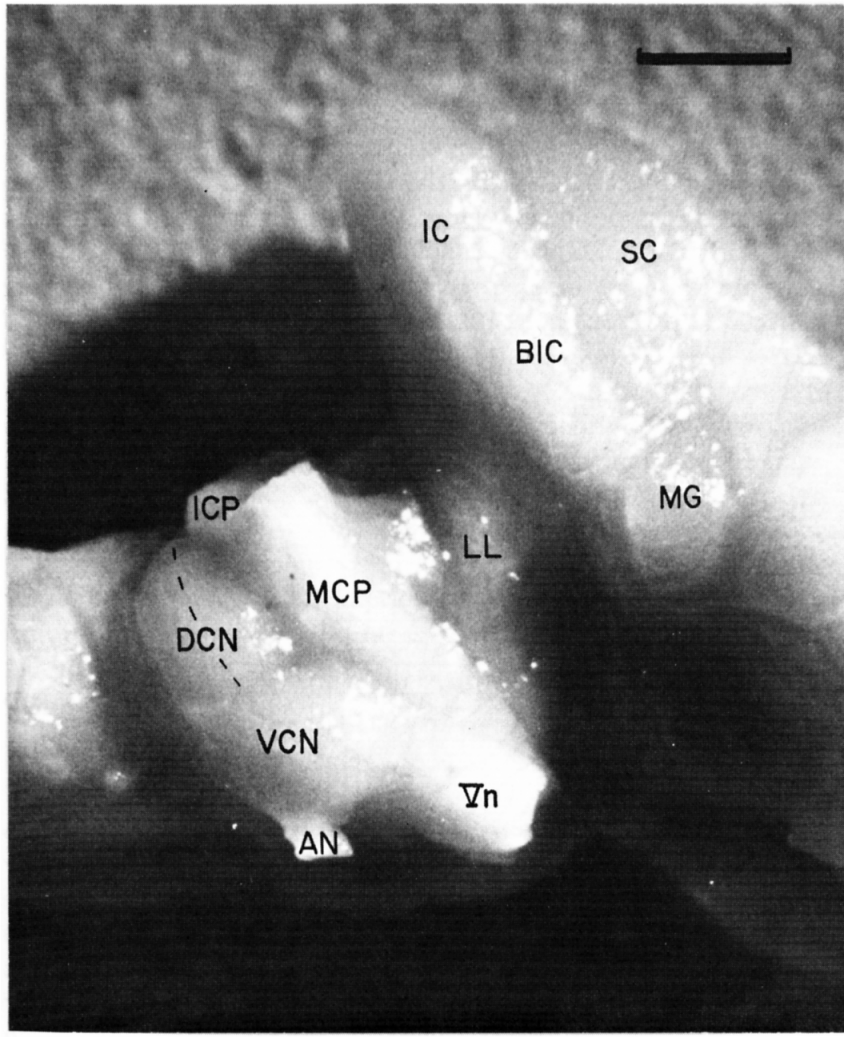


Figure 7-2. Lateral view of a mouse brain stem whose cerebral cortex and cerebellum have been removed. This photograph reveals the spatial relationship between some of the surface structures of the auditory system and other prominent landmarks. Rostral is to the right, dorsal is up. The dashed line indicates the long axis of the dorsal cochlear nucleus. Scale bar equals 1 mm. This photograph was provided by D.M. Fekete.

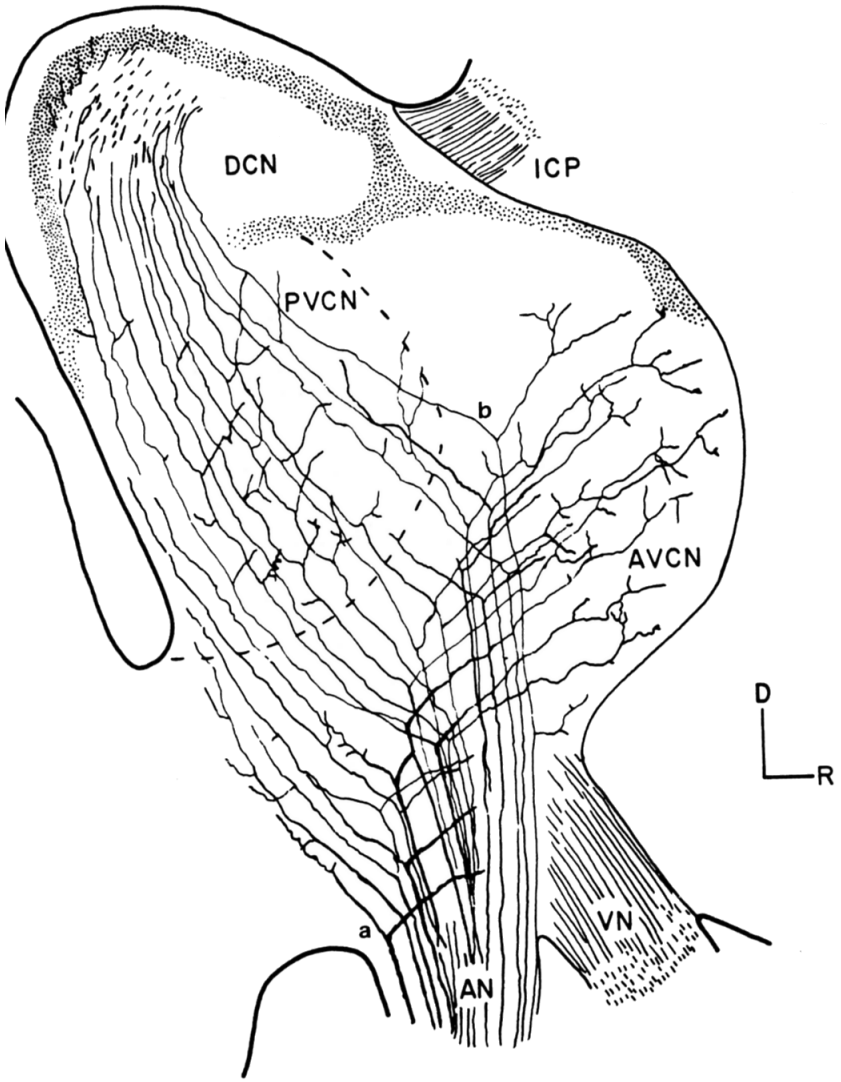


Figure 7-3. Modification of parasagittal drawing by Ramón y Cajal (fig. 329, 1909) illustrating the anatomical relationship between the auditory nerve fibers and the cochlear nucleus. Refer back to Figure 7-2 for additional orientation. Each auditory nerve fiber bifurcates upon entering the ventral cochlear nucleus. The bifurcation points and fiber trajectories maintain an orderly and stepwise spacing. Auditory nerve fibers arising from the apex of the cochlea (a) bifurcate in and project through the ventrolateral portion of the nucleus whereas fibers arising from progressively more basal regions of the cochlea (b) bifurcate in and project through progressively more dorsomedial regions of the nucleus. Stipple represents regional distribution of granule cells; note how the deep extension of granule cells delimits DCN and PVCN. The dashed line marks the approximate boundary between AVCN and PVCN. (List of abbreviations is on p. 287)

"endbulbs of Held" arise mainly from the ascending branches, whereas small boutons arise from loosely ramifying collaterals in all parts of the nucleus (Ramón y Cajal, 1909; Lorente de Nó, 1933).

The bifurcation and distribution of auditory nerve fibers are orderly within the cochlear nucleus. Fibers dividing most ventrally arise from the apex of the cochlea and are presumably most sensitive to low frequency sounds; fibers dividing in a progressively more dorsal and medial position arise from progressively more basal regions of the cochlea and are presumably most sensitive to progressively higher frequency sounds (Fig. 7-3). This arrangement of auditory nerve fibers connects points in the cochlea to neuron sheets in the cochlear nucleus, generating a topographic map of the acoustic receptors. This topographic map may be translated into a frequency map of the cochlea, and we refer to this relationship as "tonotopic organization" whereby the stimulus frequency to which neurons are maximally sensitive is found to vary systematically as a function of the neuron's position. Such tonotopic organization as determined by electrophysiological methods has been reported in the mouse (Mikaelian, 1966; *and* Chapter 8).

The Ventral Cochlear Nucleus (VCN)

The ventral cochlear nucleus appears as a prominence on the outer surface of the descending root of the trigeminal nerve. Its ventrolateral and posterior surface hangs free while its dorsolateral surface is covered by the overlying flocculus and paraflocculus of the cerebellum and the dorsal cochlear nucleus (Fig. 7-2). Medially, the ventral cochlear nucleus is bounded by fibers of the vestibular nerve and of the descending tract of the trigeminal nerve (Figs. 7-37, 38). Traditionally, the ventral cochlear nucleus has been separated into an anterior and a posterior division by the entry and bifurcation of the auditory nerve (Ramón y Cajal, 1909); however, on the basis of cytoarchitectonic criteria, the bifurcation of the auditory nerve does not determine this division (Brawer et al., 1974; Harrison and Irving, 1965; present authors). We have used the abrupt change in cell soma density as the most distinguishing feature between the two divisions (Fig. 7-4). The

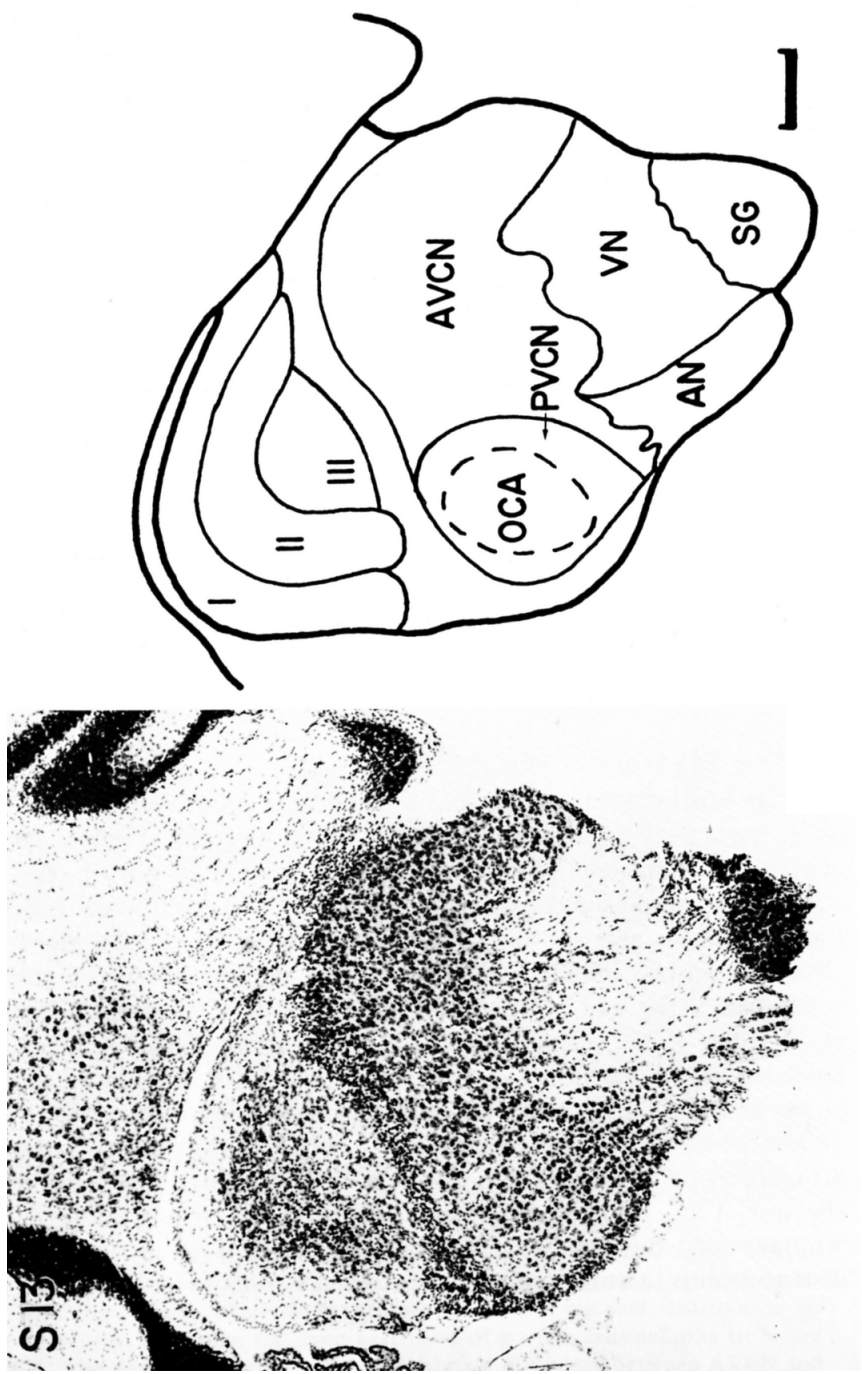


Figure 7-4. A sagittal view of the cochlear nucleus. An abrupt change in cell soma density has been used as a criterion for separating AVCN and PVCN. In the DCN of this section, three of the four layers are evident. The section is stained with cresyl violet; scale bar is equal to 200 μm.

region occupied by the bifurcations of auditory nerve fibers is termed the interstitial area (Lorente de Nó, 1933; Martin, 1981). The brief descriptions of the mouse cochlear nucleus prepared by Nissl stains (Ross, 1962, 1965; Mlonyeni, 1967; Taber-Pierce, 1967) has recently been augmented by an analysis of cell types (Fekete, 1979; Martin, 1981), applying the basic criteria developed for the cochlear nucleus of the cat (Osen, 1969).

In the ventral cochlear nucleus, spherical cells (Fig. 7-5A) tend to be concentrated in the rostral regions of the anterior division. These cells have round or oval shapes and always have a centrally placed nucleus. The cytoplasmic Nissl substance is fine and lightly staining and sometimes forms a ring of darkly staining Nissl clumps surrounding the nucleus. In the cat the Nissl "necklace" is suspended within the cytoplasm (Osen, 1969). In mice, this "necklace" of Nissl may be found immediately adjacent to the nuclear periphery (Martin, 1981) or it may appear suspended within the cytoplasm.

The globular cells (Fig. 7-5B) surround and infiltrate the zone of bifurcations, embedding themselves within the fascicles of auditory nerve fibers. The result is that globular cells characterize the interstitial area, and, therefore, are found in the adjacent parts of both anterior and posterior divisions. These cells are oval in shape and are distinguished by the eccentrically placed nuclei. The Nissl substance is fine-to-granular and characteristically demonstrates a blotchy staining pattern similar to that seen in Figure 7-5B.

The multipolar cells (Fig. 7-5C) seem to be ubiquitous throughout ventral cochlear nucleus, although they are rarely found in the octopus cell area of the posterior division (Ryugo et al., 1981). Their heterogeneity in size, shape, and Nissl patterns suggest that they do not constitute a homogeneous class. Some cells of this general class project to the contralateral inferior

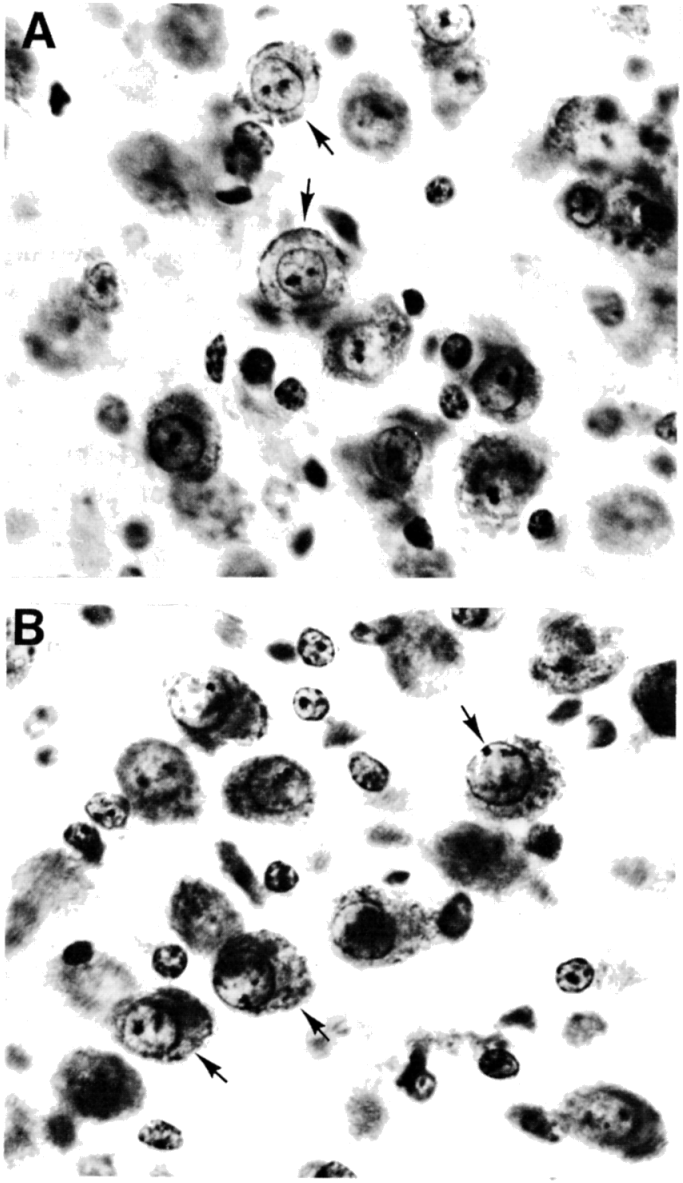
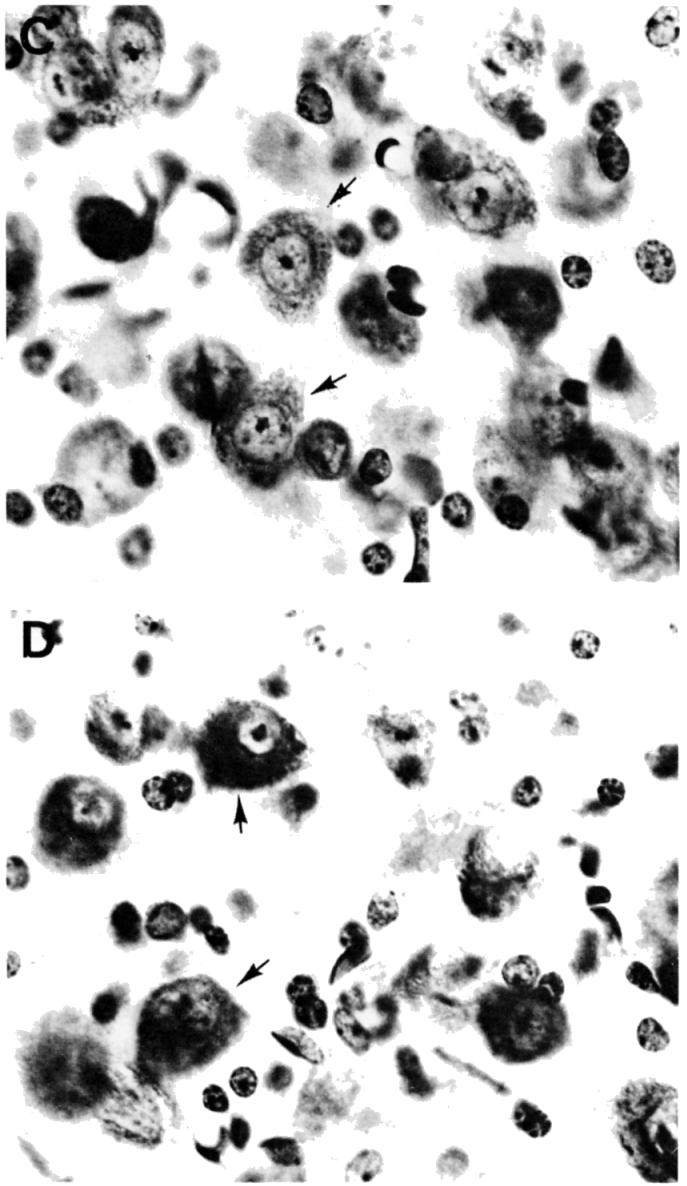


Figure 7-5. Photomicrographs of Nissl-stained sections from the ventral cochlear nucleus illustrating typical specimens from identified cell classes (arrows): (A) spherical cells; (B) globular cells; (C) multipolar cells; (D) octopus cells; and (E) auditory nerve neurons. The parasagittal diagram of the cochlear nucleus (F) indicates the region from which respective photomicrographs were taken. Photomicrographs are reproduced to the same magnification. Scale bar in (E) equals 20 μm.



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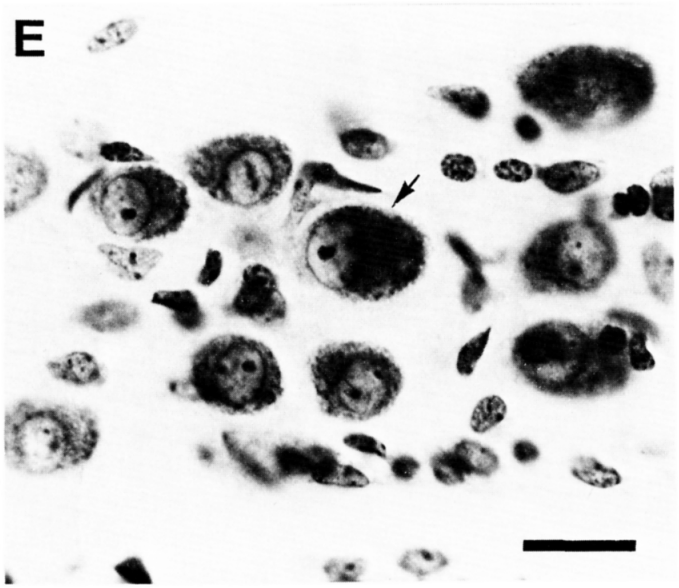


Figure 7-5 continued.

colliculus (Ryugo et al., 1981).

The octopus cells (Fig. 7-5D), also called "dark-staining" cells by Martin (1981), are confined to the caudal pole of the posterior division, a region called the octopus cell area. Octopus cells are large and exhibit evenly and densely dispersed Nissl substance. The nucleus is round and tends to be eccentrically placed. A prominent Nissl cap overlying the nucleus is characteristically located on the side closest to the cell's geometric center (Fekete, 1979). One to four primary dendritic processes may be seen, often emerging from one side of the cell in a position opposite to the eccentrically placed nucleus. Octopus cells are thought not to project to the inferior colliculus because they never contain HRP reaction product following HRP injections into the colliculus (Ryugo et al., 1981).

The so-called "auditory nerve neurons" (Harrison and Warr, 1962), not to be confused with spiral ganglion cells of the cochlea, which give rise to auditory nerve fibers, are found within the auditory nerve, located between the Schwann-glia border and the zone of bifurcations (Fekete, 1979). Their cell bodies are oval and the largest in the mouse auditory system (Fig. 7-5E). They have dense, uniformly staining Nissl substance and an eccentrically placed nucleus. The smallest of these auditory nerve neurons are strikingly similar in appearance to globular cells; however, auditory nerve neurons are not large globular cells since they differ in dendritic morphology and are HRP positive following HRP injections into the inferior colliculus (Willard et al., 1978) while globular cells are not (Ryugo et al., 1981).

The small cells form another heterogeneous group of neurons found throughout ventral cochlear nucleus. Martin (1981) considers small cells and fusiform cells as a single class; he argues that a fusiform cell sectioned across its short axis would have the same appearance as that of a small cell. Although this is certainly true, it does not mean that all small cells must be fusiform cells. The small cells have relatively little cytoplasm, but their variability in Nissl patterns and somal shapes suggest that more than one small cell type may eventually be distinguished.

The granule cells of the cochlear nucleus are found in two main areas: they congregate along the dorsal and lateral surface of the ventral cochlear nucleus, separating it from the overlying dorsal

cochlear nucleus, and they are concentrated in layer II (the granule cell layer) of dorsal cochlear nucleus. These tightly packed cells are small with round cell bodies that are 4-6 μm in diameter. Their distribution and morphology have been reported in detail by Mugnaini et al. (1980a,b).

The Dorsal Cochlear Nucleus (DCN)

The dorsal cochlear nucleus lies dorsal to the posterior region of ventral cochlear nucleus. This horn-shaped structure curves over the dorsolateral convexity of the brain stem and its long axis extends from the narrow dorsomedial apex to its broader ventrolateral base (Fig. 7-2). It is a cortical structure with four layers that may be identified on the basis of cellular composition and fibroarchitecture. We have adopted most of the nomenclature of Mugnaini et al. (1980a,b) for our discussion of the dorsal cochlear nucleus. There are two superficial layers (I and II), which envelope the wedge-shaped core (layer III), and these regions overlie the basal layer IV (Figs. 7-4, 7-6A, 7-37, 7-38).

Layer I, also called the molecular layer, is situated just beneath the ependymal cells. This most superficial layer is approximately 75 μm in depth and is composed mainly of small caliber fibers and the apical dendrites of deeper lying cells; it is conspicuous by the presence of very few cell bodies.

Layer II is characterized by a high concentration of granule cells and the presence of round cells and large multipolar cells (Fig. 7-6B, C). Accordingly, Ramón y Cajal (1909) called this layer the granule cell layer. The multipolar cells have also been called pyramidal cells (Ramón y Cajal, 1909) or bipolar cells (Lorente de Nó, 1933), although they are actually planar cells whose dendrites generate a disc-shaped domain. We shall refer to these large planar, multipolar cells as the principal cells of the dorsal cochlear nucleus.

Layer III has a lower cell density than layer II; it contains a heterogeneous population of neurons including some of those found in layer II and many large caliber fibers. Due to its complex composition, this central core of the dorsal cochlear nucleus has also been called the deep polymorphic layer (Lorente de Nó, 1933). This layer is thickest in the ventrolateral portion of the

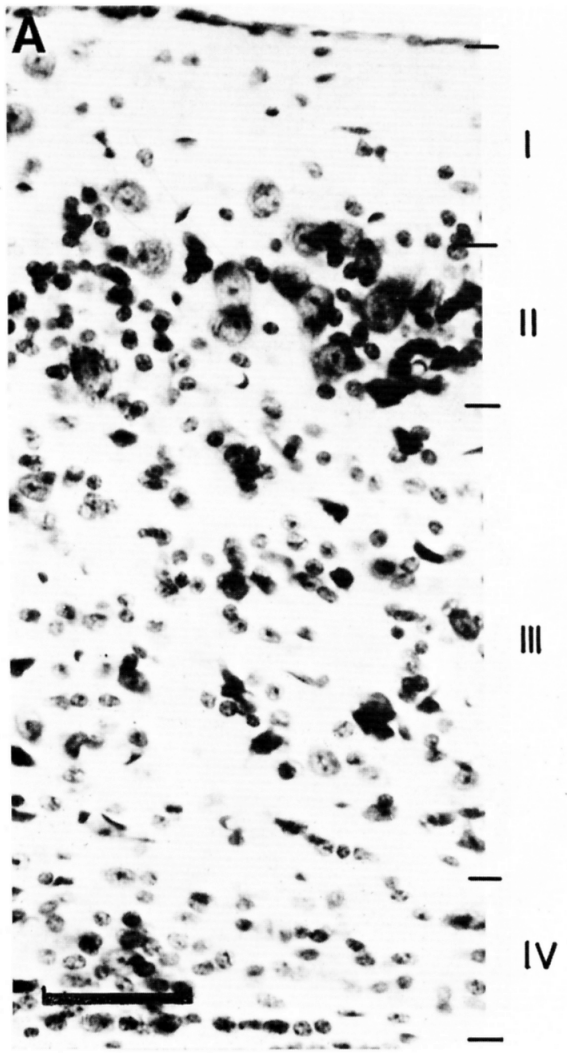
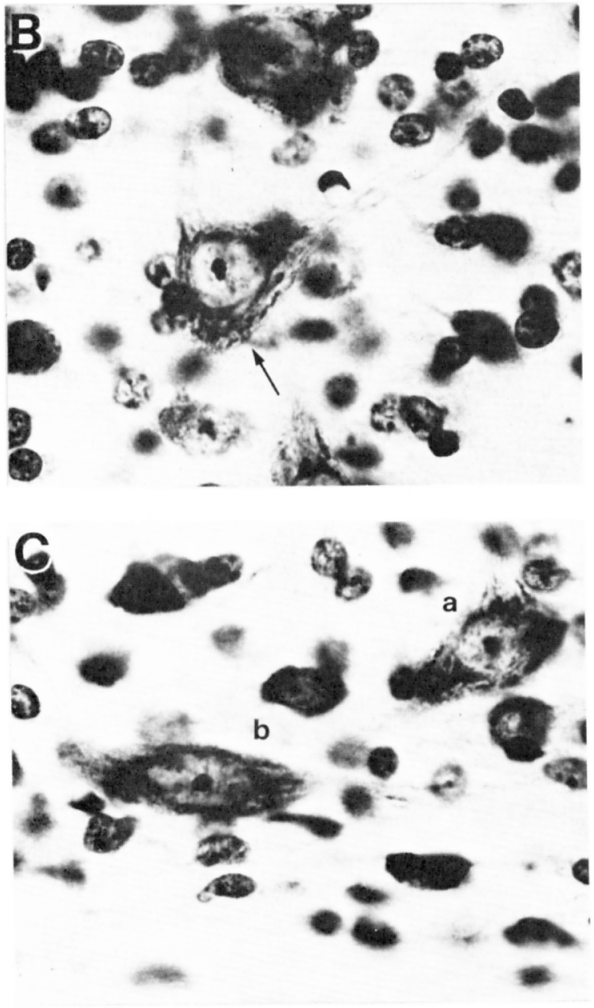


Figure 7-6. Cytoarchitecture of the dorsal cochlear nucleus. A. Photomicrograph of a section oriented perpendicular to the long axis of the dorsal cochlear nucleus and demonstrating its layered arrangement. Individual layers are labelled by Roman numerals. Scale bar equals 50 μm. B. Large multipolar neuron (arrow) in layer II. C. Large multipolar neurons in layer III (a) and IV (b). D. Small multipolar neurons (arrows) in layer III. E. Round cell (arrow) in layer II. Scale bar in E equals 20 μm and applies to photomicrographs B-E.



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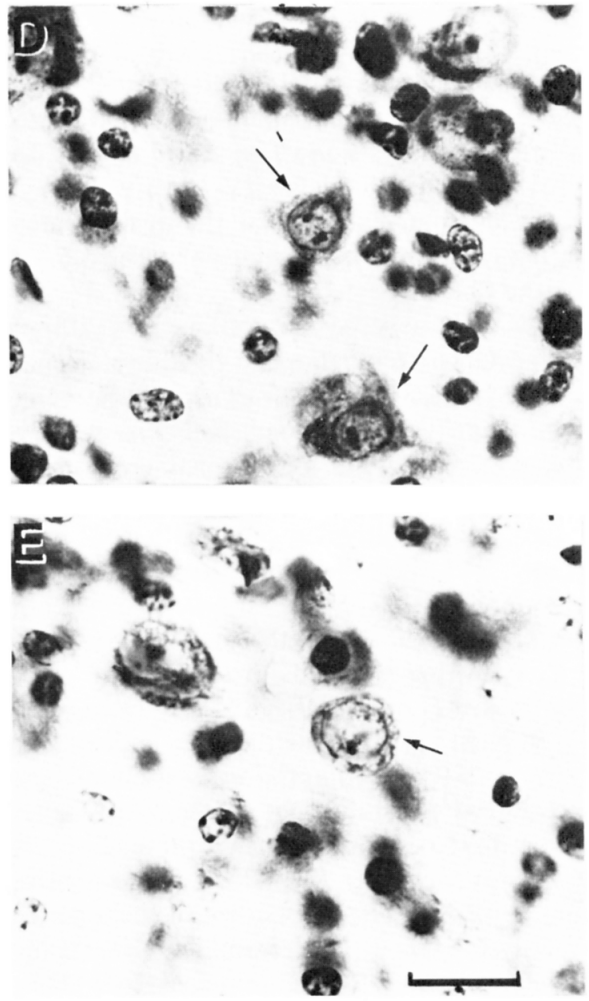


Figure 7-6 continued.

nucleus and progressively diminishes in depth at more dorsomedial levels.

Layer IV is termed the strial layer because it contains primarily the efferent fibers contributing to the dorsal acoustic stria. These efferent fibers collect in layer IV and then course dorsomedially; consequently, layer IV progressively increases in thickness as the dorsomedial apex of the nucleus is approached. There are a few scattered large multipolar cells and small cells mixed among the fibers.

There is a wide variety of morphologically different cells as seen in Nissl and Golgi preparations of the dorsal cochlear nucleus (Lorente de Nó, 1933). The cells vary according to size, shape, Nissl patterns, dendritic morphology, and position. Despite such heterogeneity, we have found three general classes of neurons, in addition to the glia and granule cells – large multipolar cells, round cells, and small multipolar cells. With additional information, we expect that these general classes can be further subdivided.

The most prominent cells of the nucleus are the large multipolar cells. Contained within this group are the pyramidal and giant cells of the cat (Lorente de Nó, 1933; Osen, 1969; Brawer et al., 1974). In Nissl preparations the large multipolar cell bodies range in size from 250 to 500 μm^2 in cross-sectional area (digital analyzer, uncorrected for shrinkage). These cells have an intensely staining cytoplasm that contains many prominent Nissl bodies. The nucleus is rounded, centrally located, and bears a single nucleolus (Fig. 7-6B, C). The cell bodies of these neurons are distributed primarily in layer II (approximately 75%) and, therefore, most certainly correspond to the principal cells; the remaining large multipolar cells are scattered in layers III (approximately 20%) and IV (approximately 5%). Regardless of their position in the layers, all of the neurons have three to five thick proximal dendrites. Most of these cells (90-95%) have dendritic arbors that exhibit very little medial-lateral spread, producing neurons that have essentially a two-dimensional shape. The orientation of these cells and their dendrites conforms to a series of planes oriented perpendicular to the long axis of the nucleus and parallel to the trajectory of primary afferent fibers. These planar-shaped principal neurons probably correspond to the pyramidal or fusiform neurons reported in other species. A few of the large multipolar neurons located in the deep portion of layer III and in layer IV have dendrites that spread out in all directions and, thereby, lack a planar shape. Such nonplanar cells appear similar to the giant cells of the cat, an observation corroborated by Mugnaini (personal communication). All of the large multipolar neurons, planar and nonplanar, project axons to the inferior colliculus (Ryugo et al., 1981).

The round cells have a somal size that ranges from 125 to 250 μm^2 in cross-sectional area. Each cell has a thin rim of cytoplasm that surrounds the centrally located nucleus (Fig. 7-6E). These cells are found mainly in layer II, but are also scattered within layer I and the upper part of layer III. In Golgi preparations, it becomes possible to distinguish at least two different types of round cells. The first type exhibits one or two thin dendrites, which have a limited number of branches. The distal dendrites are smooth and each dendrite terminates in a small, beaded enlargement. These cells seem to coincide with the Golgi cells of the dorsal cochlear nucleus described by Mugnaini et al. (1980a,b). The second type of round cell has one or two thin proximal dendrites, but these dendrites undergo extensive branching within layer I and are studded with spines. These latter cells share similar morphological features with the cartwheel cells of the cat described by Brawer et al. (1974).

The small multipolar cells have a cell body that varies in size from 75 to 250 μm^2 in cross-sectional area and is quite irregular in profile. The cytoplasm contains fine, granular Nissl substance that stains with a wide range of intensity. These cells are primarily located in Layer III, but may be found in all layers of the nucleus (Fig. 7-6D). Their variability in size, shape, and location suggests that there may be more than one cell type assigned to this class, but the critical data are lacking.

Connections of the Cochlear Nucleus

The cochlear nucleus is a key structure in the auditory pathway. All ascending pathways in the brain are thought to originate in the cochlear nucleus, since no primary fibers of the auditory

nerve bypass the nucleus (Ramón y Cajal, 1909). Consequently, the manner in which the cochlear nucleus establishes its connections with other auditory nuclei is basic to understanding the anatomical organization of the central auditory system. Some general features of the ascending auditory pathways in mammals have been reviewed (Harrison and Howe, 1974; Harrison, 1978a,b), but such information pertaining to the mouse has been wholly lacking. Furthermore, virtually nothing is known about intrinsic connections. We have found only one illustration of descending fibers entering the deep layers of the dorsal cochlear nucleus from the trapezoid body (Lorente de Nó, 1933); however, the origin of the descending fibers remains to be determined.

We have studied the anatomical connections between the inferior colliculus and the cochlear nucleus using both retrograde and anterograde methods (Ryugo et al., 1981). We demonstrated that narrow, vertical sheets of neurons are arrayed along the rostrocaudal dimension of the cochlear nucleus and project to restricted laminae in the central nucleus of the inferior colliculus. This sheet-like arrangement of efferent neurons corresponds to the course and termination of the primary afferent fibers (Ramón y Cajal, 1909) and is consistent with the reported tonotopic organization of the cochlear nucleus (Mikaelian, 1966). Presumably, the topography of these connections accounts for, at least in part, the tonotopicity reported for the central nucleus of the inferior colliculus (Harnischfeger, 1978). In addition, we demonstrated a projection from the dorsal cochlear nucleus to the external cortex of the inferior colliculus. Thus, it becomes apparent that the cytoarchitectonic distinctions within the cochlear nucleus are complemented by their differential pattern of connections with the inferior colliculus. The next step is to identify those cell classes which issue these projections.

We have confirmed our HRP data on dorsal cochlear nucleus connections using anterograde degeneration techniques (Willard and Ryugo, 1979): lesions in the dorsal acoustic stria, the efferent pathway for the dorsal cochlear nucleus, produced degeneration within the contralateral ventral nucleus of the lateral lemniscus and in the central nucleus and external cortex of the inferior

colliculus. In this material, some degenerating axons clearly branched and innervated both regions of the inferior colliculus We have been unable to detect any projections from the cochlea nucleus to the dorsal cortex of the inferior colliculus.

The ascending projections of the cochlear nucleus are summarized in Figure 7-7. The dashed lines represent pathways re

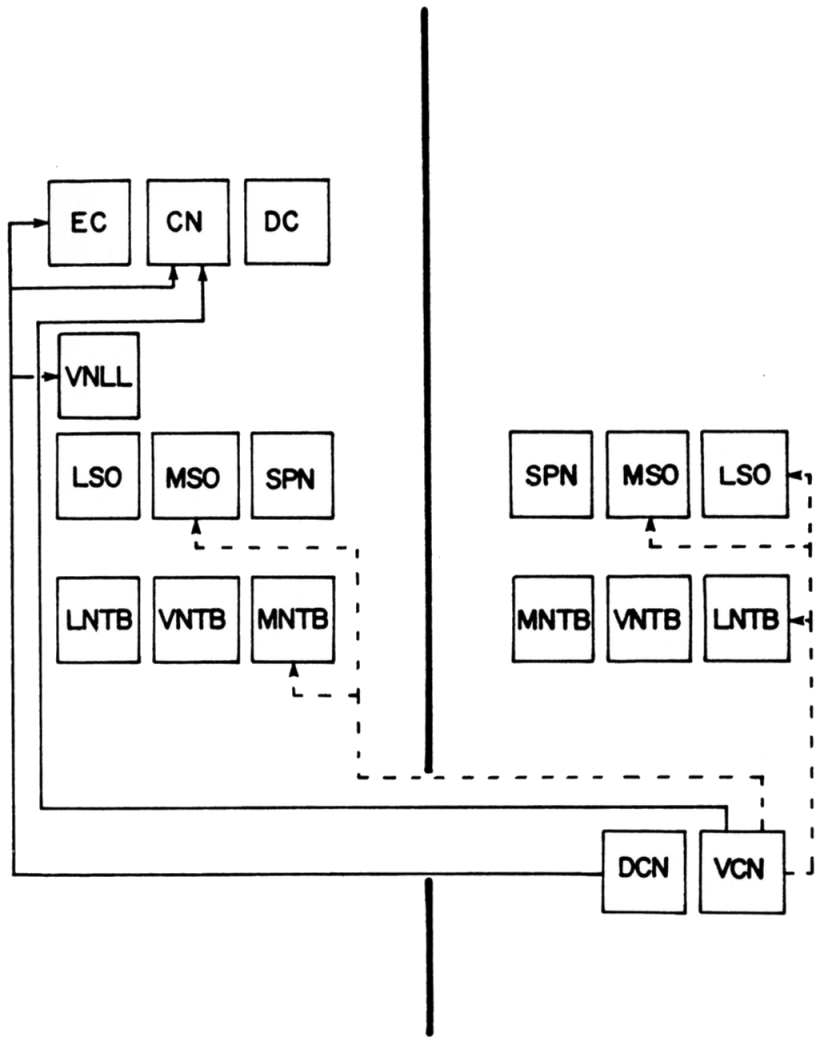


Figure 7-7. A schematic diagram summarizing the known projections fror the cochlear nucleus to other brain stem nuclei. The solid lines represen pathways demonstrated in the mouse (Ryugo et al., 1981) and the dashe lines indicate pathways demonstrated in the rat (Harrison and Irving, 1966) The thick, vertical line represents the midline.

ported for the rat (Harrison and Irving, 1966); the solid lines represent the known pathways of the mouse (Ryugo et al., 1981).

The Superior Olivary Complex (SOC)

The superior olivary complex is a collection of neuronal groups located in the ventral tegmentum of the posterior pons, just rostral to the facial nucleus and caudal to the ventral nucleus of the lateral lemniscus. The cells of the superior olivary complex are embedded in a dense matrix of neuropil and delimited from the surrounding brain tissue by a thin fiber capsule. On the basis of spatial relationships and the morphological characteristics of the constituent neurons, six nuclear groups have been identified in the mouse complex (Ollo and Schwartz, 1979; present authors); these are the lateral superior olive, medial superior olive, superior paraolivary nucleus, and the medial, lateral, and ventral nuclei of the trapezoid body (Fig. 7-39). The relative spatial relationships among the four most prominent components in the superior olivary complex are illustrated in Figure 7-8.

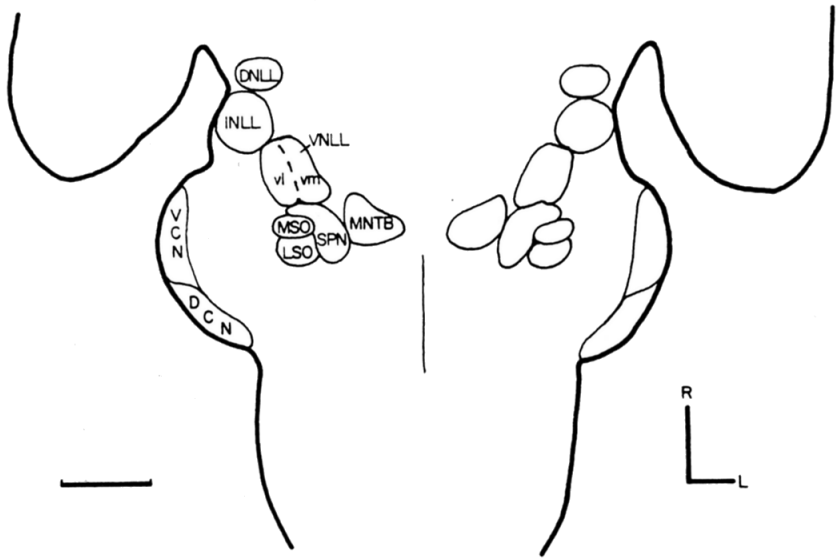


Figure 7-8. A schematic diagram of a horizontal section through the brain stem illustrating the spatial relationships of auditory nuclei. Scale bar is equal to 1 mm.

Lateral Superior Olive (LSO)

The lateral superior olive occupies the lateral position within the olivary complex (Fig. 7-8; Fig. 7-39 section C21, C24). This nucleus consists of a 200 to 300 μm thick slab of cells that is folded back on itself so that when viewed in the coronal plane, the nucleus is S-shaped (Fig. 7-9). Three types of cells have been identified in the lateral superior olive; they are principal cells, marginal cells, and spindle cells (Ollo and Schwartz, 1979).

The principal cells form the core of the nucleus and are arranged in rostrocaudally oriented sheets; in coronal sections, these sheets appear as cords of cells radiating from a prominent dorsal hilus and a less prominent ventral hilus (Fig. 7-9A). The principal cell has an oval to pear-shaped cell body whose dimensions are approximately 12 X 15 μm (Fig. 7-10A).

The cytoplasm consists of fine-grained Nissl substance that stains intensely. The nucleus is oval and pale in appearance and occupies a significant portion of the cell body. In Golgi preparations, several additional features of these cells are revealed; the main characteristic of the principal cells is the planar shape of their dendritic field. The dendrites exhibit many varicosities, branch frequently, and project along the dorsoventral and rostrocaudal axis but not along the mediolateral axis. The common alignment of these planar-shaped neurons endows the nucleus with a laminar appearance when viewed in the coronal or horizontal plane. A similar arrangement of principal cells is seen in the lateral superior olive of the cat (Scheibel and Scheibel, 1974).

The largest cells of the lateral superior olive are found along the caudal, dorsal, and lateral margins of the nucleus; consequently, they have been named marginal cells. Marginal cells have pyramidal-shaped cell bodies having dimensions of 20 X 20 μm (Fig. 7-10B). Their nuclei are round and centrally located and the cytoplasm has coarse, granular Nissl substance that aggregates into several intensely staining patches. The dendrites of the marginal cells tend to form a sheath that conforms to the contours of the nucleus. Rostrally, the marginal cells merge with the cells of the ventral nucleus of the lateral lemniscus and superior paraolivary nucleus.

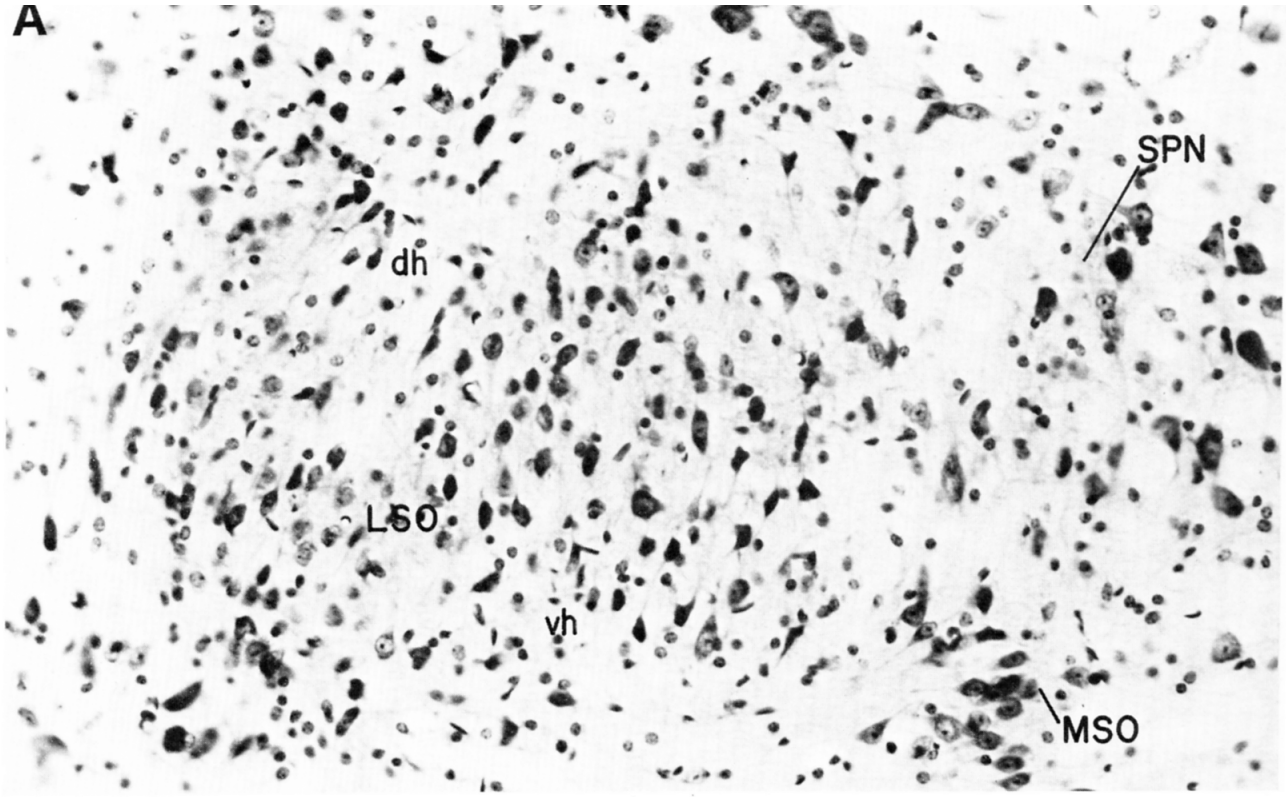
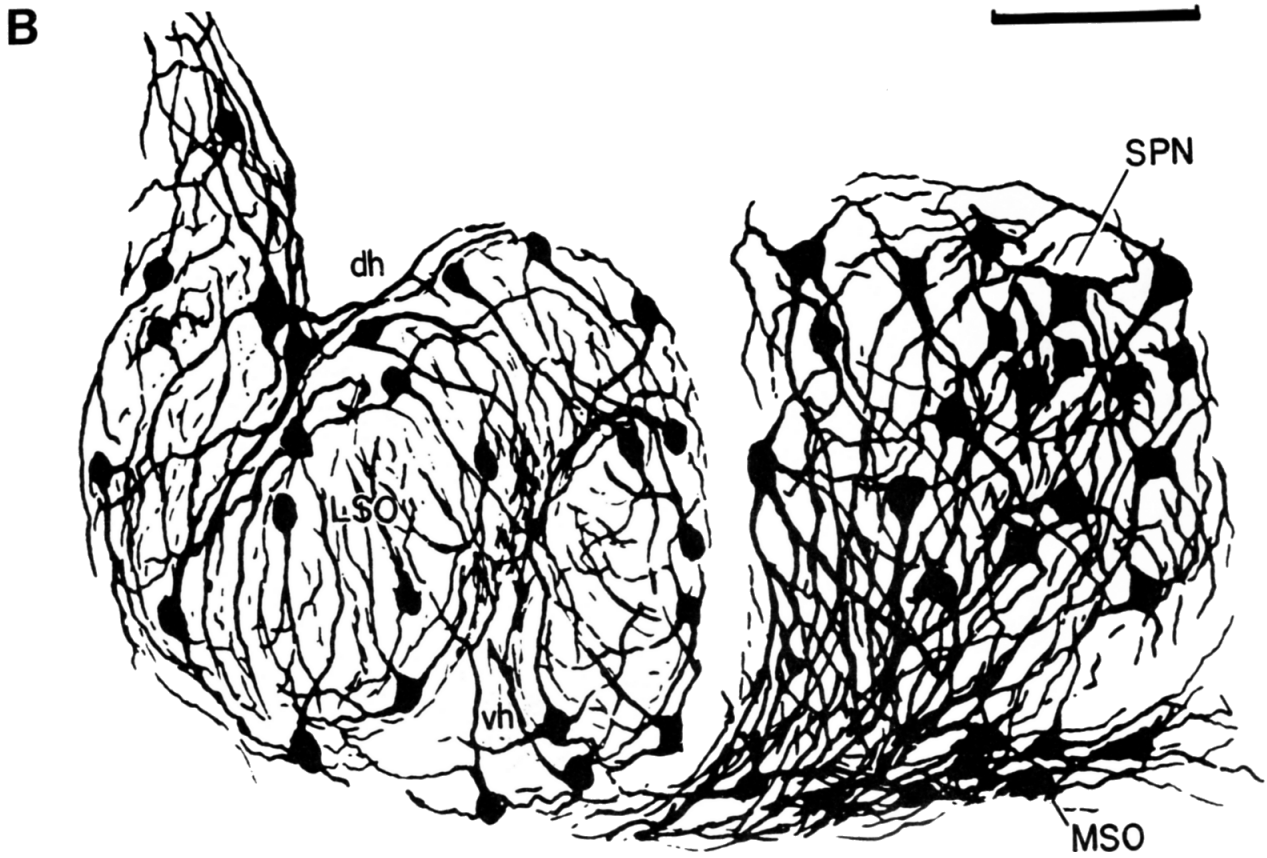


Figure 7-9. The neuronal architecture of three nuclei of the superior olivary complex. A. Photomicrograph of a Nissl-stained coronal section illustrating the lateral and medial superior olivary nuclei and the superior paraolivary nucleus. B. Drawing from a Golgi-stained preparation illustrating the dendroarchitecture of the same three nuclei. (Modified from R. Lorente de Nó, (1947). By permission of Alan R. Liss, Inc.) Scale bar equals 100 μm for both figures.



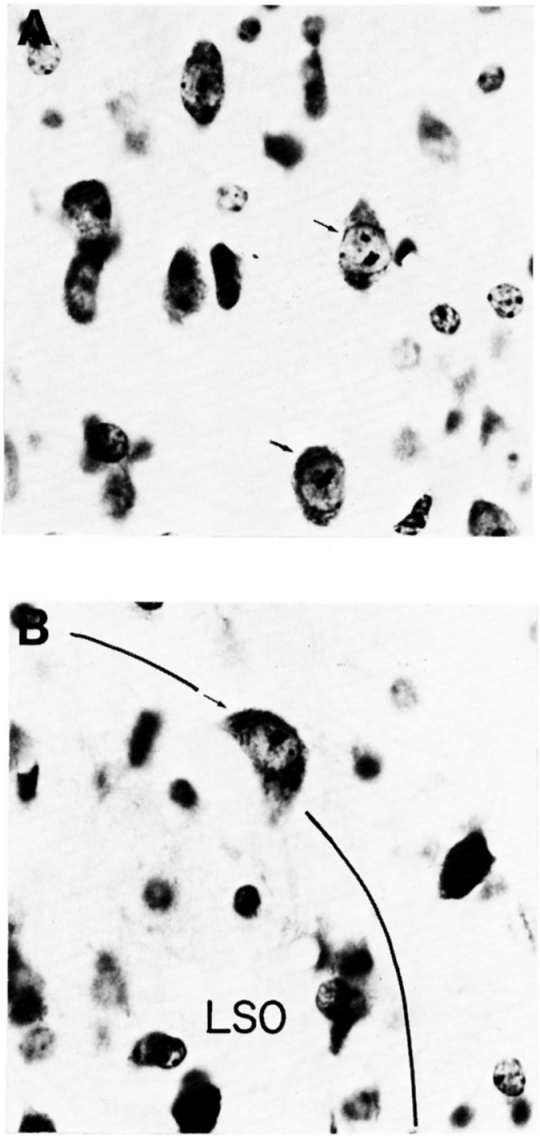
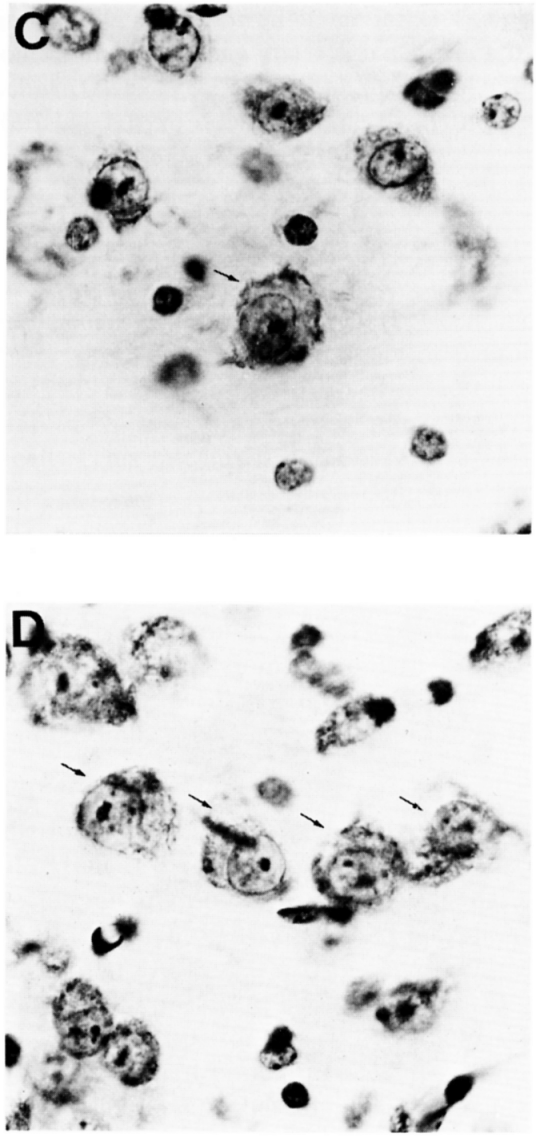


Figure 7-10. Photomicrographs of Nissl-stained preparations from the superior olivary complex, illustrating typical specimens from identified cell classes: (A) principal cells (arrows) of the lateral superior olive; (B) marginal cells (arrows) located on the boundary (solid line) of the lateral superior olive; (C) typical cells of the lateral nucleus of the trapezoid body; (D) typical cells of the ventral nucleus of the trapezoid body (arrows); (E) principal cells of the medial nucleus of the trapezoid body (arrows); and (F) large multipolar neurons of the superior paraolivary nucleus. Scale bar equals 20 μm for A-F.



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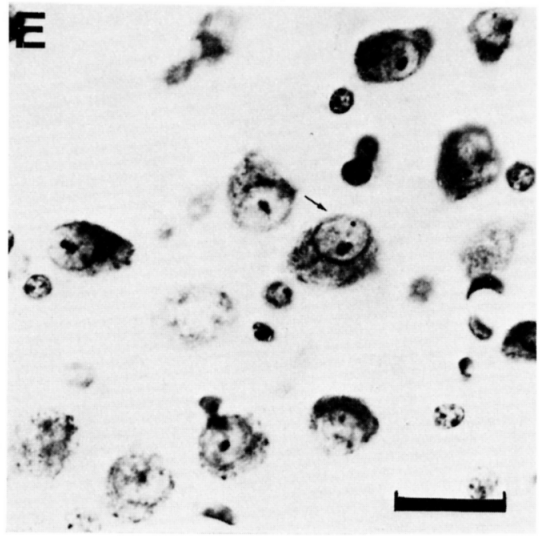


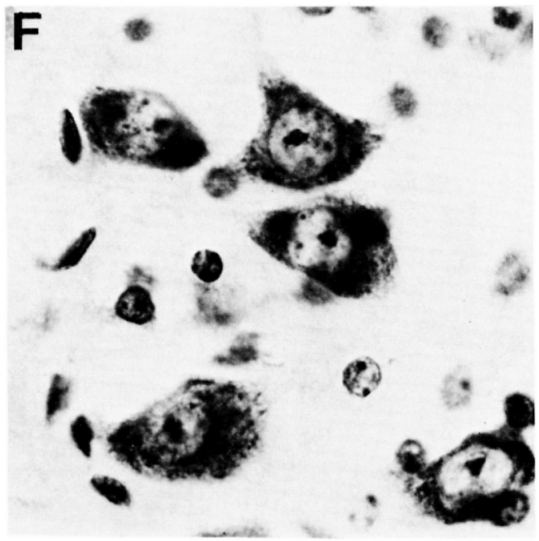


Figure 7-10 continued.

The spindle cells are reported to be larger than principal cells and are located mainly along the medial border of the nucleus (Ollo and Schwartz, 1979). Using Nissl, protargol, Golgi, and HRP stained material, we have not been able to distinguish the spindle cells.

The Medial Superior Olive (MSO)

The medial superior olive is a somewhat inconspicuous nucleus in the mouse, especially when compared to that of the cat or monkey. The caudal half of the nucleus lies between and slightly ventral to the lateral superior olive and superior paraolivary nucleus (Figs. 7-8B, 7-39). More anteriorly, the lateral superior olive disappears and the medial superior olive remains as a short, vertical column of cells. This nucleus is composed of approximately 200 cells, a number greatly reduced when compared to that of other mammals (Irving and Harrison, 1967).

We have been able to distinguish only a single cell type in this nucleus. These neurons have oval-shaped cell bodies that are elongated along the horizontal axis. Their nuclei are round and pale, suspended in darkly staining cytoplasm that contains granular Nissl substance. The dendrites generate a planar dendritic tree having a predominantly horizontal orientation (Fig. 7-11).

The Superior Paraolivary Nucleus (SPN)

The superior paraolivary nucleus extends along the entire rostrocaudal extent of the superior olivary complex, in a position between the lateral superior olive and the medial nucleus of the trapezoid body (Fig. 7-8). This nucleus is morphologically similar to that reported in the rat (Harrison and Feldman, 1970), although it does not appear to be present in the cat (Ollo and Schwartz, 1979). The superior paraolivary nucleus may be characterized by its predominant population of large, multipolar neurons (Fig. 7-9B). This cell type has an oval-to-round, pale nucleus with a distinct nucleolus, contained in a triangular-shaped cell body. The cell body measures approximately 25 μm in diameter (longest dimension) and exhibits darkly staining cytoplasm and many prominent Nissl bodies. In Golgi preparations, the dendrites of these cells are long and relatively unbranched, but reveal no

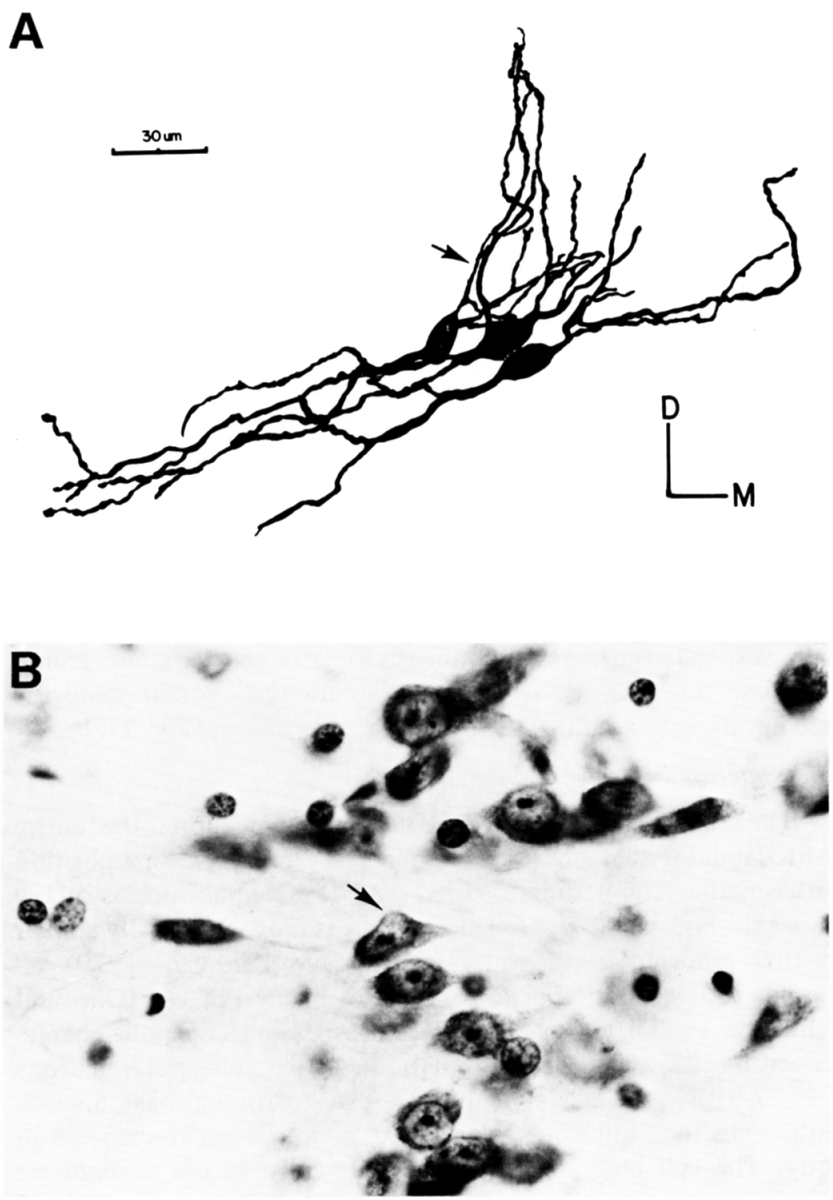


Figure 7-11. The neuronal architecture of the medial superior olivary nucleus. A. Camera lucida drawing of three bipolar neurons. Note the predominant horizontal orientation of the dendrites, plus the occasional dorsally directed dendrite (arrow). B. Photomicrograph of Nissl-stained neurons of the medial superior olive. The faintly stained dendrites reveal these cells to be bipolar with an occasional dorsally directed dendrite (arrow). A and B were reproduced at the same magnification.

particular orientation. A much smaller population (less than 5%) of cells is present that appear as small multipolar cells or spindle cells; however, since they have the same cytological characteristics as the large multipolar neurons, they may simply represent cell fragments as a result of tissue sectioning or different views of the large multipolar neurons.

The Medial Nucleus of the Trapezoid Body (MNTB)

The medial nucleus of the trapezoid body is the most medial neuronal group of the superior olivary complex, situated dorsolateral to the corticospinal tract. This nucleus is easily recognized by virtue of the fact that its darkly staining cells appear compressed into a compact zone, embedded within the fibers of the trapezoid body (Fig. 7-39). There are at least two types of neurons, principal cells and stellate cells, which compose this nucleus.

The principal cells typically have a tear-drop shaped soma and an eccentrically placed nucleus (Fig. 7-10E); their cytoplasm is intensely staining, revealing the fine, granular Nissl substance. Each neuron gives rise to 1-2 long, thin, untapering proximal dendrites that do not seem to exhibit any particular orientation. Usually, the primary dendrites terminate in a complex tuft, formed by the multiple branching of shorter, secondary dendrites. Occasionally, the primary dendrite branches into two long secondary dendrites, each of which then forms a terminal tuft of short, tertiary dendrites. These principal cells are similar in appearance to that described in the medial nucleus of the trapezoid body in the cat (Morest, 1968).

Each principal cell receives a single calyx of Held; these large, axosomatic terminal endings arise from large caliber fibers of the trapezoid body. In the cat, these large endings have been shown to arise from globular cells in the contralateral cochlear nucleus (Tolbert, 1978). In the mouse, the calycine endings consist of elongated, finger-like processes that totally encircle the principal cell (Fig. 7-12).

The stellate cells of the medial nucleus are few in number and scattered among the principal cells. Their cytoplasm is lightly staining and contains fine, granular Nissl substance and many prominent Nissl bodies. These cells have thick, tapering proximal dendrites that radiate throughout the nucleus.

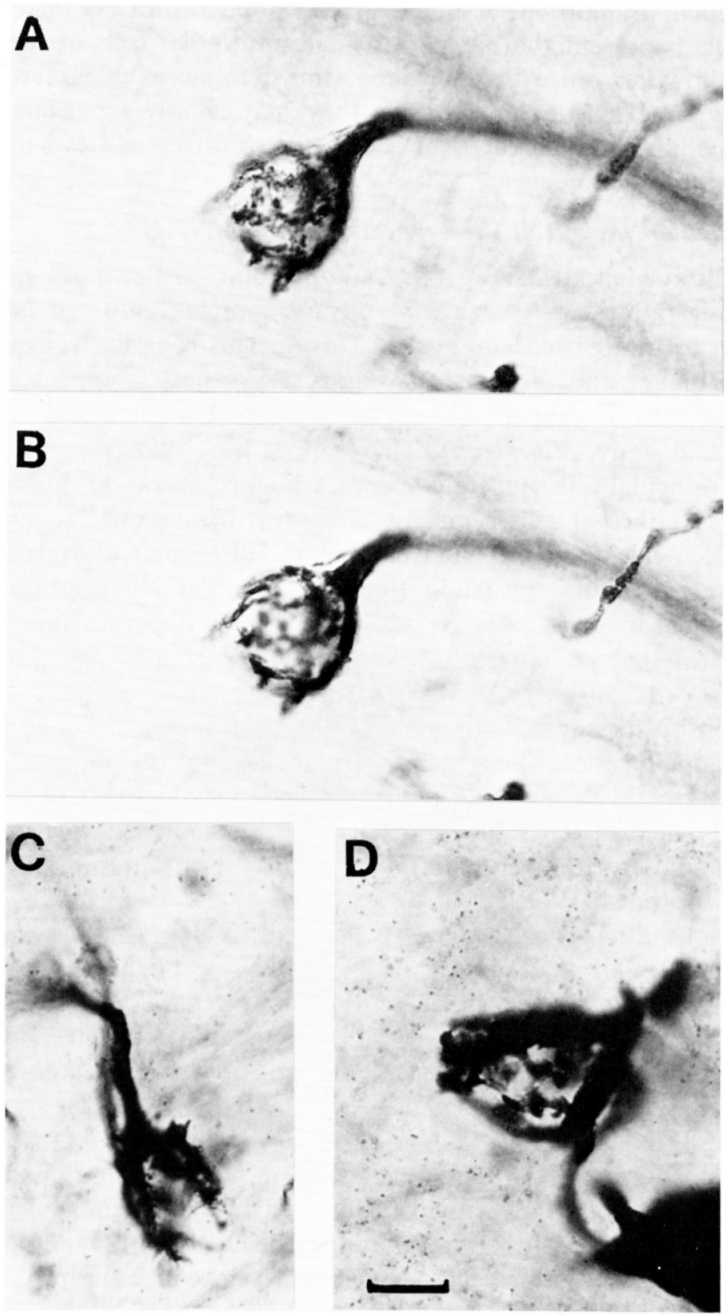


Figure 7-12. Photomicrographs of the large calycine endings (of Held) in th medial nucleus of the trapezoid body. A, B. Single calyx of Held, photo graphed in 2 planes of focus. C, D. Examples of additional calyces of Hel A single calyx arises from the end of large axons (5 μm in diameter). Eac calyx is composed of several thick, gnarled processes (2-3 μm in diameter which surround the cell body of the principal neurons. The main processe are linked together by a more delicate network of finer fibers and varicositie The scale bar equals 10 μm.

The Lateral and Ventral Nuclei of the Trapezoid Body

These two diffuse nuclei are formed by a plate of scattere neurons intertwined among the fibers of the trapezoid body an located along the ventral and ventrolateral surface of the brai stem (Fig. 7-39). They are separated from each other by thic fascicles of fibers from the trapezoid body. The lateral nucleu of the trapezoid body flanks the ventrolateral surface of the latera superior olive. The ventral nucleus of the trapezoid body lie below the medial superior olive and the superior paraolivar nucleus; its lateral extension inserts between the ventral surfac of the brain stem and the medial part of the lateral nucleus of th trapezoid body while its medial extension merges with the latera border of the medial nucleus of the trapezoid body.

The neurons which comprise these nuclei have been describe as small (15 μm), medium (19.5 μm), and large (25 μm) cell which are often elongated along the horizontal axis (Ollo an Schwartz, 1979). We have examined histological preparations c this region in the three standard planes of section. The constituer neurons comprise a seemingly heterogeneous population, althoug we have distinguished a predominant cell type. Typically, th cell is pale staining with fine, granular Nissl substance; occasion ally, the Nissl substance is condensed into dark patches that su round the centrally located nucleus (Fig. 7-10C, D). The nucleu is round and pale and contains a prominent nucleolus. The den drites radiate in all directions, are long and relatively unbranche and exhibit no particular orientation. The remaining neurons i these nuclei could represent additional cell types or could be th result of viewing the same cell from different perspectives or fro viewing various fragments of sectioned cells.

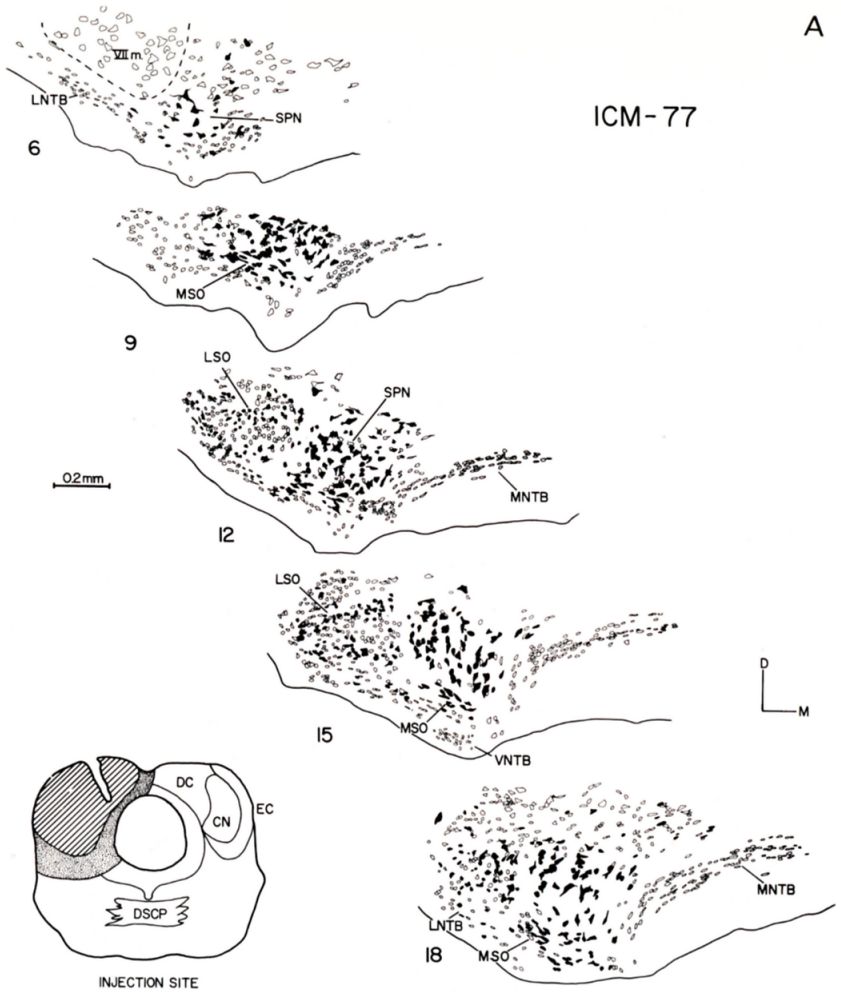


Figure 7-13. Distribution of neurons in the superior olivary complex that project to the ipsilateral inferior colliculus. A large injection of HRP was placed in the inferior colliculus of mouse ICM-77. The brain was cut in the coronal plane and processed with benzidine dihydrochloride. Each section of the brain stem was assigned a number; on every third section, all neurons through the superior olivary complex were drawn with our camera lucida system. The solid figures represent those neurons containing HRP-reaction product. Inset A represents the center of the HRP injection site (stripes) and the surrounding fringe (stipple). Inset B provides an expanded view of the superior olivary complex for orientation purposes. Inset in Figure 7-14 provides the plane of section for ICM-77. A summary of the data is presented in Figure 7-15.

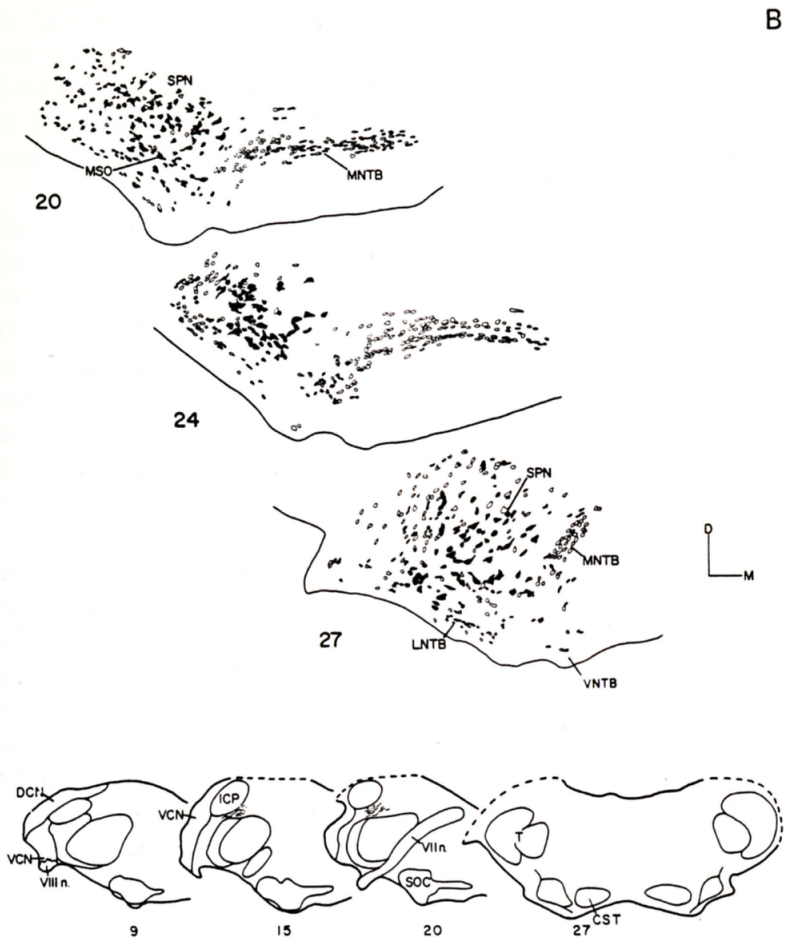


Figure 7-13 continued.

Connections of the Superior Olivary Complex

There are no published reports on the connections of the superior olivary complex in the mouse, although they have been reviewed for the cat, rat, and monkey (Harrison and Howe, 1974; Harrison, 1978a,b). We have determined the projections of the superior olivary nuclei to the inferior colliculus using the retrograde transport of HRP (Willard et al., 1978).

The lateral superior olive has a bilateral and topographic projection to the inferior colliculus, an observation in agreement with studies done on other species (Beyerl, 1978; Adams, 1979; Roth et al., 1978). In addition, we have demonstrated an asymmetry in the spatial origin of these projections. The ipsilateral projection arises from marginal cells and from principal cells located along the borders of the nucleus; in contrast, the contralateral projection arises from marginal cells and from principal cells located more centrally within the nucleus (Fig. 7-13, section 9, 12).

The cells of the medial superior olive exhibit a distinctly ipsilateral projection to the inferior colliculus (Fig. 7-13, sections 9-24). Some unidentified neurons in the vicinity of the medial superior olive project to the contralateral inferior colliculus (Fig. 7-14, section 9, 12). The issue of whether the medial superior olive has a contralateral projection to the inferior colliculus remains unresolved. We have also identified a predominantly ipsilateral projection to the inferior colliculus from the principal cells of the superior paraolivary nucleus (Fig. 7-13, 14); this projection is topographic such that cells in the lateral portion of the nucleus project to the dorsolateral inferior colliculus and cells in the medial portion of the nucleus project to the ventromedial inferior colliculus.

Projections of the mouse medial nucleus of the trapezoid body remain to be determined. A differential projection pattern to the inferior colliculus is observed to arise in the lateral and ventral nuclei of the trapezoid body (Fig. 7-13, 14). Cells of the lateral nucleus project bilaterally to the inferior colliculus whereas cells of the ventral nucleus establish ipsilateral projections to the inferior colliculus. We have used these differential projections

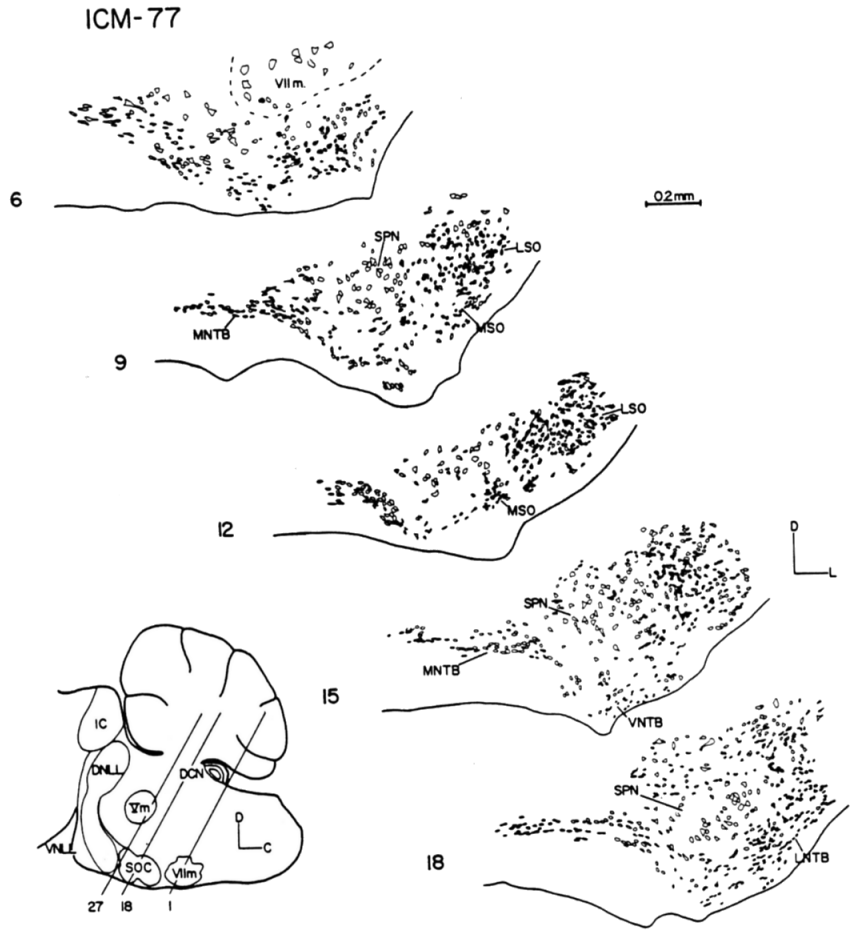


Figure 7-14. Distribution of neurons in the superior olivary complex that project to the contralateral inferior colliculus (ICM-77; histological and analytical procedures are described in Fig. 7-13). The neurons represented in black project their axons to the contralateral inferior colliculus. Inset: provides plane of section for tissue. The data have been summarized in Figure 7-15.

as a guide for partitioning the cells of the trapezoid body into a ventral and lateral nucleus, but much more work is needed in this area.

The projections of the superior olivary nuclei to the inferior colliculus are summarized in Figure 7-15. Clearly, there is much work remaining to determine the afferent, efferent, and intrinsic connections of these nuclei.

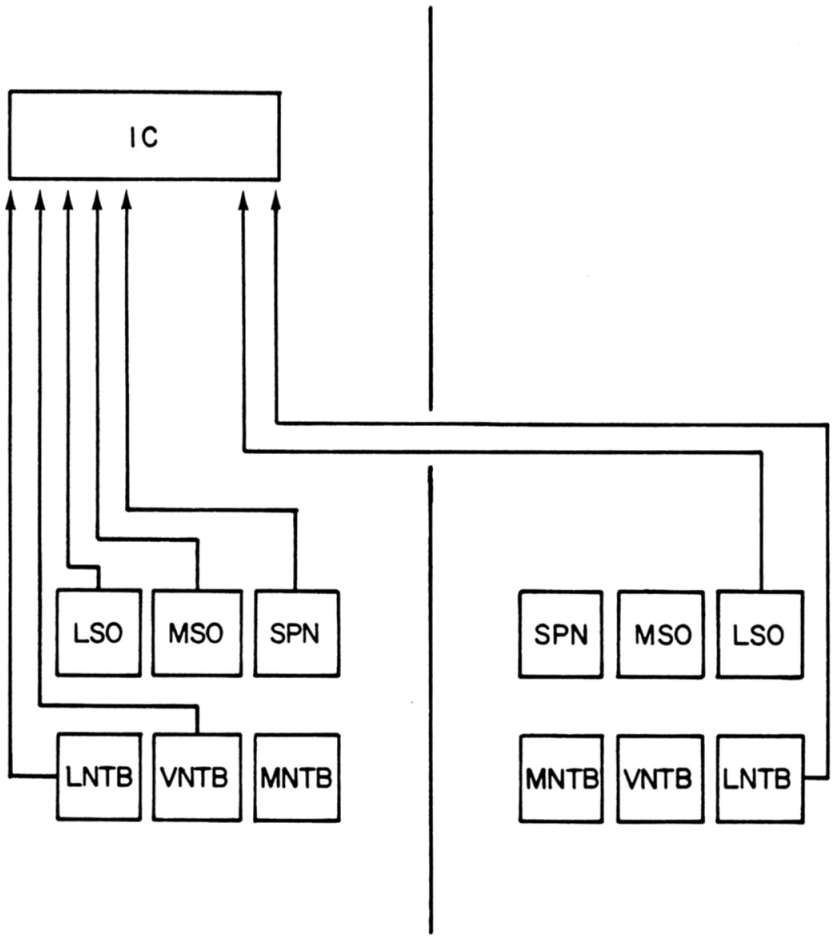


Figure 7-15. Summary diagram of the projections from the superior olivary complex to the inferior colliculus. These data were obtained by analyzing the retrograde transport of HRP from the inferior colliculus to the superior olivary complex.

Nuclei of the Lateral Lemniscus

The lateral lemniscus is a prominent auditory pathway which begins at the level of the superior olivary complex and courses through the pons to terminate in the inferior colliculus (*see* Fig. 7-2). Neurons are intermingled among these fibers all along their trajectory. Based on relative spatial position, certain cytoarchitectonic features, and differential connections, these neurons may be segregated into three separate nuclei: they are the ventral, intermediate, and dorsal nuclei of the lateral lemniscus.

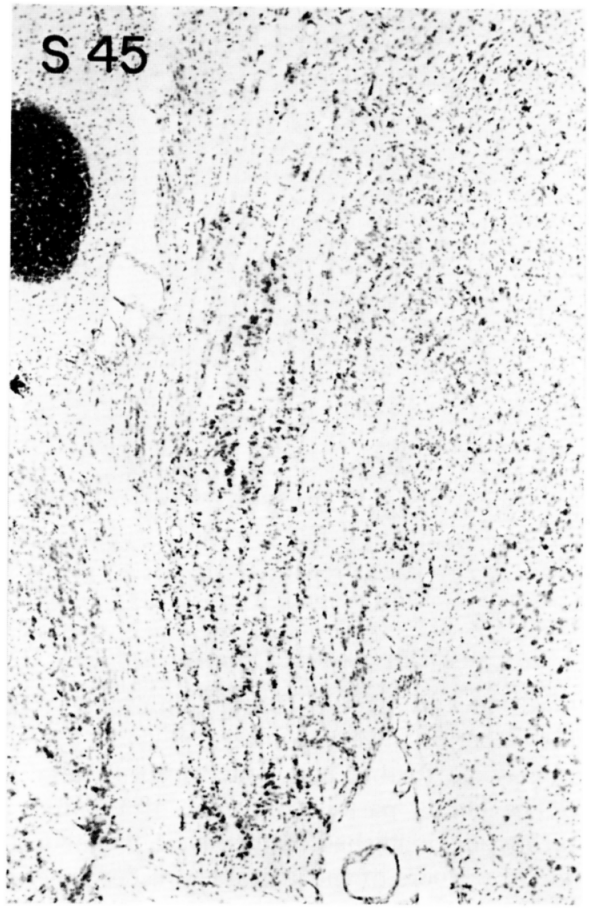


Figure 7-16. A sagittal view of the lateral lemniscus illustrating its 3 nuclear divisions. The section was stained with cresyl violet; the scale bar is equal to 200 μm.

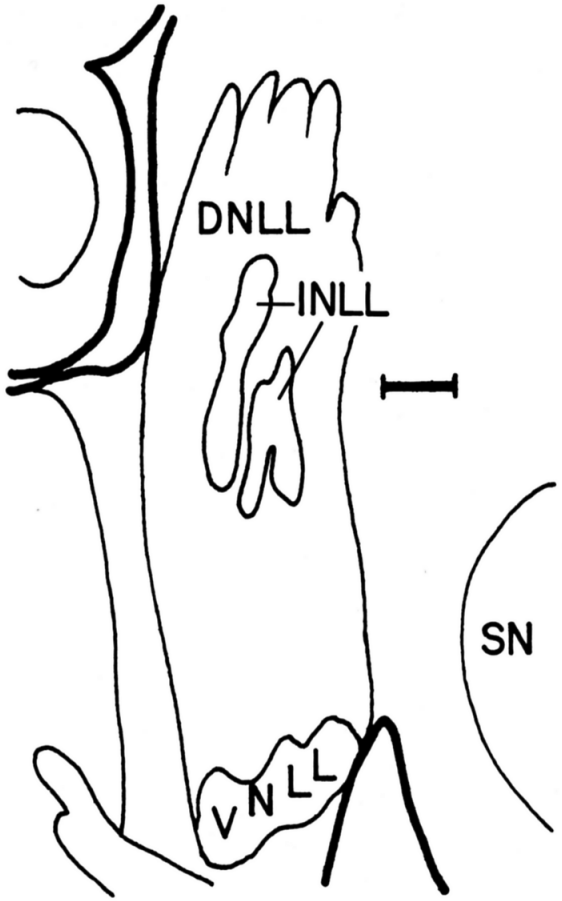


Figure 7-16 continued.

The Ventral Nucleus of the Lateral Lemniscus (VNLL)

The ventral nucleus of the lateral lemniscus is located just rostral to the superior olivary complex (Figs. 7-8, 7-16, 7-40). This nucleus may be further subdivided into a lateral part and a medial part. The lateral part is composed of a compact accumulation of neurons, distinguished by an enveloping neuropil capsule and surrounded by fibers of the lateral lemniscus. The constituent neurons have small (10 × 15 μm) rounded cell bodies (Fig. 7-17B)

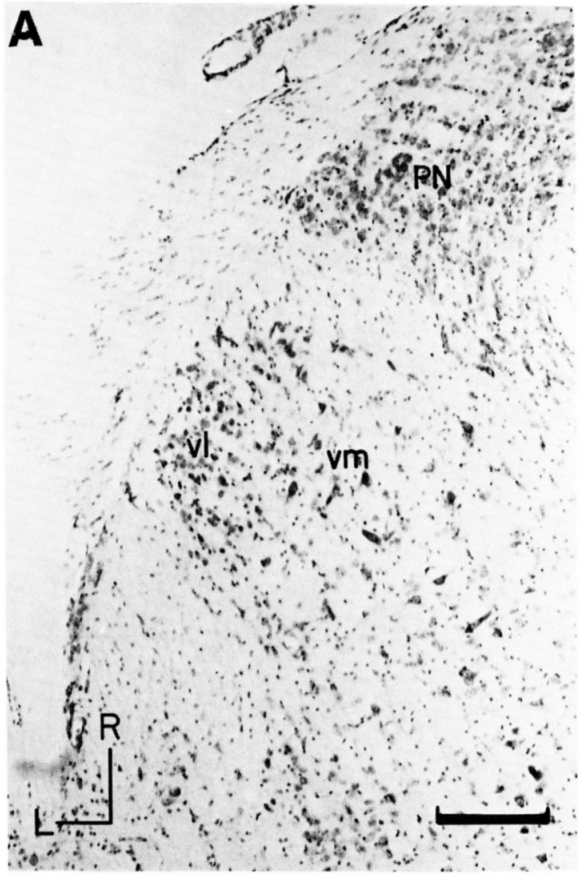
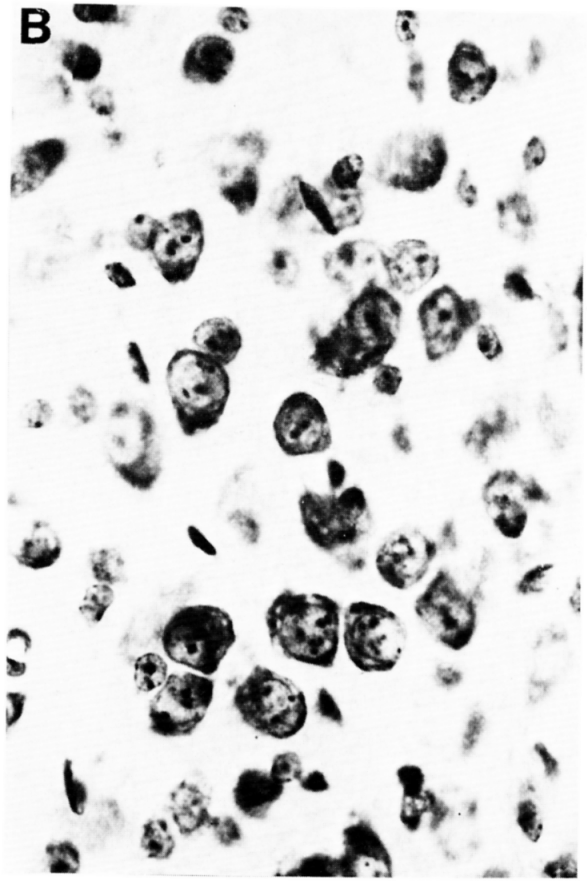


Figure 7-17. Neuronal architecture of the ventral nucleus of the latera lemniscus. A. Low magnification photomicrograph of the ventral nucleu in horizontal section (Nissl stain). Scale bar equals 200 μm. B, C. High magni fication photomicrographs of neurons in the two divisions of the ventra nucleus of the lateral lemniscus. Globate neurons (B) seen in the ventrolatera division and the larger, multipolar neurons (C, arrow) seen in the ventro medial division. Scale bar equals 20 μm.



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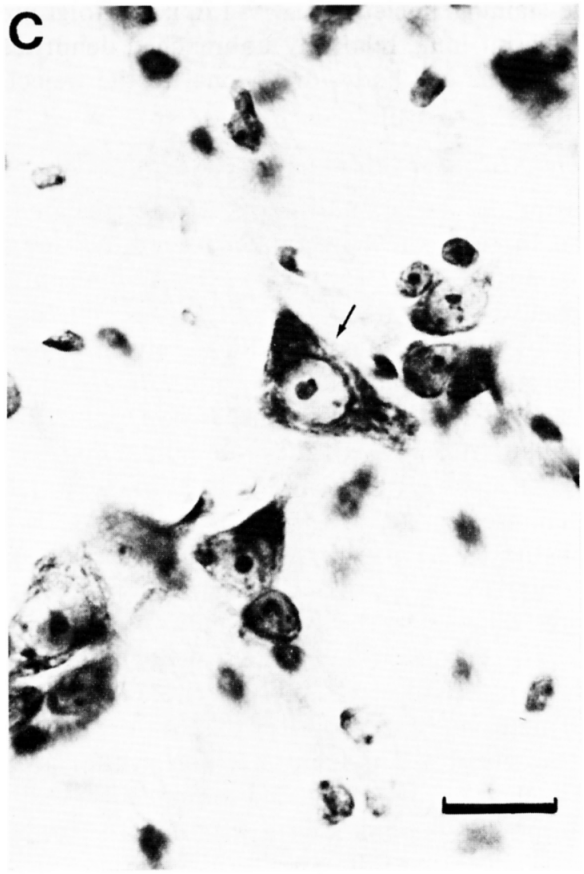


Figure 7-17 continued.

and long, relatively thin dendrites that tend to be oriented parallel to the trajectory of the lemniscal fibers. In protargol preparations, these cells may be seen receiving large, axosomatic calycine endings; these large endings are similar in form, but smaller than the calyx of Held endings found in the medial nucleus of the trapezoid body. In contrast, the medial part is composed of large (15 × 20 μm) multipolar neurons that are loosely scattered among the lemniscal fibers (Fig. 7-17A). These cells have darkly staining cytoplasm, filled with coarse granules of Nissl substance and a

round, pale-staining nucleus (Fig. 7-17C); in Golgi preparations, these cells exhibit long, relatively unbranched dendrites that radiate away from the cell body, orthogonal to the trajectory of the lemniscal fibers.

The Dorsal (DNLL) and Intermediate (INLL) Nuclei

Neurons of the dorsal and intermediate nuclei are less densely packed than those of the ventral nucleus and they are arranged in vertical columns (Figs. 7-16, 7-41). The columns are separated by and aligned with the fibers of the lateral lemniscus. A striking arrangement of the dendrites from these neurons is demonstrated in Golgi-prepared material; the dendritic domains are essentially two-dimensional, flattened along the horizontal plane. These vertical columns of cells with their horizontal dendrites generate an image of a stack of flattened cells through which fibers of the lateral lemniscus pass (Fig. 7-27).

The constituent neurons exhibit a characteristic arrangement within any horizontal section through this region (Fig. 7-18). The dendrites of cells in the central core form a reticulum with their dendrites, through which lemniscal fibers pass. Most of the dendrites lie within the plane of the section. The more peripherally located neurons have dendrites that are organized in a series of concentric sheaths. This neuronal organization extends from the ventral nucleus border to the inferior colliculus.

Despite this common arrangement of cells, several features serve to separate the dorsal nucleus from the intermediate nucleus. The neurons of the intermediate nucleus have intensely staining Nissl substance (Fig. 7-41, section C112; Fig. 7-16), in contrast to the more lightly staining neurons of the dorsal nucleus. Furthermore, each nucleus has differential connections with the inferior colliculus (Figs. 7-19, 7-20).

Connections of the Nuclei of the Lateral Lemniscus

There have been no published reports on the afferent projections to the nuclei of the lateral lemniscus. Using anterograde degeneration techniques and lesions to the dorsal cochlear nucleus or the dorsal acoustic stria, we have observed agyrophilia characteristic of terminal degeneration in the ventral, but not in the in-

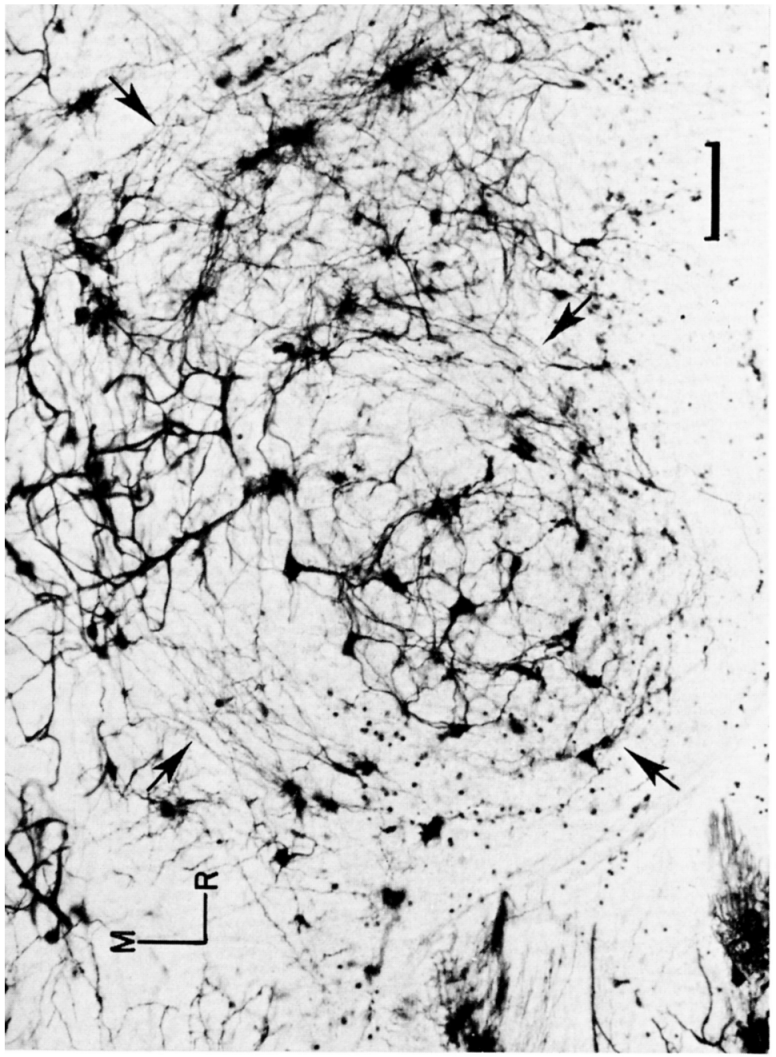


Figure 7-18. Neuronal architecture of the dorsal nucleus of the lateral lemniscus. A Golgi-Cox stained preparation of this nucleus photographed in the horizontal plane. The central portion contains a reticulum of neurons. Surrounding neurons are arranged in a spiral pattern. The arrows denote the nuclear boundary. Scale bar equals 100

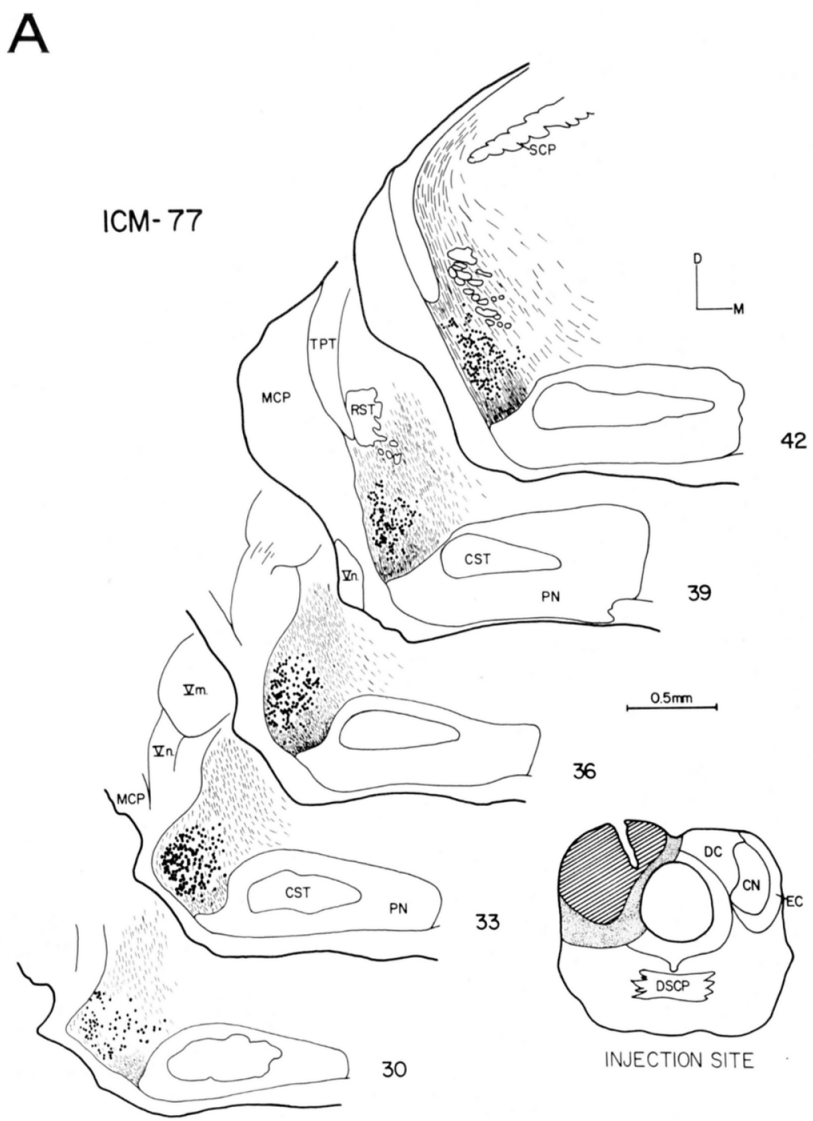
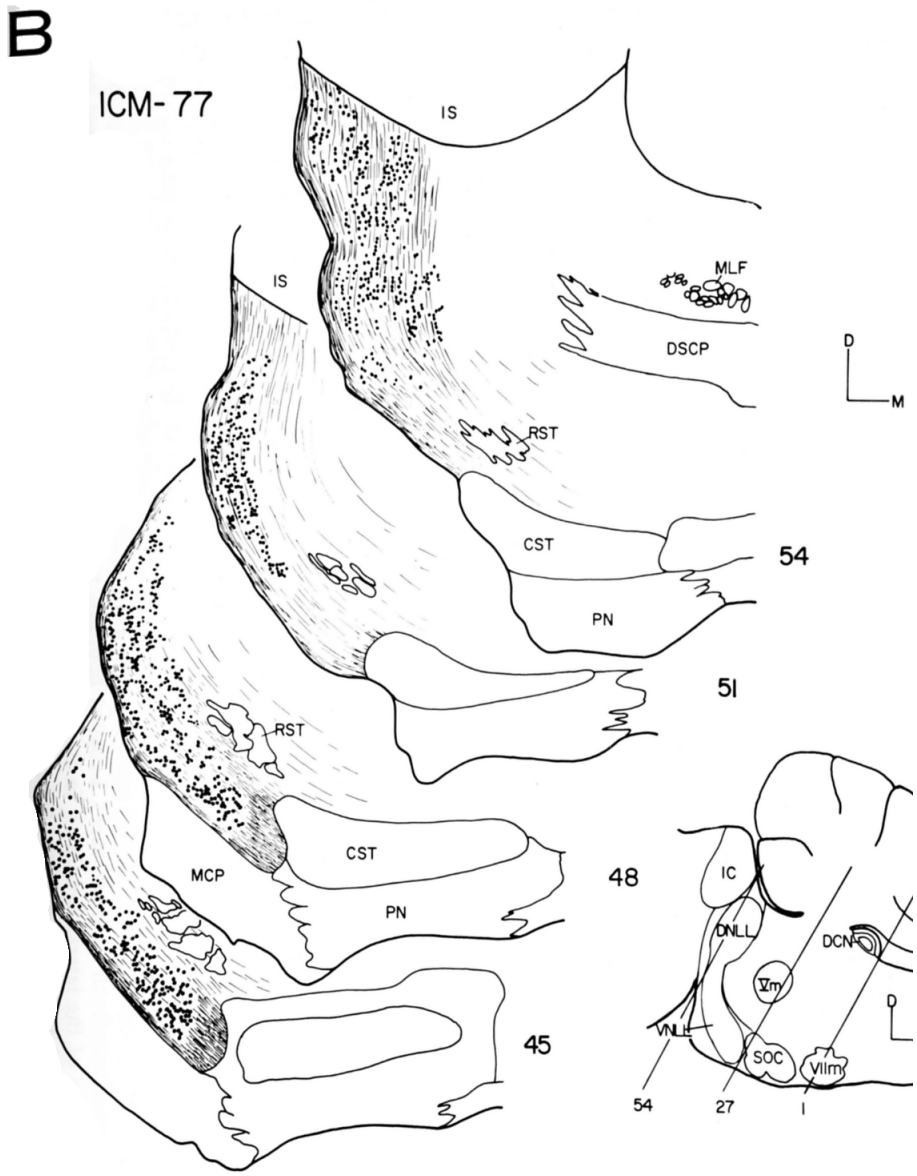


Figure 7-19. Distribution of cells in the nuclei of the lateral lemniscus that project to the ipsilateral inferior colliculus. A large injection of HRP into the inferior colliculus (ICM-77) revealed labelled neurons throughout the ipsilateral nuclei of the lateral lemniscus of ICM-77. Labelled neurons are represented by dots and labelled axons are represented by dashes. The inset in the lower right of Diagram A represents the extent of the HRP injection site. The striped area contains the darkest HRP reaction product; the stippled area contains the HRP "haze." Inset in Diagram B orients the plane of section. A summary of these data is presented in Figure 7-21.



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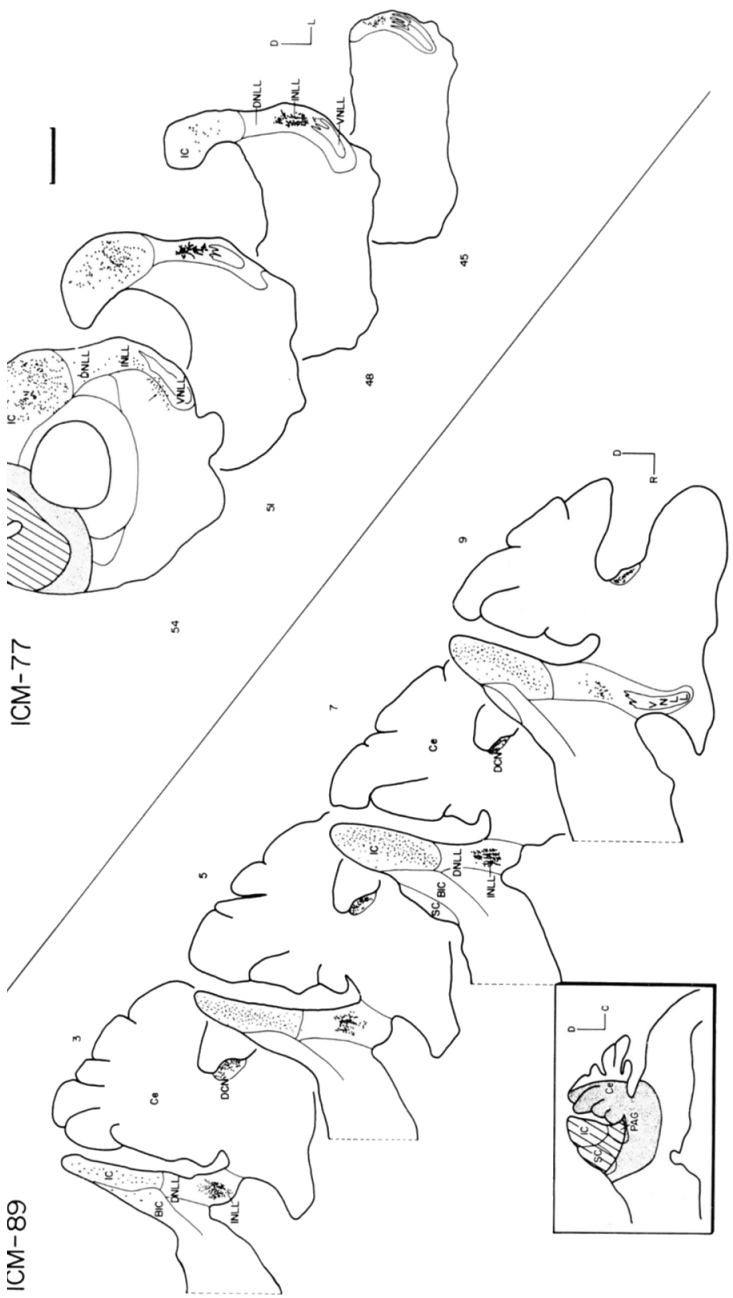


Figure 7-20. Distribution of cells in the nuclei of the lateral lemniscus that project to the contralateral inferior colliculus. ICM-77 and ICM-89 received large injections of HRP into the inferior colliculus; ICM-77 was sectioned in the coronal plane and ICM-89 was sectioned in the sagittal plane. This figure presents sequential sections through the contralateral lemniscus from both of these cases. Labelled neurons, represented by dots, are generally confined to the intermediate nucleus of the lateral lemniscus. In the rostral-most section (54) of ICM-77, a cluster of labelled neurons (arrow) is seen medial to the fibers of the lateral lemniscus. These neurons seem to belong to the paralemniscal nucleus. Scale bar equals 1 mm.

termediate or dorsal nucleus. Our conclusion from such degeneration studies is that the dorsal cochlear nucleus has a direct projection to neurons of ventral nucleus.

We have also examined the connections of the nuclei of the lateral lemniscus with the inferior colliculus, using HRP techniques (Figs. 7-19, 7-20). Both medial and lateral parts of the ventral nucleus project to the ipsilateral inferior colliculus, specifically to the central nucleus and the external cortex (Fig. 7-19A). No projections from ventral nucleus have been observed to the contralateral inferior colliculus. Neurons of the intermediate nucleus project bilaterally to the inferior colliculus (Figs. 7-19B, 7-22). Neurons of the dorsal nucleus only project to the ipsilateral inferior colliculus (Fig. 7-19B). A schematic diagram of these connections is illustrated in Figure 7-21.

The Inferior Colliculus (IC)

The inferior colliculus is a prominent midbrain structure (Fig. 7-2) that is visible on the dorsal surface of the brain between the cerebral hemispheres and the cerebellum. In addition, the inferior colliculus separates the lateral lemnsicus from the brachium of the inferior colliculus. This structure has received much attention because of its posture as a major synaptic station for ascending and descending auditory pathways (Adams, 1979; Geniec and Morest, 1971). We have taken advantage of this anatomical observation and have charted many of the connections between the inferior colliculus and other auditory structures using HRP histochemistry.

Initially, Ramón y Cajal (1909) divided the inferior colliculus of mammals into three regions: (1) the nucleus of the posterior quadrigeminal tubercle; (2) the external cortex; and (3) the dorsal cortex (Figs. 7-42, 7-43). These three regions have been identified in the mouse; in addition, the nucleus of the posterior quadrigeminal tubercle may be further subdivided into a central nucleus and a dorsomedial nucleus (Willard et al., 1978; Ryugo et al., 1981). All four divisions of the inferior colliculus have been observed in a variety of mammalian species, including man (Merzenich and Reid, 1974; Fitzpatrick, 1975; Oliver and Hall, 1978; Geniec and Morest, 1971; Ryugo and Killackey, 1975; Rockel and Jones, 1973).

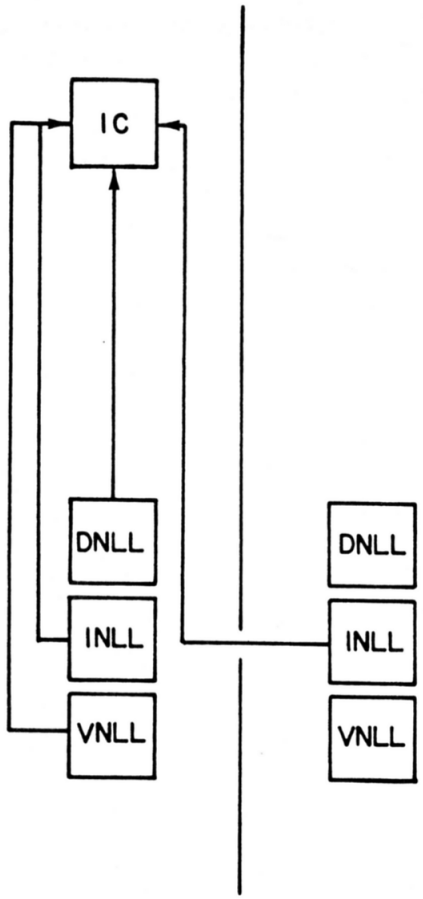


Figure 7-21. Summary diagram illustrating the known ascending projections of the nuclei of the lateral lemniscus to the inferior colliculus in the mouse.

The inferior colliculus is associated with three large fiber systems: the lateral lemniscus, the brachium of the inferior colliculus, and the commissure of the inferior colliculus. Regional differences in fiber density and fiber pattern resulting from these bundles form important morphological criteria for the definition of subdivisions in the inferior colliculus.

The lateral lemniscus is the major source of ascending projections to the inferior colliculus. Many of these fibers pass directly into the central nucleus and the external cortex, while other fibers bifurcate along the lateral border of the central nucleus and innervate both regions (Fig. 7-22).

The brachium of the inferior colliculus contains the bulk of the ascending fibers of the inferior colliculus; many pass perpendicularly through the layers of the central nucleus, penetrate the external cortex and emerge as a superficial capsule (Fig. 7-22A). These fibers sweep dorsolaterally, enter the brachium, and travel upward to the thalamus. Descending fibers from the thalamus and the auditory cortex also travel within the brachium to innervate the inferior colliculus.

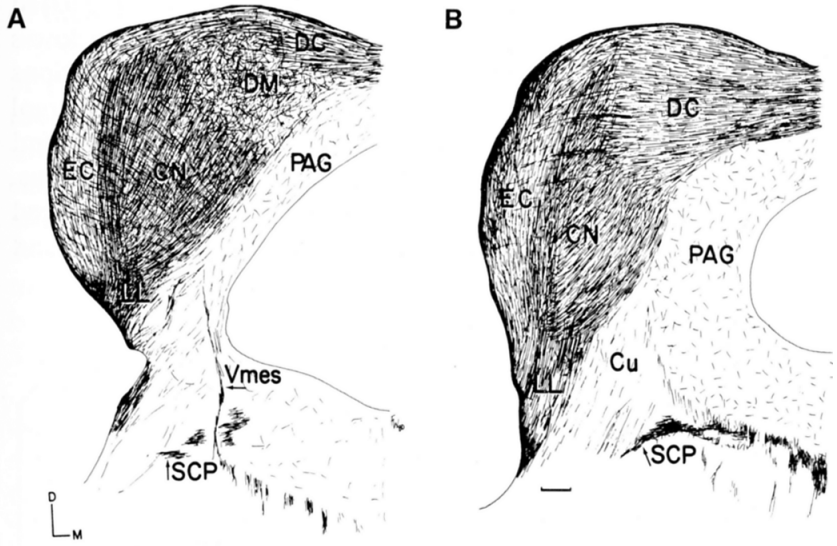


Figure 7-22. Projection drawing of protargol-stained material illustrating the fibroarchitecture of the inferior colliculus. The central nucleus is evident by its dense neuropil, characterized by the innervation from the lateral lemniscus. The central nucleus also has efferent fibers that proceed dorsolaterally to penetrate the external cortex before entering the brachium of the inferior colliculus (Section A). The dorsal cortex is characterized by the presence of horizontally directed fascicles of fibers from the commissure of the inferior colliculus (Section B). The dorsomedial nucleus exhibits a criss-cross neuropil pattern (Section A). Scale bar equals 0.2 mm.

The third major fiber system of the inferior colliculus is contained within the commissure of the inferior colliculus. These fibers pass above the cerebral aqueduct in the anterior two-thirds of the inferior colliculus, and essentially interconnect the two colliculi. The dorsal cortex is most heavily infiltrated by these commissural fibers (Fig. 7-22B). Except for the ventromedial laminae of the central nucleus, all parts of one colliculus are homotopically connected through the commissure to the other colliculus.

The Central Nucleus (CN)

The central nucleus occupies the central core of the inferior colliculus. It is an egg-shaped mass with a dent in its dorsomedial pole. The boundaries of the central nucleus are best appreciated in Nissl preparations sectioned between 40 and 60 μm thickness or in protargol-stained preparations. The thicker Nissl sections reveal the cell-sparse margins of the central nucleus; in protargol sections, fiber bundles appear to fill the cell-sparse margins and delimit the dense neuropil so characteristic of the central nucleus. The most striking feature of the central nucleus is its pronounced laminar organization (Fig. 7-23): the neurons, their dendrites, and

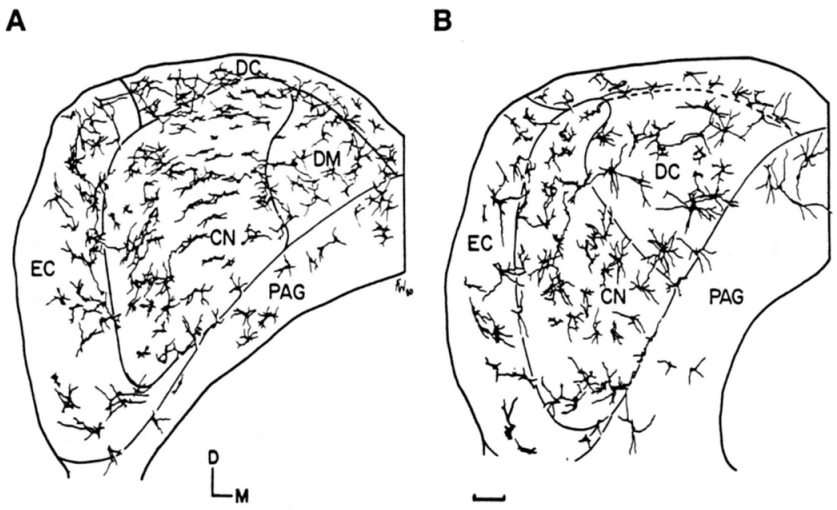


Figure 7-23. Neuronal architecture of the inferior colliculus. Camera lucida drawings taken from a juvenile mouse (Golgi-Kopsch method, Stensaas modification). Sections A and B correspond repectively to Sections A and B of Figure 7-22. Note how subdivisions based on cell composition are similar to the subdivisions based on fibroarchitecture. Also evident is the laminar arrangement of neurons and dendrites in the central nucleus (Section A).

afferent axons tend to be aligned into rows. Two general classes of neurons may be identified in the central nucleus: principal cells and stellate cells. It must be emphasized, however, that additional subpopulations within these classes probably exist, since many neurons cannot be neatly classified.

Principal cells have a characteristic planar shape, imparted by the arrangement of their dendritic arborizations (Fig. 7-24B). The proximal dendrites are thin (1-3 μm diameter) and untapering; they branch repeatedly yet maintain a flattened domain; the distal dendrites are studded with spines. The cell body has an oval-to-fusiform appearance and contains an oval-shaped nucleus. These neurons are major contributors to the laminar appearance of the central nucleus.

Stellate cells display a wide range of sizes and shapes. In Nissl preparations, these cells are multipolar and typically have a rounded nucleus (Fig. 7-24A). Their cytoplasm stains intensely and has many small Nissl bodies. In Golgi preparations, these cells emit 3-5 thick, proximal dendrites; the proximal dendrites are usually short, but give rise to relatively long, variably branching dendrites that are virtually spineless. Stellate cells have a spherical-to-elliptical dendritic domain, and their dendrites do not particularly conform to the laminar organization of the central nucleus. Stellate cells are found freely intermixed with the principal cells.

The other main contributor to the laminar appearance of the central nucleus is the fiber architecture (Fig. 7-22). Long segments of the ascending fibers of the lateral lemniscus can be followed in coronal sections, as they project across the central nucleus in a ventrolateral-to-dorsomedial trajectory. These fiber segments, while of varying lengths, nevertheless seem to maintain regular spacing distances, further emphasizing their banded distribution. In addition to their characteristic trajectory, these fibers also exhibit a characteristic morphology despite their origin from different brain stem nuclei. We have analyzed Golgi-like images of these lemniscal fibers stained by HRP methods. These fibers are of large caliber (2 μm diameter) and give rise to numerous short collaterals; these collaterals emerge at right angles to the parent fiber and terminate as one or several boutons (Fig. 7-25A, B).

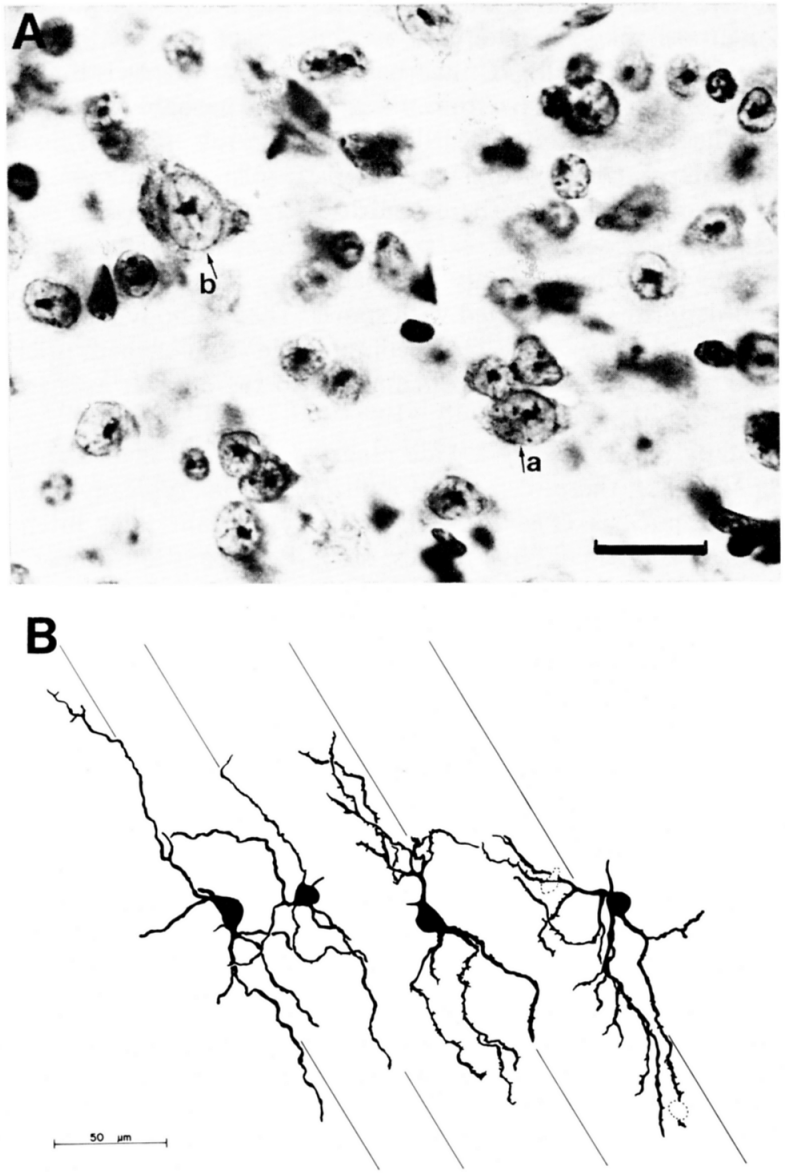


Figure 7-24. Neurons of the central nucleus of the inferior colliculus. A. Photomicrograph of Nissl-stained principal cell (a) and multipolar cell (b). Scale bar equals 20 μm. B. Camera lucida drawing of four principal cells stained by the Golgi-Kopsch method. Notice how the dendritic arbors of each neuron are rather planar and how they are aligned in parallel with one another and with the trajectory of lemniscal fibers (indicated by the thin lines).

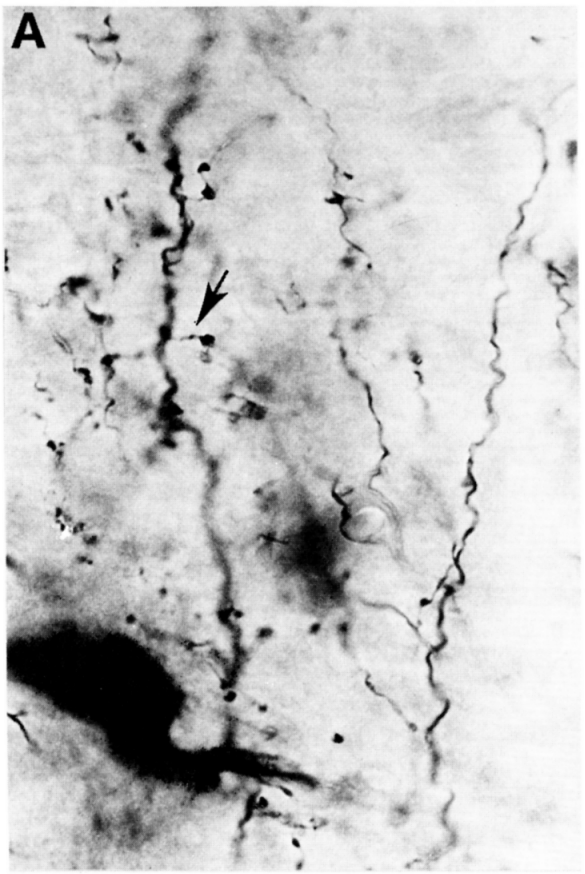
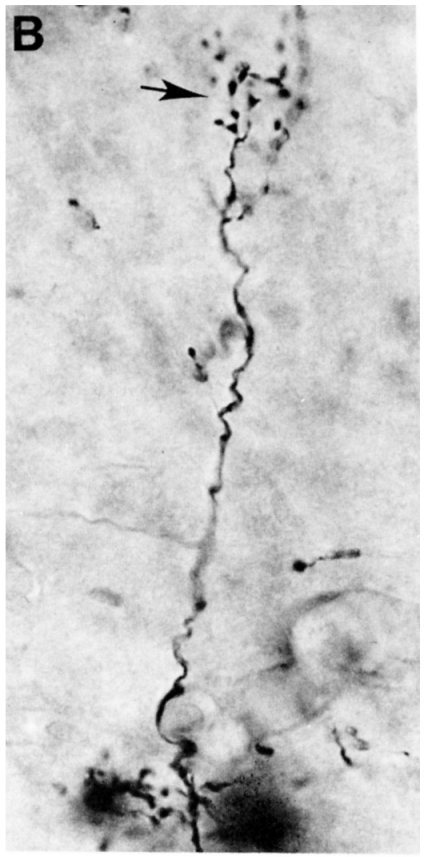
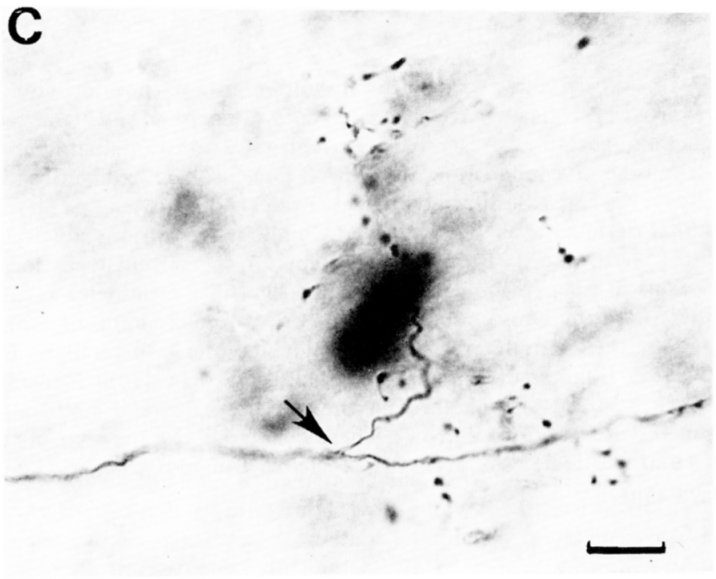


Figure 7-25. Axonal and terminal morphology in the inferior collicu These axons were filled by the anterograde movement of HRP and rea with diaminobenzidine. A. Photomicrograph of axons originating in lateral lemniscus and innervating the central nucleus. The parent fiber is μm in diameter and exhibits modest varicosities along its length. Short laterals that terminate as one or several bulbous expansions are freq features of these axons. B. Photomicrograph of the terminal portion lateral lemniscal fiber in the central nucleus. The fiber terminates as a s of collaterals and bulbous endings (arrow). C. Photomicrograph of axon originated in the contralateral inferior colliculus and collateralized in dorsal cortex. Commissural fibers are usually less than 1 μm in diam course on a horizontal plane through the dorsal cortex, and emit long laterals in the dorsal cortex (arrow). These collaterals give rise to many s branches that terminate as boutons. The scale bar equals 10 μm and appli all photographs.





The Dorsomedial Nucleus (DM)

The dorsomedial nucleus is a small group of cells that fits into the dorsomedial and caudal dent of the central nucleus (Figs. 7-23A, 7-42). Its dorsal and caudal surfaces are covered by the superficial layer of the dorsal cortex. The neurons are small to medium sized stellate cells. Although their dendrites have a spherical domain, many of the distal dendritic segments curve to conform with the gradually disappearing laminae of the central nucleus. This area does not seem to receive a significant contribution of fibers from the lemniscus, brachium, or commissure; instead its neuropil is characterized by loosely arranged reticulum of fibers of unknown origin (Fig. 7-22A).

The External Cortex (EC)

The external cortex wraps around the lateral, ventral, and rostral borders of the central nucleus (Figs. 7-42, 7-43).This structure may be divided into a superficial and deep layer (Ramón y Cajal, 1909). The superficial layer is located rostral and dorsal in the inferior colliculus (Fig. 7-43). It consists of densely packed, small stellate cells with lightly staining cytoplasm. The deep layer underlies the superficial layer, but also extends back to reach the caudal portion of the dorsal cortex and hooks ventromedially to underlie the central nucleus. A distinguishing feature of the deep layer is its population of loosely packed, large neurons (Fig. 7-42). Many of these cells have pyramidal-shaped cell bodies containing granular, intensely staining Nissl substance and thick primary dendrites that taper distally; these dendrites are long and relatively unbranched. In many cases, individual cells extend their dendrites into the superficial layer, while also projecting dendrites into the central nucleus (Fig. 7-23). The ventrolateral portion of the deep layer contains the largest neurons of the inferior colliculus (Fig 7-26).

The parcellation of the external cortex into two layers is supported by our observation that each layer receives different innervation. Specifically, the superficial layer receives somatic sensory input from the dorsal column nuclei and the trigeminal complex while the deep layer receives input from the dorsal cochlear nucleus and only scattered input from somatosensory sources (Willard and Ryugo, 1979).

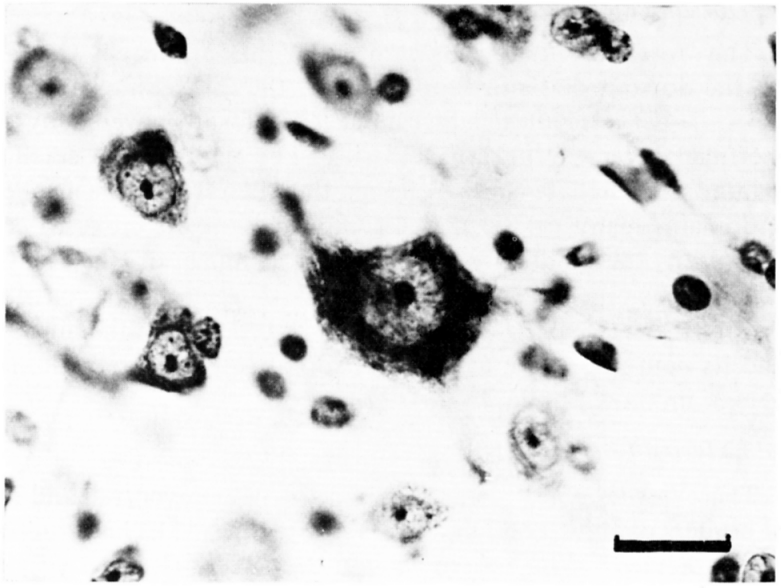


Figure 7-26. Photomicrograph of a large multipolar neuron in the ventral portion of the deep layer of the external cortex. Scale bar equals 20 μm.

The Dorsal Cortex (DC)

The dorsal cortex consists of a superficial cap, which covers the dorsal and caudal surfaces of the central nucleus, and a deep zone, which lies adjacent to the dorsomedial and rostral corner of the central nucleus (Fig. 7-43). The superficial layer is composed of small stellate cells and small planar cells (Fig. 7-23B); they have lightly staining Nissl substance in their cytoplasm and their thin, untapering dendrites are covered with spines. The flattened, planar cells have their "face" oriented parallel to the collicular surface. The deep zone contains a mixture of large and small stellate cells (Fig. 7-23). The large stellate cells have a darkly staining Nissl substance and thick, tapering proximal dendrites. These dendrites extend throughout the deep layer without any obvious orientation, and often penetrate into the superficial layer of the dorsal cortex. The small stellate cells exhibit a thin rim of lightly staining cytoplasm surrounding their oval nucleus; their dendrites tend to course parallel or perpendicular to the trajectory of the commissural fibers.

The commissural fibers enter the dorsal cortex medially and course on a horizontal plane across this structure (Fig. 7-22). We have observed many of these fibers filled with HRP following injections into the contralateral inferior colliculus (Fig. 7-25C). They appear thinner than the fibers of the lemniscus (less than 1 micron in diameter) and give off long collateral branches at right angles to the parent fiber.

The Interstitial Nucleus (IN)

The interstitial nucleus represents the rostromedial portion of Ramón y Cajal's (1909) internuclear cortex. This nucleus is composed of small multipolar neurons intercalated in the commissure of the inferior colliculus as it crosses the midline (Fig. 7-43 section C140). The neurons of this structure are present in lower density than those of the dorsal cortex. The dendrites of these cells tend to course either perpendicular or parallel to the trajectory of the fibers in the commissure. Nothing is known about the connections of this structure.

The Parabrachial Nucleus (PBN)

The parabrachial nucleus is a diffuse population of cells located within and medial to the brachium of the inferior colliculus (Fig. 7-43, section C140). These neurons are multipolar and have a wide range of sizes. Many of the dendrites of these cells course perpendicular to the trajectory of the brachial fibers (Fig. 7-27). Rostrally these neurons merge with those of the medial division of the medial geniculate body (Fig. 7-27B).

Connections of the Inferior Colliculus

The inferior colliculus receives direct ascending projections from virtually every major auditory structure of the mouse brain with the exception of the medial nucleus of the trapezoid body. These projections are summarized in Figures 7-7, 7-15, and 7-21. Using small injections of HRP, we have been able to determine the projections to specific subdivisions of the inferior colliculus. Essentially, the ascending projections to the central nucleus and the external cortex appear very similar, with the exception that the ventral cochlear nucleus does not project to the external cor-

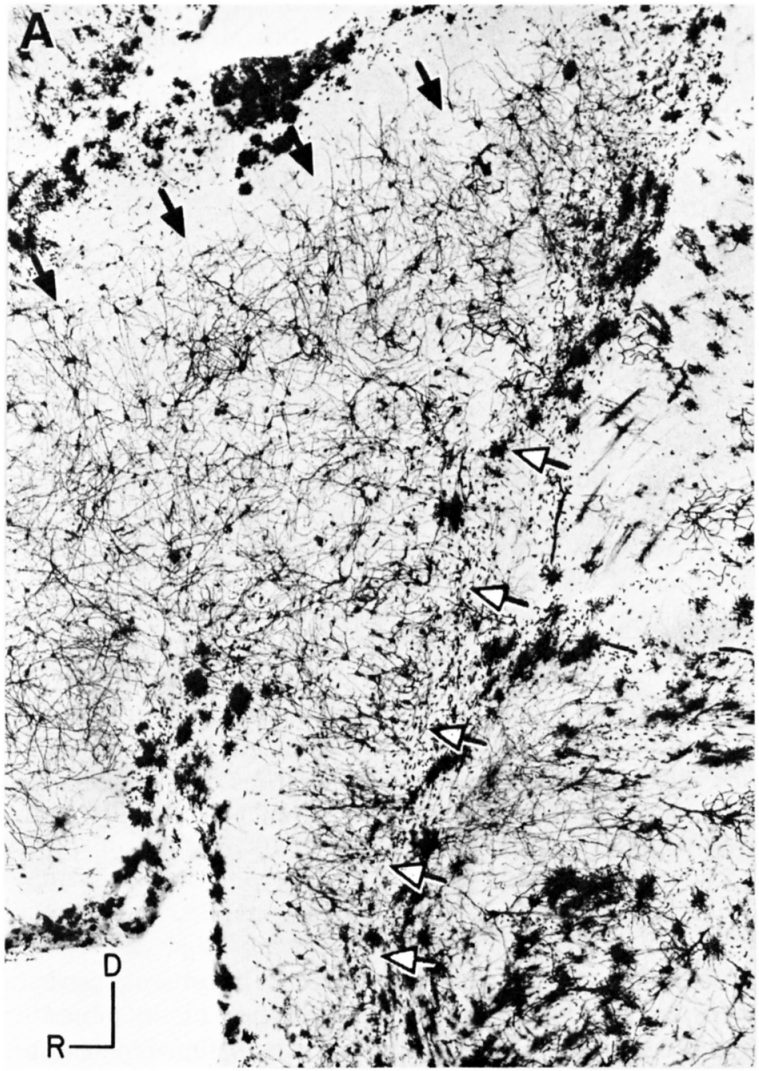
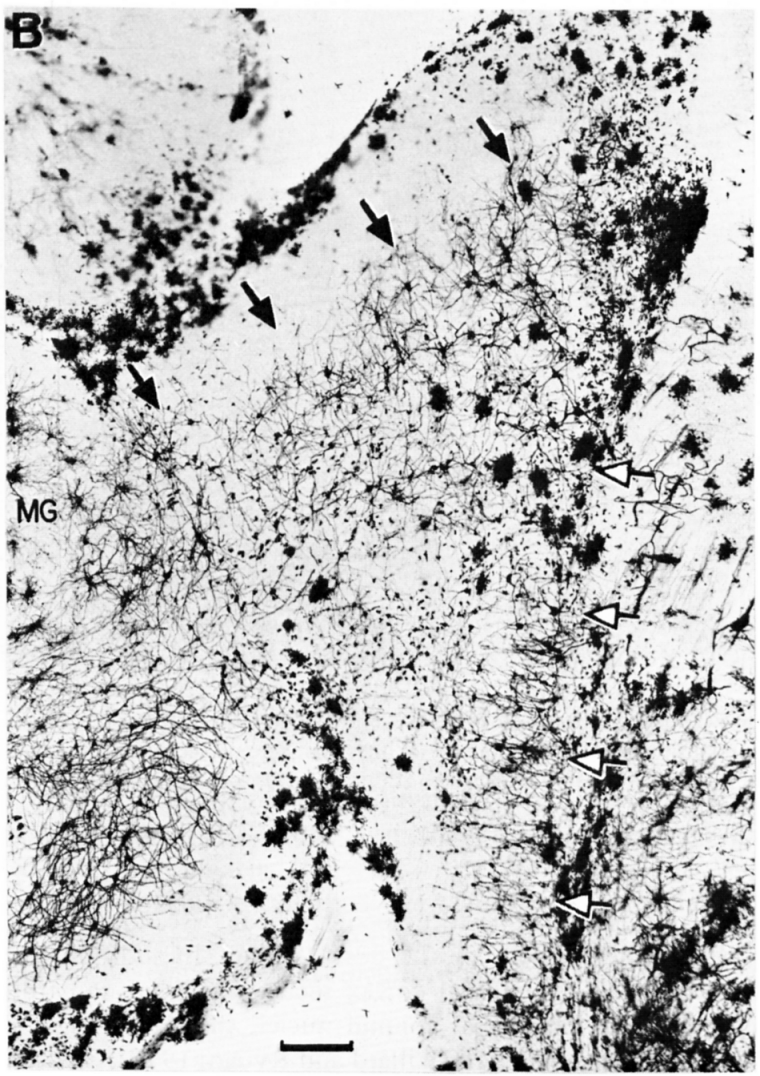


Figure 7-27. Neuronal organization in the lateral lemniscus and the brachium of the inferior colliculus. Photomicrographs of Golgi-Cox stained parasagittal sections (A is more medial than B) through the lateral midbrain. The lateral lemniscus is marked by open arrows; the brachium of the inferior colliculus is marked by solid arrows. Neurons within these fiber systems tend to have their dendrites oriented perpendicularly to the trajectory of the fiber bundles. Scale bar equals 0.25 mm.



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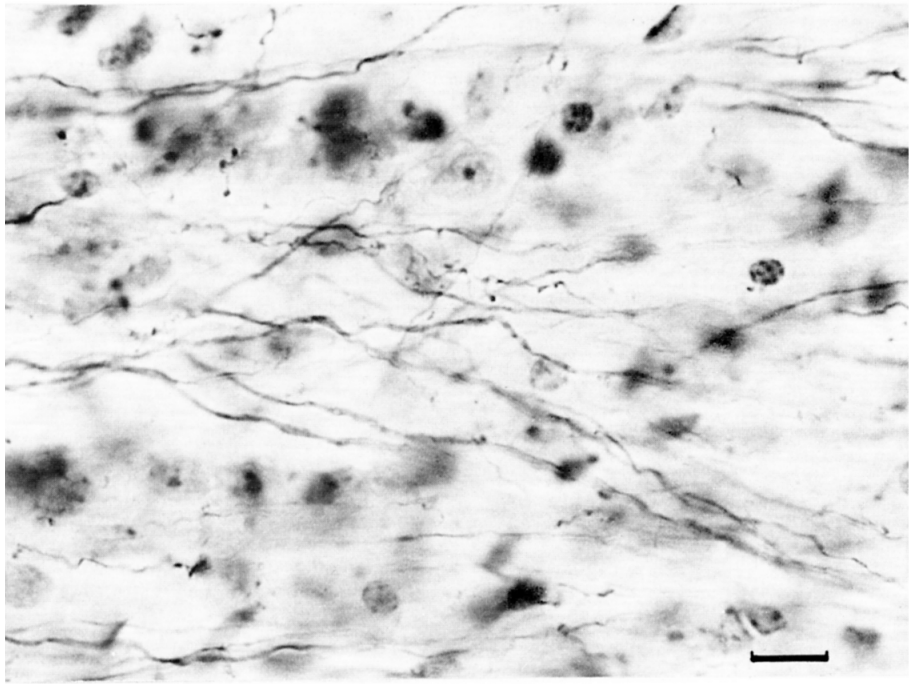


Figure 7-28. Axon morphology in the brachium of the inferior colliculus. A. Photomicrograph of HRP-stained axons that are projecting to the medial geniculate body. They are relatively thin, 1 μm or less in diameter, and emit many collateral boutons. B. Photomicrograph of terminal bouton (arrow) ending on the cell body of a parabrachial neuron. Scale bars equal to 20 μm.

tex. We have been unable to detect significant ascending input to the dorsomedial nucleus or the dorsal cortex. In addition to the auditory input, the external cortex receives afferent somatosensory fibers from the dorsal column nuclei, the spinal trigeminal nucleus, and the spinal cord (Willard and Ryugo, 1979).

The commissural connections of the inferior colliculus are quite orderly but also quite complex. We can report with confidence three basic observations on this subject: (1) all portions of

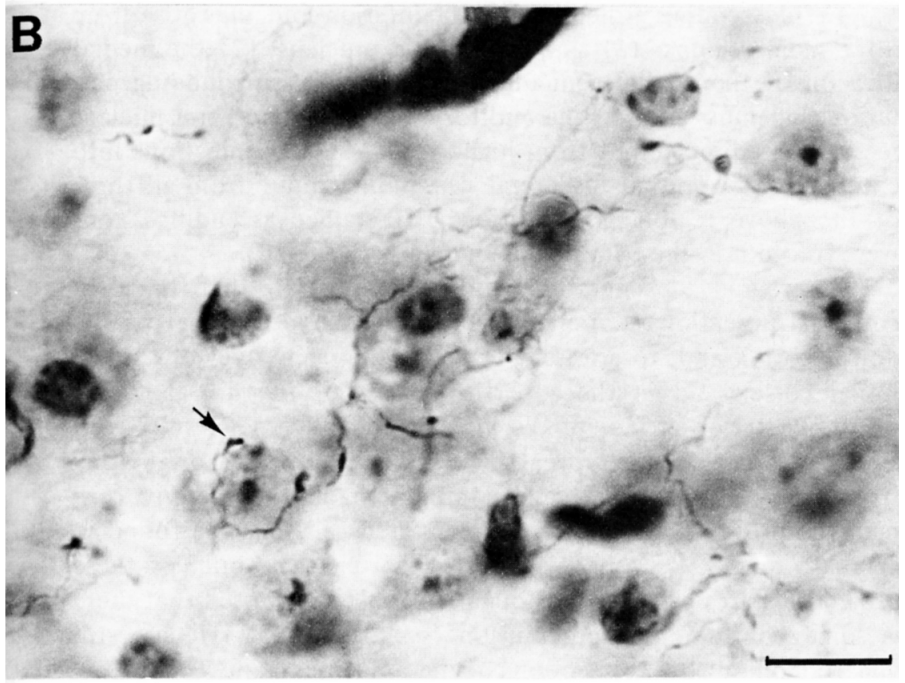


Figure 7-28 continued.

the inferior colliculus are homotopically connected through the commissure, with the exception of the ventromedial-most laminae of the central nucleus; (2) there is a symmetrical, lamina-to-lamina relationship established between the two central nuclei and (3) neurons projecting through the commissure exhibit two targets in the contralateral colliculus, their homotopic site, and the dorsal cortex.

The descending projections to the inferior colliculus arise from three main regions: (1) the parabrachial nucleus; (2) the medial division of the medial geniculate body and the surrounding posterior thalamus; and (3) the auditory cortex. The central nucleus receives no direct input from higher centers. HRP injections into external cortex reveal ipsilateral descending input from all three of the above regions; in addition HRP-stained ascending axons were traced into the parabrachial nucleus (Fig. 7-28).

Anterograde degeneration studies demonstrate that the corticotectal projections terminate heavily in the deep layer of the dorsal cortex and, to a lesser degree, in the deep layer of the external cortex and in the superficial layer of the dorsal cortex on the posterior surface of the inferior colliculus. HRP injections into the dorsal cortex reveal descending projections originating from layer V pyramidal cells confined mainly to area 41 (primary auditory cortex), although scattered cells may be found in areas 36 and 22 (secondary auditory cortex); the bulk of these projections are ipsilateral although it should be stressed that there is some contralateral contribution (*see* Fig. 7-35). We are still uncertain about the connections of the dorsomedial nucleus.

We have made some progress on unravelling the connections between ipsilateral subdivisions of the mouse inferior colliculus; we will refer to these connections as "associational." It appears that all of the subdivisions have axonal projections into the central nucleus. In turn, the neurons of the central nucleus have a projection to the deep layer of the external cortex. This projection arises as collaterals from fibers entering the brachium.

The Medial Geniculate Body (MGB)

The medial geniculate body is visible on the posterolateral surface of the thalamus as a rounded protrusion, marking the rostral end of the brachium of the inferior colliculus, and situated laterally and beneath the superior colliculus (Fig. 7-2). It is not a homogeneous structure and may be subdivided into a varying number of component nuclei on the basis of cytoarchitectonics, Golgi analysis, and patterns of connections (Morest, 1964; Oliver and Hall, 1978; Rámon y Cajal, 1909; Ross, 1962, 1965; Ryugo and Killackey, 1975). The ventral, medial, and dorsal subdivisions

emerge as three major components of the medial geniculate body that are common to a number of mammalian species (Fig. 7-29).

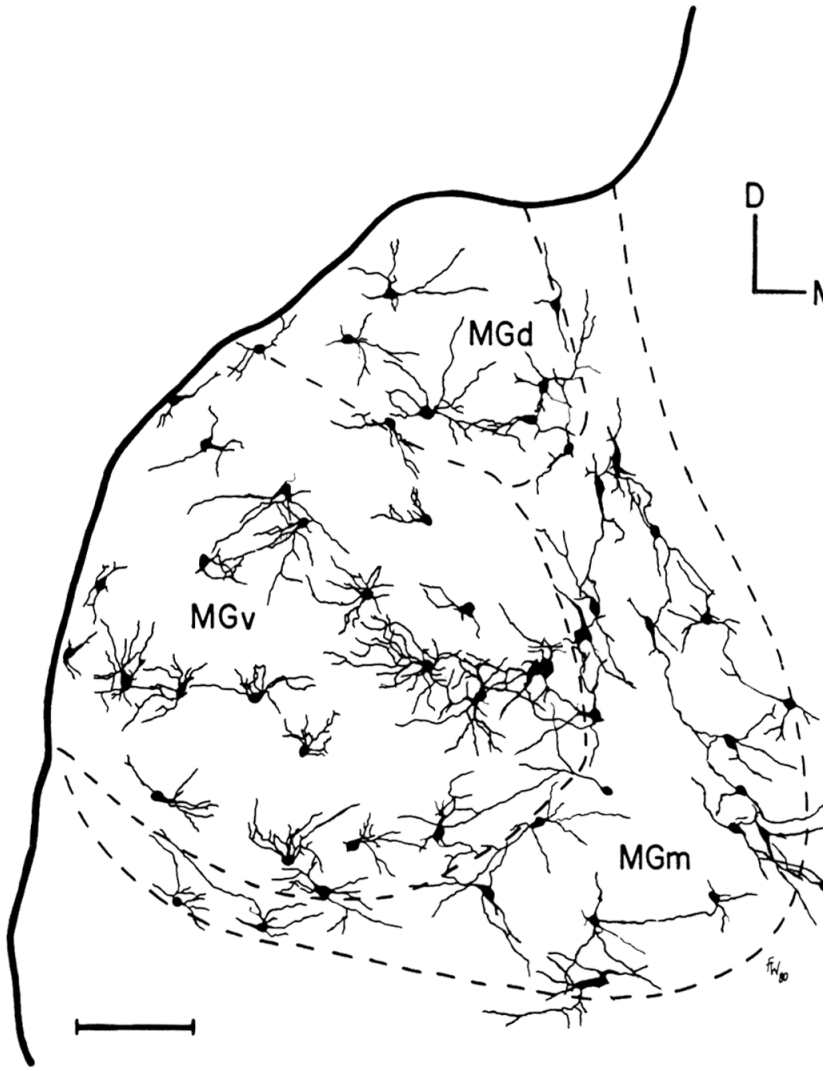


Figure 7-29. Neuronal architecture of the medial geniculate body. Camera lucida drawing of single Golgi-stained coronal section of a juvenile mouse (Golgi-Kopsch, Stensaas modification). The major subdivisions of the medial geniculate body are illustrated. Scale bar equals 100 μm.

The ventral division of the medial geniculate body (MGv) constitutes the principal mass of this complex. It is composed of densely packed small and medium sized neurons and is heavily penetrated by myelinated fibers. Examination of Nissl-stained sections reveals that the cell bodies are arranged in curved rows, forming a pattern of concentric swirls (Fig. 7-45, section C192), which is replicated by the trajectory of the myelinated fibers. The presence of two types of cell bodies in Nissl material is corroborated in our Golgi material. The small cells, presumably homologous to Golgi II cells of the cat (Morest, 1975), are inconsistently and rarely impregnated. The larger cells are characterized by 3-5 stout primary dendrites, each of which terminates by giving rise to a tuft of much thinner, secondary dendrites; such neurons are probably homologous to the thalamocortical relay cells described in the ventral division of the medial geniculate body of the cat (Morest, 1964).

The dorsal division of the medial geniculate caps the ventral division on its dorsal and caudal boundaries. It is composed of round cells that are somewhat smaller but whose cytoplasm stains slightly darker than those medium-sized cells of MGv. The cells have a round, centrally placed nucleus, which is surrounded by a thin rim of cytoplasm. This division stains negligibly with myelin stains. In Golgi preparations, the neurons have dichotomously radiating dendrites that ultimately form a spherical dendritic field. Neither the cell bodies nor the dendrites appear to be oriented in any particular fashion.

The medial division of the medial geniculate body embraces the medial and rostral boundaries of the ventral division. The medial division is characterized by the presence of rather large multipolar neurons and many myelinated fibers that are running in a rostral-caudal direction. In addition, cells having round or elongate perikarya are also found in this region. Regardless of the cell body shape, these neurons have long and relatively unbranched dendrites.

Our parcellation of the medial geniculate into three subdivisions does not coincide with the parcellation by Caviness and Frost (1980). Basically, Caviness and Frost (1980) divide this structure into two components, a principal division (MG) and a

medial division (MGm). Our dorsal division appears to encompass the dorsal portion of their MG and the caudal portion of their lateral posterior nucleus (LPc). Caviness and Frost (1980) apparently consider LPc to be nonauditory because its cortical target, area 36a, is considered a part of the visual field. In contrast, we feel that the dorsal division (their LPc) is part of the auditory thalamus. First, the dorsal division receives afferent projections from the inferior colliculus; second, HRP injections that encroach into area 36 and 36a, the homologous auditory belt cortex of the rat (Ryugo and Killackey, 1974), produce HRP-labelled cells in the dorsal division. Resolution of this issue seems to revolve around whether area 36a is more concerned with audition or vision. Finally, we feel that the rostral-most pole of MG, illustrated in their atlas sections 2.0 and 2.2 (*see* Fig. 1 of Caviness and Frost, 1980), is actually the rostral extension of the medial division because this region receives somatosensory projections from the dorsal column nuclei (unpublished observations).

Connections of the Medial Geniculate Body

There is no published information on tectothalamic projections in the mouse, although our preliminary data suggest the basic connections are similar to what has been reported for the rat (Ryugo and Killackey, 1975; Fullerton, 1978). That is, the central nucleus of the inferior colliculus projects to the ventral division of the medial geniculate body, the external cortex projects to the medial division of the medial geniculate body, and the dorsal cortex projects to the dorsal division of the medial geniculate body.

The thalamocortical projections have recently been reported for the mouse and two general categories of axons are observed (Caviness and Frost, 1980; Frost and Caviness, 1980). Class I axons are of large caliber and terminate heavily in cortical layers III and IV; collateral branches of these axons are found to a much smaller extent in cortical layers I and VI. Class I projections therefore have axon terminals distributed in three tiers. In contrast, Class II axons are described as small-caliber and are diffusely distributed in all layers of cortex but have their heaviest concentration of terminals in cortical layers I and VI. Class II projections

have axon terminals distributed in two tiers. These two classes of thalamocortical projections seem to be related to the specific (Class I) and unspecific (Class II) thalamocortical afferents described by Lorente de Nó (1938). The ventral division of the medial geniculate body gives rise to Class I projections that terminate primarily in cortical area 41 (Fig. 7-32). The dorsal division of the medial geniculate body gives rise to Class I projections in cortical areas 36 and 36a. The medial division of the medial geniculate body gives rise to Class II projections in cortical areas 41, 22, 36, and 36a (Fig. 7-32).

Descending projection from the medial geniculate body have been observed following injections of HRP into external cortex of the inferior colliculus. These projections arise from the ipsilateral medial division and, to a much smaller extent, from the ipsilateral dorsal division. There were never any HRP-labelled cells found in the ventral division. In some cases, it was also possible to observe anterogradly labelled axons; such axons were distributed principally within the medial division, suggesting a reciprocity of connections between it and the external cortex.

A summary of these connections of the medial geniculate body is illustrated in Figure 7-30. The basic relationship between auditory structures of midbrain, thalamus, and cortex appears to be similar to what has been found in other species, particularly in the rat (Ryugo, 1976; Fullerton, 1978).

Auditory Cortex

The auditory cortex is located on the posterolateral surface of the cerebral hemispheres, just dorsal to the rhinal fissure. A number of cytoarchitectonic maps of the mouse cerebral cortex have been constructed (De Vries, 1912; Droogleever Fortuyn, 1914; Isenschmid, 1911; Ramón y Cajal, 1909; Rose, 1912, 1929), but until Woolsey (1967) compared the results of his electrophysiological experiments to these cortical maps, a defined anatomical entity in cortex could not be directly related to a functional system.

Before continuing further, it is necessary to establish the definitions for two terms that may cause some confusion due to their interchangeable usage. The term "area" will be used in

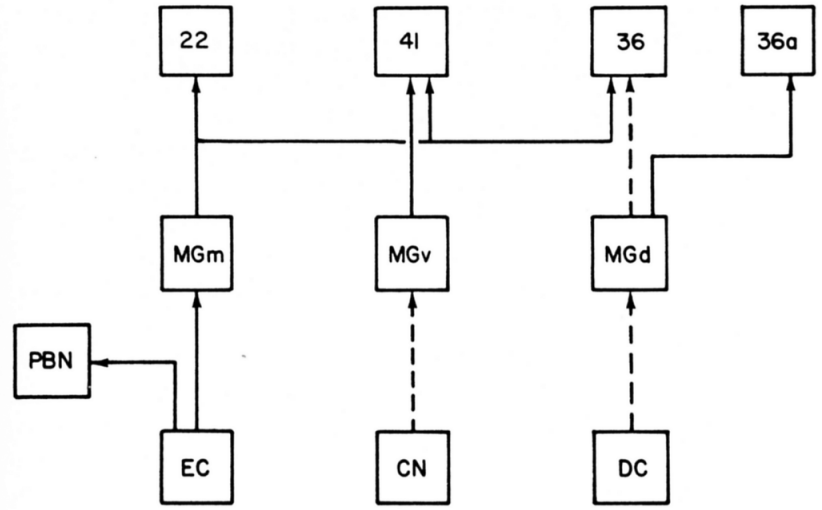


Figure 7-30. Summary diagram illustrating the ascending afferents and efferents of the medial geniculate body. The solid lines indicate the known pathways for the mouse (Caviness and Frost, 1980; Frost and Caviness, 1980; authors' observations); dashed lines represent pathways that have been found in the rat (Fullerton, 1978; Ryugo, 1976). The pathways that have been studied in both mouse and rat are wholly consistent with each other.

referring to a distinct cytoarchitectonic entity; in contrast, a "field" is composed of one or more areas that are unified because they all receive physiologically defined projections from specified regions of the thalamus.

The auditory field of the mouse has been partitioned into three cytoarchitectonic areas (Caviness, 1975). Primary auditory cortex or koniocortex is so named because of its dense population of granule cells in cortical layer IV and the presence of large pyramidal cells in layer V; Caviness (1975) calls this area 41. Area 41 is surrounded rostrally and dorsally by area 22 and caudally and ventrally by area 36. Although cytoarchitectonic boundaries between these auditory areas in the mouse are not sharp, several features may be emphasized which characterize each cortical area (Fig. 7-31).

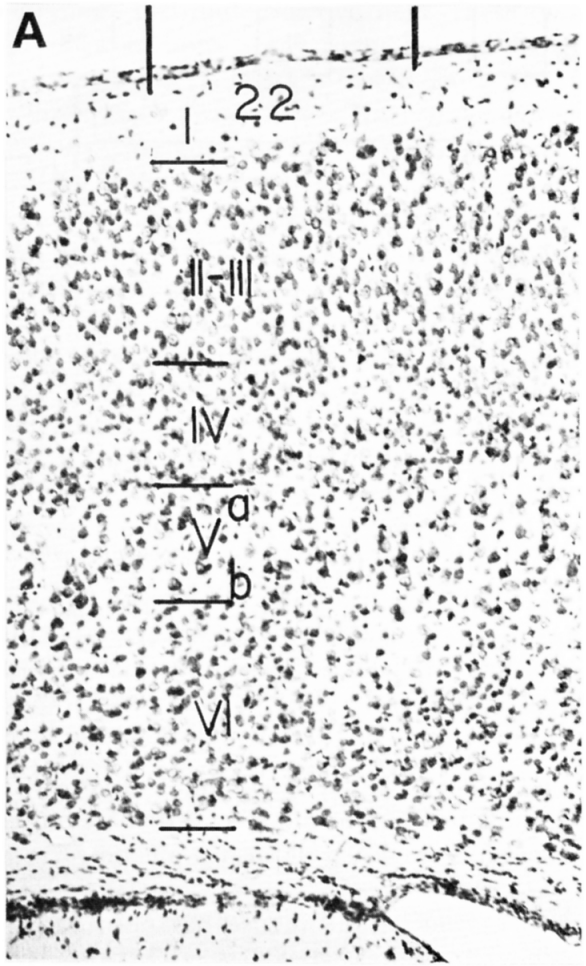
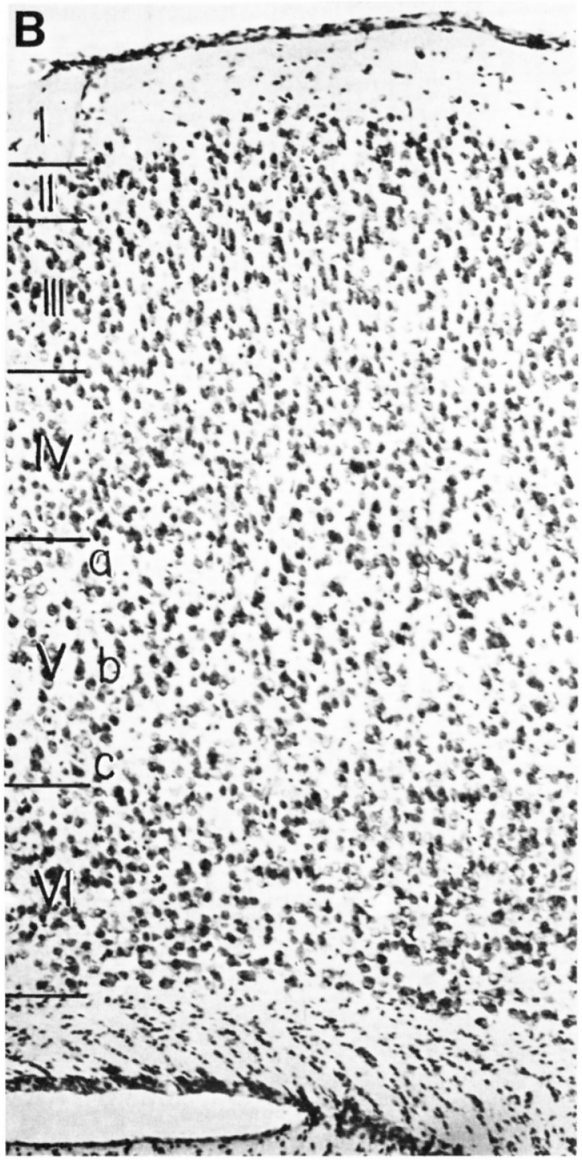


Figure 7-31. Photomicrographs from three different cortical areas which comprise auditory cortex (Nissl stain). The cortical layers are labelled by Roman numerals and their boundaries are indicated by horizontal bars. A. Area 22 is indicated by the vertical lines. This area is squeezed between temporal and parietal cortex and does not have distinct boundaries. B. Area 41 or primary auditory cortex (koniocortex). C. Area 36 or secondary auditory cortex. This cortical region is sandwiched between area 41 dorsally and the rhinal sulcus ventrally. Scale bar equals 0.1 mm.



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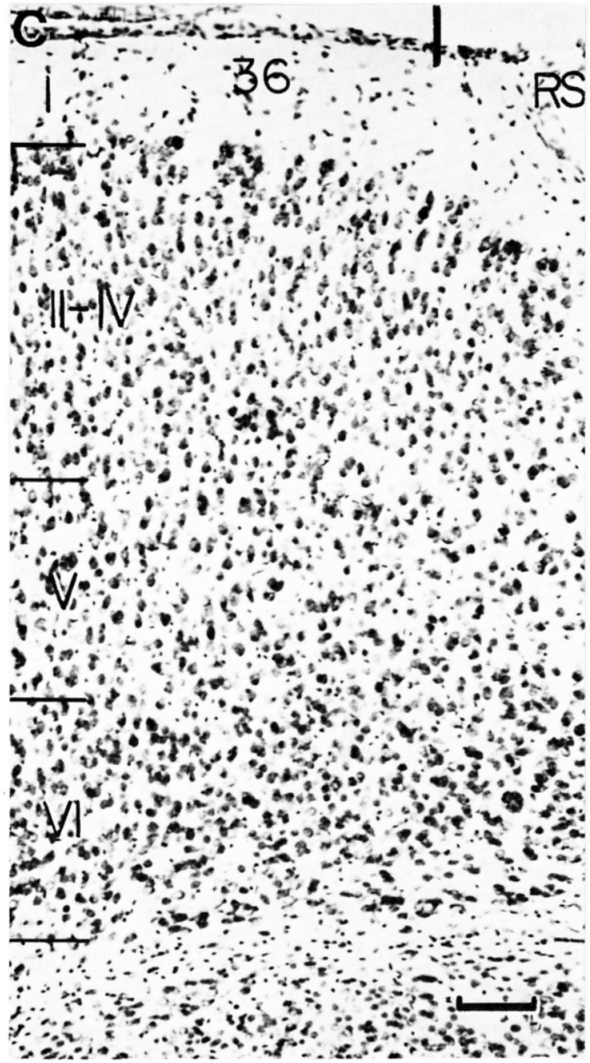

Figure 7-31 continued.

Area 41 has the greatest cortical depth of the three areas (Fig. 7-31). Layer I is thin and composed mainly of fibers and a few scattered cell bodies. Its appearance does not change throughout the auditory cortex. Layer II contains small pyramidal cells and has a slightly greater cell density than that of layer III, which also contains small pyramidal cells. Layer IV consists of densely packed granule cells. Layer V contains large pyramidal cells and may be separated into three sublayers: V_a shows a decrease in cell density from the layer IV; V_b is the broadest and densest of the three sublayers; and V_c is markedly diminished in cell density. Layer VI contains densely packed, globular-shaped neurons.

Area 22 is a narrow region which is squeezed between the temporal cortex and the occipital cortex. It is marked by a decrease in cortical depth compared to that of area 41, an accompanying increase in neuronal density, and a general blurring of the layers (Fig. 7-31). Layers II – IV closely resemble each other in neuronal size and density. Layer V has a hypocellular sublayer V_a, the characteristic sublayer V_b with its large pyramidal cells, but no sublayer V_c. Layer VI may be separated from V by an increase in cell density and the presence of the globular-shaped neurons.

Area 36 forms the ventrolateral and caudal border of area 41. It extends along the dorsal edge of the rhinal fissure and passes caudally between areas 18a and 35 (*see* Fig. 1, Frost and Caviness, 1980). Area 36 has a decreased cortical depth and increased neuronal density when compared to area 41 (Fig. 7-31). Layers II – IV tend to blend together. The layer V pyramidal cells are smaller than those in area 41 and there are no hypocellular zones marking sublayers V_a and V_c. Layer VI is delineated by a slight increase in cell density from that of V and the presence of globular-shaped cells.

Connections of Auditory Cortex

The afferent projections into auditory cortex arise from the thalamus (*see* Fig. 7-32 as discussed previously), from ipsilateral regions of cerebral cortex (association fibers, about which we know virtually nothing), and from commissural fibers which arise from contralateral regions of cerebral cortex (Yorke and Caviness, 1975).

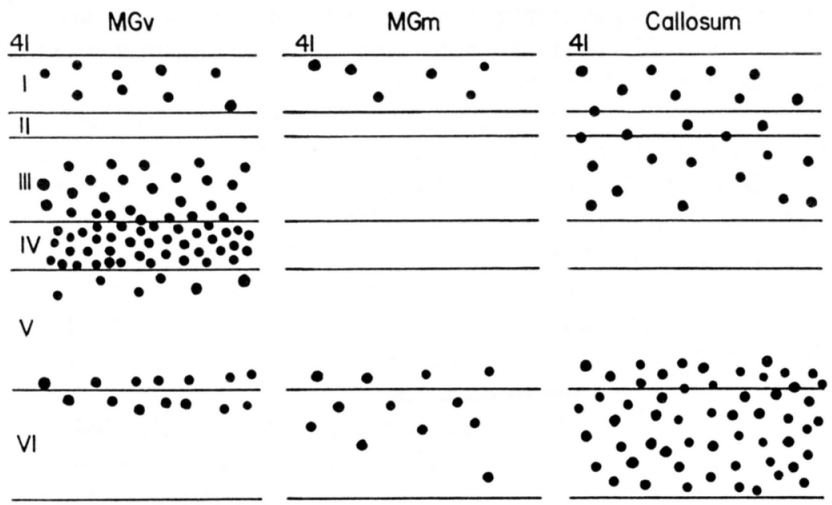

Figure 7-32. Diagram that illustrates the laminar distribution, density, and source of axon terminals in area 41. Thalamocortical projections arise from the ventral (MGv) and medial (MGm) divisions of the medial geniculate body whereas the contralateral hemisphere contributes to the projections through the corpus callosum. This information is from data of Yorke and Caviness (1975), Caviness and Frost, (1980), Frost and Caviness (1980).

The commissural projections arise in the contralateral hemisphere and reach the auditory cortical fields by passing through the corpus callosum. The distribution of commissural terminals within the auditory cortical fields was determined by anterograde degeneration methods following surgical transsection of the corpus callosum; basically, the commissural terminals are distributed in two horizontal strips, one above layer IV and one below (Fig. 7-32). Areas 41 and 22 are marked by terminal degeneration in cortical layers I, II, and III, and in layer VI and the adjacent part of layer V. In contrast, Area 36 has terminal degeneration in cortical layers I and II, and in layer VI and the adjacent part of layer V.

The regional and laminar distribution of those neurons that give rise to commissural projections were determined by the retrograde transport of HRP (Yorke and Caviness, 1975). Neurons

with commissural projections were found in all cortical layers, but most were the medium-to-large pyramidal cells within cortical layers III and V. As many as 50 percent of the cells in layers III and V project across the corpus callosum; a slightly lower percentage of cells in layer VI also give rise to commissural projections. There is a high degree of overlap between the cortical regions of origin and the regions of termination of callossal fibers.

The origin and distribution of descending (corticofugal) projections has been partially determined using both anterograde degeneration and HRP techniques. Following hemidecortication, degenerating axons and terminals are found in both the medial geniculate body and the inferior colliculus. The ipsilateral ventral division of the medial geniculate receives a heavy corticothalamic projection, whereas the ipsilateral dorsal and medial divisions receive a significantly smaller projection. In the inferior colliculus, the ipsilateral dorsal cortex receives a significant projection. There is also scattered degeneration within the ipsilateral cortex, but no direct projection to the central nucleus of the inferior colliculus.

We have confirmed the corticotectal projections using HRP methods (Fig. 7-33). The corticotectal projections originate from pyramidal cells of various sizes which are concentrated in layer Vb of area 41 (Fig. 7-34). HRP-labelled pyramidal cells are found in much fewer numbers in area 36 or 22. The terminal field of these corticotectal projections is in the dorsal cortex. A summary of the connections of auditory cortex are presented in Figure 7-35.

Conclusion

Although we have presented a seemingly myriad of anatomical details concerning the central auditory system of the mouse, there is still a paucity of data, due primarily to the magnitude of the task of organizing the tremendous number of neurons within the bewildering complexity of the nervous system. Nevertheless, the conclusion emerges that the mouse is well-suited for anatomical studies on the auditory system; it has all of the basic components and does not seem unusually specialized in any particular

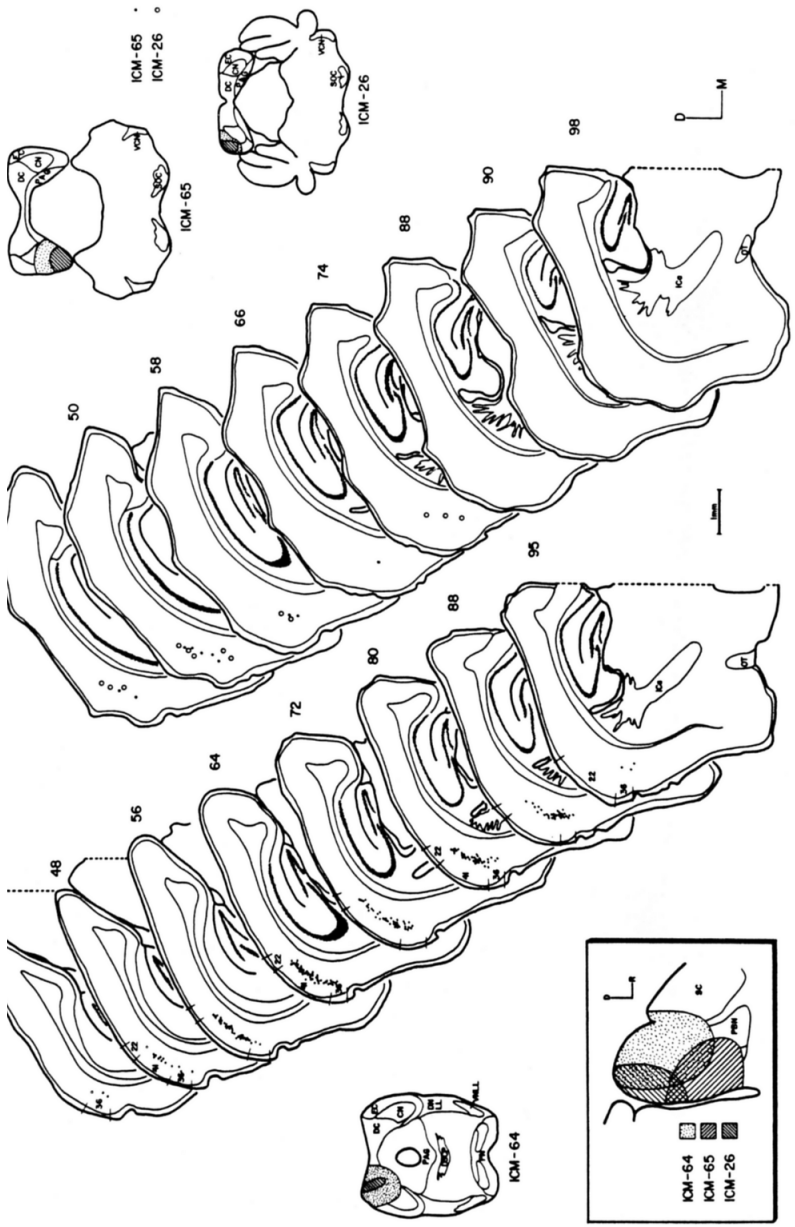

Figure 7-33. Areal distribution of layer V pyramidal cells that project to the ipsilateral inferior colliculus. Nearly all of these projections arise from area 41. HRP injections that center in the dorsal cortex of the inferior colliculus (e.g. ICM-64) produce many labelled cells in auditory cortex. More caudal injections of HRP (ICM-26 and ICM-65) which are outside the dorsal cortex produce relatively few labelled cells in auditory cortex. These data are consistent with anterograde degeneration studies where lesions of auditory cortex result in terminal degeneration primarily confined to dorsal cortex.

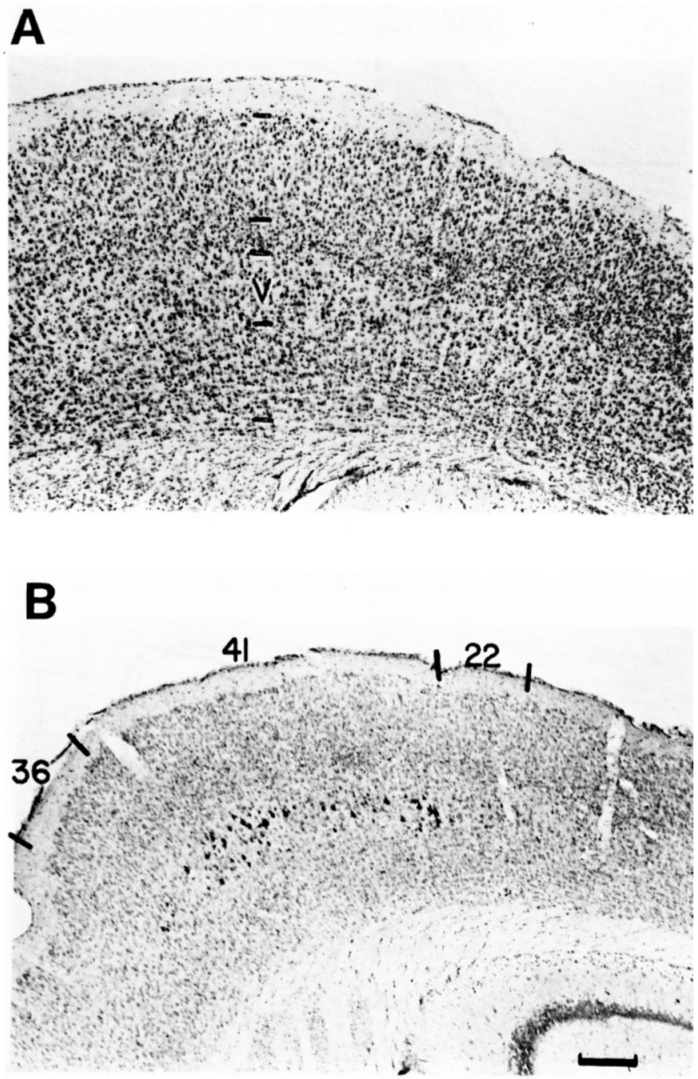

Figure 7-34. Laminar distribution of cortical pyramidal cells that project to the ipsilateral inferior colliculus. Corticotectal projections arise primarily from layer Vb pyramidal cells of area 41. A. Photomicrograph of Nissl-stained coronal section through auditory cortex illustrating the cortical layers, particularly layer V. B. Photomicrograph of HRP-reacted and neutral red counterstained coronal section through auditory cortex (comparable to that shown in A) from mouse ICM-64. Notice that most of the HRP-labelled neurons arise from layer Vb in area 41; however, a few labelled cells are seen in layers Va and Vc. Scale bar equals 0.2 mm. C. Coronal section through the inferior colliculus illustrating the HRP-injection site. D. Coronal drawing through brain ICM-64 outlining the region photographed in A and B.

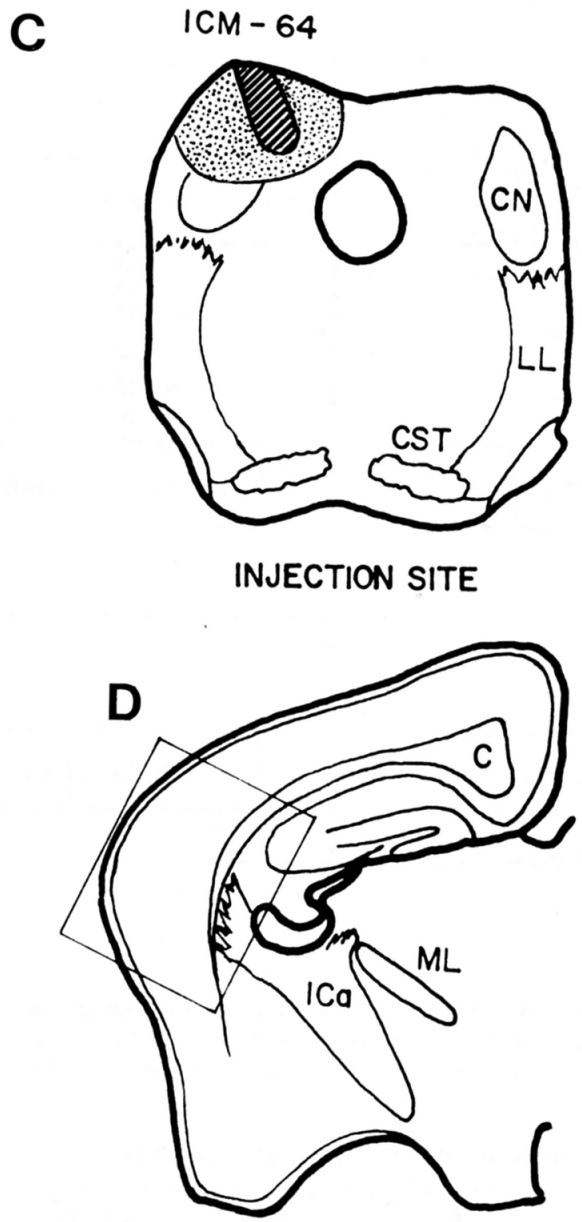

Figure 7-34 continued.

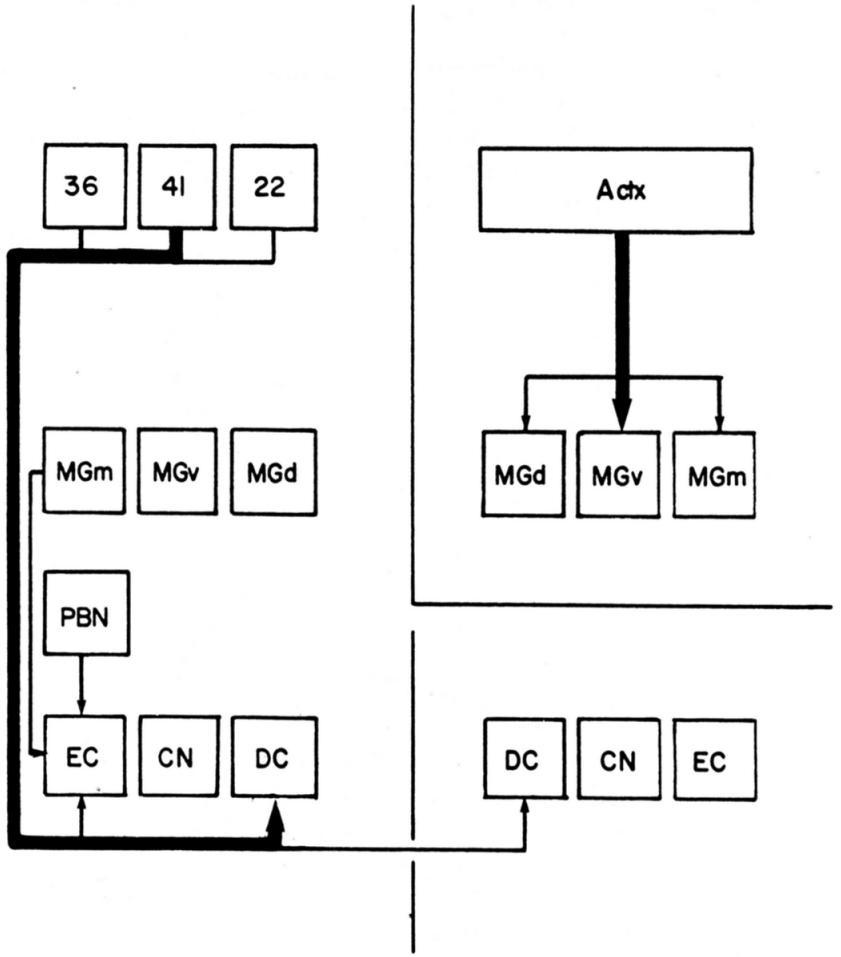

Figure 7-35. Summary diagram illustrating the known descending pathways that originate in auditory cortex and the medial geniculate body. The relative innervation density is reflected by the relative thickness of the line.

way. In the analysis of the comparative anatomy of the nervous system, the problem of selection of criteria for defining cell groups requires careful consideration. Typically, such analysis begins with regions of the nervous system where relative spatial position of cell groups are important. Descriptions of cell groups based primarily

on spatial position have often proven inadequate in comparative studies since anatomically similar nuclei (defined by the constituent cell morphology, input terminations, and output connections) in different species may not occupy the same position relative to other structures. This is especially the case where there may be species differences in cell migration and/or cell segregation that do not affect synaptic connections.

Ultimately, we seek anatomical resolution at the cellular and synaptic level. However, the cell-by-cell analysis of neuronal morphology and input and output connections represents an imposing task. No single technique will provide all of the necessary information due to the selectivity of the available histological methods. Consequently, the identification of neuron classes requires a large sample of cells prepared in various ways so that numerous and diverse features can be observed and catalogued for each neuron encountered. The common features of cells must be extracted and circuit hypotheses may then be formed regarding the resulting cell categories. At virtually every level of the mammalian auditory system, such information is incomplete (Table 7-I).

All of the available evidence reveals that the mouse auditory system follows the general plan for mammals. The cellular composition and axonal connections of the major auditory structures in the mouse brain confirm and extend what has been reported for other mammalian species (*see* Table 7-I; *also see* reviews by Harrison, 1978a,b; Harrison and Howe, 1974). There are some reports of anatomical variations between comparable brain structures in different mammals, but such variations could simply reflect differences in analytic methods or nomenclature criteria. On the other hand, it is possible that certain auditory structures are associated with behaviorally different aspects of hearing, and variations in these structures might be associated with differences in the auditory behavior of the species (Irving and Harrison, 1966; Masterton et al., 1975; Moore and Moore, 1971).

Table 7 – I-A

COCHLEAR NUCLEUS – CELL TYPE

	Mouse		Harrison & Irving, 1965, 66 Rat		Distelhoft et al., 1980 Rabbit		Osen, 1969 Brawer et al., 1974 Cat		Moskowitz & Liu, 1973 Squirrel Monkey		Moore & Osen, 1979 Konigsmark, 1973 Human	
	N	G	N	G	N	G	N	G	N	G	N	G
VENTRAL COCHLEAR NUCLEUS												
Sperical cells/Bushy cells	+	+	+	+	–	+	+	+	+	–	+	+
	endbulbs		endbulbs									
Multipolar cells/Stellate cells	+	+	+	+	–	+	+	+	+	–	+	+
Globular cells/Bushy cells	+	+	+	+	–	–	+	+	+	–	+	+
Small cells	+	+	+	+	–	–	+	+	–	–	+	+
Octopus cells	+	+	+	+	–	+	+	+	+	–	+	+
Auditory nerve neurons	+	+	+	+	–	–	0	0	–	–	–	–
Giant cells	+	+	+	+	–	–	+	+	–	–	–	–
Granule cells	+	+	+	+	–	–	+	+	–	–	0	0
DORSAL COCHLEAR NUCLEUS												
Principal cells (pyramidal, fusiform)	+	+	+	+	–	+	+	+	+	–	+	+
Small cells	+	+	+	–	–	–	+	+	–	–	+	+
Giant cells	+	+	+	+	–	+	+	+	0	–	+	+
Granule cells	+	+	+	+	–	+	+	+	–	–	rare	

N = Nissl stain
G = Golgi stain
+ = present
0 = absent
– = no data

Table 7 – I-B

DORSAL COCHLEAR NUCLEUS CYTOARCHITECTURE

	Mouse	Cat	Prosimians: Galago	Prosimians: Loris	Ceboid: Marmoset	Ceboid: Owl Monkey	Ceboid: Cebus	Ceboid: Spider	Ceboid: Wooly	Cerocopithecoid: Macaque	Cerocopithecoid: Vervet	Gibbon	Human
DORSAL COCHLEAR NUCLEUS													
Pontobulbar fiber layer	0	0	0	0	0	0	0	+	+	+	+	+	+
Ext. granule cell layer	0	0	+	+	+	+	+	+	+	ant-lat. side only		0	0
Molecular layer/marginal zone	+/0	+/0	+/0	+/0	+/0	+/0	+/0	+/0	+/0	+/+	+/+	0/+	vestige
Fusiform cell layer / Granule cell layer	+/+	+/+	+/+	+/+	+/0	+/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
Central region (polymorphic layer)	+ fc	+ fc	+ fc	+ fc	+ fc	+ fc	+ fc	+ fc	+ fc	+ fc	+ fc	+ fc	+ fc

fc = fusiform cells present
\+ = present
0 = not present

Data from Moore, 1980 and Moore and Osen, 1979

Table 7 – I-C

COMPONENTS OF THE SUPERIOR OLIVARY COMPLEX

	Ramón y Cajal, 1909	Willard & Ryugo	Ollo & Schwartz, 1979	Harrison & Warr, 1962	Webster et al., 1968	Morest, 1968	Scheibel & Scheibel, 1974	Schwartz, 1977	Moore & Moore, 1971	Moore & Moore, 1971	Moore & Moore, 1971
	Cat Rabbit Mouse	ICR mouse	C57 BL/6 mouse	Rat	Kangaroo Rat	Cat	Cat	Cat	Monkey	Gibbon	Human
SUPERIOR OLIVARY COMPLEX	+	+	+	+	+	+	+	+	+	+	+
LATERAL NUCLEUS	+	+	+	+	+	+	+	+	+	+	+
Principal cells	+	+	+	–	+	–	+	–	–	–	–
Marginal cells	+	+	+	–	–	–	–	–	–	–	–
Spindle cells	–	0	+	–	–	–	–	–	–	–	–
MEDIAL (ACCESSORY) NUCLEUS	+	+	+	+	+	+	+	+	+	+	+
Principal cells	+	+	+	–	+	–	–	+	–	–	–
Marginal cells	+	0	0	–	+	–	–	+	–	–	–
Multipolar cells	–	0	0	–	–	–	–	+	–	–	–
Rostrocaudal cells	–	0	0	–	–	–	–	+	–	–	–
MEDIAL NUCLEUS OF TRAPEZOID BODY	+	+	+	+	+	+	–	–	+	+	0
Principal cells	+	+	+	–	+	+	–	–	–	–	–
Stellate cells	–	+	–	–	–	+	–	–	–	–	–
Elongate cells	–	–	–	–	–	+	–	–	–	–	–
DORSAL PERIOLIVARY CELL MASS	+	+	+	+	+	+	–	–	+	+	+
Retro-olivary nucleus	+	0	0	0	0	DPLO	–	–	–	–	–
Superior paraolivary nucleus	–	+	+	+	RO	0	–	–	–	–	–
DMPO/DPO	–	0	0	0	0	+	–	–	–	–	–
VENTRAL PERIOLIVARY CELL MASS	+	+	+	+	+	+	–	–	+	+	+
External periolivary nucleus	+	LNTB	LNTB	LNTB	LPN	LNTB	–	–	–	–	–
Internal periolivary nucleus	+	VNTB	VNTB	VNTB	MPN	VNTB	–	–	–	–	–
VMPO	–	0	0	0	0	+	–	–	–	–	–

\+ = present
– = no data
0 = absent

Table 7 – I-D

NUCLEI OF THE LATERAL LEMNISCUS

	Willard & Ryugo MOUSE	Ramón y Cajal, 1909 MOUSE/RABBIT	Taber, 1961 Berman, 1968 CAT
VENTRAL NUCLEUS	+	+	+
Medial division – large multipolar cells	+	large star cells	-
Lateral division – small-med. multipolar cells	+	–	–
INTERMEDIATE NUCLEUS	+	trail of cells	0
Medium multipolar cells – dark staining	+	–	–
DORSAL NUCLEUS	+	+	+
Medium multipolar cells – light staining	+	fusiform cells	–

+ = present
– = no data
0 = absent

Table 7 – I-E

COMPONENTS OF THE INFERIOR COLLICULUS

Ramón y Cajal, 1909 Cat, rabbit, mouse, dog	Willard & Ryugo Mouse	Ryugo, 1976 Rat	Rockel & Jones, 1973 Cat	Oliver & Hall, 1978 Tree shrew	Fitzpatrick, 1975 Squirrel monkey	Geniec & Morest, 1971 Human
NUCLEUS OF THE OSTERIOR TUBERCLE	CENTRAL NUCLEUS	CENTRAL NUCLEUS	CENTRAL NUCLEUS	CENTRAL NUCLEUS	CENTRAL NUCLEUS	CENTRAL NUCLEUS
Multipolar cells (L + M)	Principal cells	Principal cells	Principal cells	Disc-shaped cells (M + S)	Disc-shaped neurons	Disc-shaped neurons (M + S)
Star-shaped cells (S)	Stellate cells	Multipolar cells (L + M)	Multipolar cells (L + S)		Stellate neurons	
Spindle-shaped cells						
	DORSOMEDIAL NUCLEUS	DORSOMEDIAL NUCLEUS	DORSOMEDIAL REGION	MEDIAL NUCLEUS		DORSOMEDIAL NUCLEUS
	Stellate cells (M + S)	Multipolar cells (L + M)	Large cells	S + M Cells		Multipolar neurons (S + M)
DORSAL CORTEX	DORSAL CORTEX	PERICENTRAL NUCLEUS	PERICENTRAL NUCLEUS	ROOF NUCLEUS	PERICENTRAL NUCLEUS	DORSAL CORTEX
I. Fiber layer	Fiber layer	Fiber layer	Fiber layer			
II. Star neurons (M + S) Spindle cells	I. Stellate and planar cells (S)	Spiney and nonspiney cells (S + M)	Spiney cells (L + M)	I. Small cells		I. Flattened neurons (S) II. Multipolar neurons (S + M)
III. Multipolar cells (L) Spindle-shaped cells	II. Stellate cells (L + S)		Multipolar cells (L) Fusiform cells (L)	II. Larger cells		III. Multipolar neurons (M) IV. Multipolar neurons (L)
EXTERNAL CORTEX	EXTERNAL CORTEX	EXTERNAL NUCLEUS	EXTERNAL NUCLEUS	LATERAL ZONE	EXTERNAL NUCLEUS	VENTROLATERAL NUCLEU LATERAL ZONE
I. Star & spindle cells (S)	I. Stellate cells	Multipolar cells (S + L)		1. Dorsolateral nucleus small cells		1. Multipolar neurons (S + M)
II. Triangular & pyramidal cells (M)	II. Multipolar cells (L)			2. Ventrolateral nucleus large cells		2. Multipolar neurons (L + S)

L = Large M = Medium S = Small

Table 7 – I-F

COMPONENTS OF THE MEDIAL GENICULATE BODY

Ramón y Cajal, 1966 Cat, Mouse, Rabbit, Dog	Ross, 1962 Mouse	Willard and Ryugo Mouse	Ryugo, 1976 Rat	Morest, 1964 Cat	Oliver and Hall, 1978 Tree shrew
INFERIOR LOBE	PARS PRINCIPALIS	VENTRAL DIVISION	VENTRAL DIVISION	VENTRAL DIVISION	VENTRAL DIVISION
Star-shaped cells: long axons	*Ventral Group* "Chief" mass	Principal cells	Principal cells	*Ventral Nucleus* Tufted cells	*Ventral Nucleus* Tufted cells
Small multipolar cells: short axons		Small multipolar cells	Small multipolar cells	Golgi Type II cells	Golgi Type II cells
ACCESSORY OVOID NUCLEUS				*Pars Ovoidea*	
Elongated cells: concentric laminar appearance				*Pars Lateralis* *Ventrolateral Nucleus*	*Caudomarginal Nucleus*
SUPERIOR LOBE		DORSAL DIVISION	DORSAL DIVISION	DORSAL DIVISION	DORSAL DIVISION
Superficial fusiform cells Multipolar cells	*Dorsal Group* Dark-staining cells (M)	Dark-staining multipolar cells (M)	Small multipolar cells	*Dorsal Nucleus* Multipolar cells	*Dorsal Nucleus*
				Deep Dorsal Nucleus Radiate neurons	*Deep Dorsal Nucleus*
				Suprageniculate Nucleus Radiate neurons	*Suprageniculate Nucleus*
					Anterodorsal Nucleus
MEDIAL (OR DEEP) NUCLEUS	PARS MAGNOCELLULARIS	MEDIAL DIVISION	MEDIAL DIVISION	MEDIAL DIVISION	MEDIAL DIVISION
Large multipolar cells	Large polygonal cells Small round and spindle cells	Large multipolar cells	Large multipolar cells Small multipolar cells	Radiate neurons Tufted neurons	
					Rostral Nucleus *Caudal Nucleus*

M = medium

Abbreviations

Actx	auditory cortex
AN	auditory nerve
AVCN	anteroventral cochlear nucleus
BIC	brachium of the inferior colliculus
C	caudal
Ce	cerebellum
CN	central nucleus of the inferior colliculus
CNS	central nervous system
CST	corticospinal tract
Cu	cuneiform nucleus
D	dorsal
d	dorsal division of the medial geniculate (Figs. 7-37 – 45 only)
DC	dorsal cortex of the inferior colliculus
DCN	dorsal cochlear nucleus
dh	dorsal hilus of the lateral superior olive
DLPO	dorsolateral periolivary
DM	dorsomedial nucleus of the inferior colliculus
DMPO	dorsomedial periolivary nucleus
DNLL	dorsal nucleus of the lateral lemniscus
DPO	dorsal periolivary nucleus
DSCP	decussation of the superior cerebellar peduncle
EC	external cortex of the inferior colliculus
IC	inferior colliculus
ICA	intercollicular area
ICa	internal capsule
ICP	inferior cerebellar peduncle
IN	interstitial nucleus of the inferior colliculus
INLL	intermediate nucleus of the lateral lemniscus
IPN	interpeduncular nucleus
IS	injection site
L	lateral
LL	lateral lemniscus
LNTB	lateral nucleus of the trapezoid body
LPN	lateral periolivary nucleus
LSO	lateral superior olive
M	medial

m	medial division of the medial geniculate (Figs. 7-37 – 45 only)
MCP	middle cerebellar peduncle
MG	medial geniculate
MGd	dorsal division of the medial geniculate
MGm	medial division of the medial geniculate
MGv	ventral division of the medial geniculate
ML	medial lemniscus
MLF	medial longitudinal fasciculus
MNTB	medial nucleus of the trapezoid body
MPN	medial periolivary nucleus
MSO	medial superior olive
OCA	octopus cell area of the posteroventral cochlear nucleus
PAG	periaqueductal gray
PBG	parabigeminal nucleus
PBN	parabrachial nucleus
PN	pontine nucleus
PNS	peripheral nervous system
PVCN	posteroventral cochlear nucleus
R	rostral
RN	red nucleus
RO	retro-olivary nucleus
RS	rhinal sulcus
RST	rubrospinal tract
SC	superior colliculus
SCp	superior colliculus, deep layer
SCP	superior cerebellar peduncle
SN	substantia nigra
SOC	superior olivary complex
SPN	superior paraolivary nucleus
TPT	tectopontine tract
VCN	ventral cochlear nucleus
v	ventral division of the medial geniculate (Figs. 7-37 – 45 only)
vh	ventral hilus of the lateral superior olive
vl	ventrolateral portion of the ventral nucleus of the lateral lemniscus
vm	ventromedial portion of the ventral nucleus of the lateral lemniscus

VN	vestibular nerve
VNLL	ventral nucleus of the lateral lemniscus
VNTB	ventral nucleus of the trapezoid body
VMPO	ventromedial periolivary nucleus
Vmes	trigeminal mesencephalic nucleus
Vm	trigeminal motor nucleus
Vn	trigeminal nerve
VIIm	facial motor nucleus
VIIn	facial nerve
VIIIn	vestibulocochlear nerve

Appendix

A histological series of brain stem sections are presented in the form of an atlas. The atlas consists of photomicrographs through auditory structures paired with line drawings that depict nuclear boundaries (thin lines) and their subdivisions (dashed lines). This atlas has two main functions: to present the histological appearance and spatial relationships between auditory nuclei; and to facilitate comparisons and discussions of experimental results.

The atlas brain was obtained from a young adult ICR albino mouse (3 months old, 30-35 g). Using the following procedure we were unable to detect any shrinkage in the tissue. The animal was given a lethal dose of Nembutal® and then perfused through the heart with physiological saline (25ml), Bouin's fixative (250 ml), and 0.1M phosphate buffered 10% formalin (250ml). The brain was removed from the skull and post-fixed for several days in fresh changes of the buffered formalin. Dehydration, clearing and embedding were accomplished in the following manner:

1. Wash in tap water	1hr
2. Dehydrate in 50% EtOH	1hr
3. Dehydrate in 70% EtOH	1hr
4. Solution A (40% Abs. EtOH, 20% *t*-butanol, 40% water)	1hr

5. Solution B (50% Abs. EtOH, 35% *t*-butanol, 15% water) — 1hr
6. Solution C (45% Abs. EtOH, 55% *t*-butanol) — 1hr
7. Solution D (25% Abs. EtOH, 75% *t*-butanol) — 1hr
8. 100% *t*-butanol — Overnight in 40°C oven
9. Paraffin — 2 hr at 60°C under vacuum
10. Fresh Paraffin — 2 hr at 60°C under vacuum
11. Standard embedding procedure
12. Tissue sectioned at 20 μm and stained with cresyl violet

The coronal atlas has been prepared in a plane that is parallel to the back of the inferior colliculus (Fig. 7-36). This orientation has the advantage that sections from the caudal inferior colliculus do not separate from the rest of the brain stem, thereby preserving the spatial relationships between brain stem nuclei. An added advantage is that this plane is also parallel to the long axis of the dorsal cochlear nucleus, expediting the analysis of that structure. Sections 1 and 128 are indicated by diagonal lines on MTK-54 (Fig. 7-36). The atlas sections are evenly spaced through the auditory nuclei and are labeled C (for coronal plane) followed by their section number.

We are including the following measurements from an ICR mouse to facilitate the use of this atlas for stereotaxic surgery. The mouse was positioned in a standard small animal stereotaxic apparatus (Kopf) with the incisor bar set 9.0 mm below ear bar zero.

Structure	Stereotaxic Position (±5%)	Brain atlas Section Number
Posterior surface of DCN	AP = −1.5 mm	0
Intercollicular fossa	AP = +2.9 mm, ML=O	160
Lateral surface of VCN	ML = 2.9 mm	0
Midline	ML = 0	133

All calibration bars on the atlas plates are equal to 200 μm.

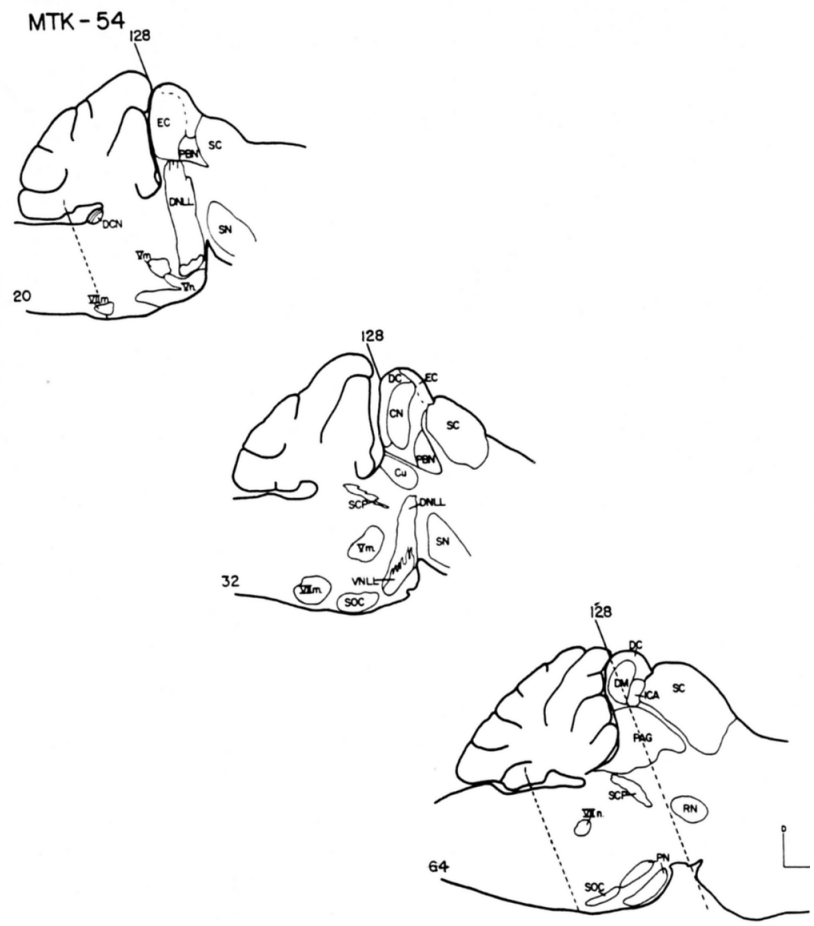

Figure 7-36. Plane-of-section diagram for the coronal mouse brain atlas The parasagittal sections (numbered 10, 16, and 34) are marked by diagonal lines labelled 1 and 128. These diagonal lines illustrate the position and orientation of the coronal atlas sections. The scale bar equals 1.0 mm.

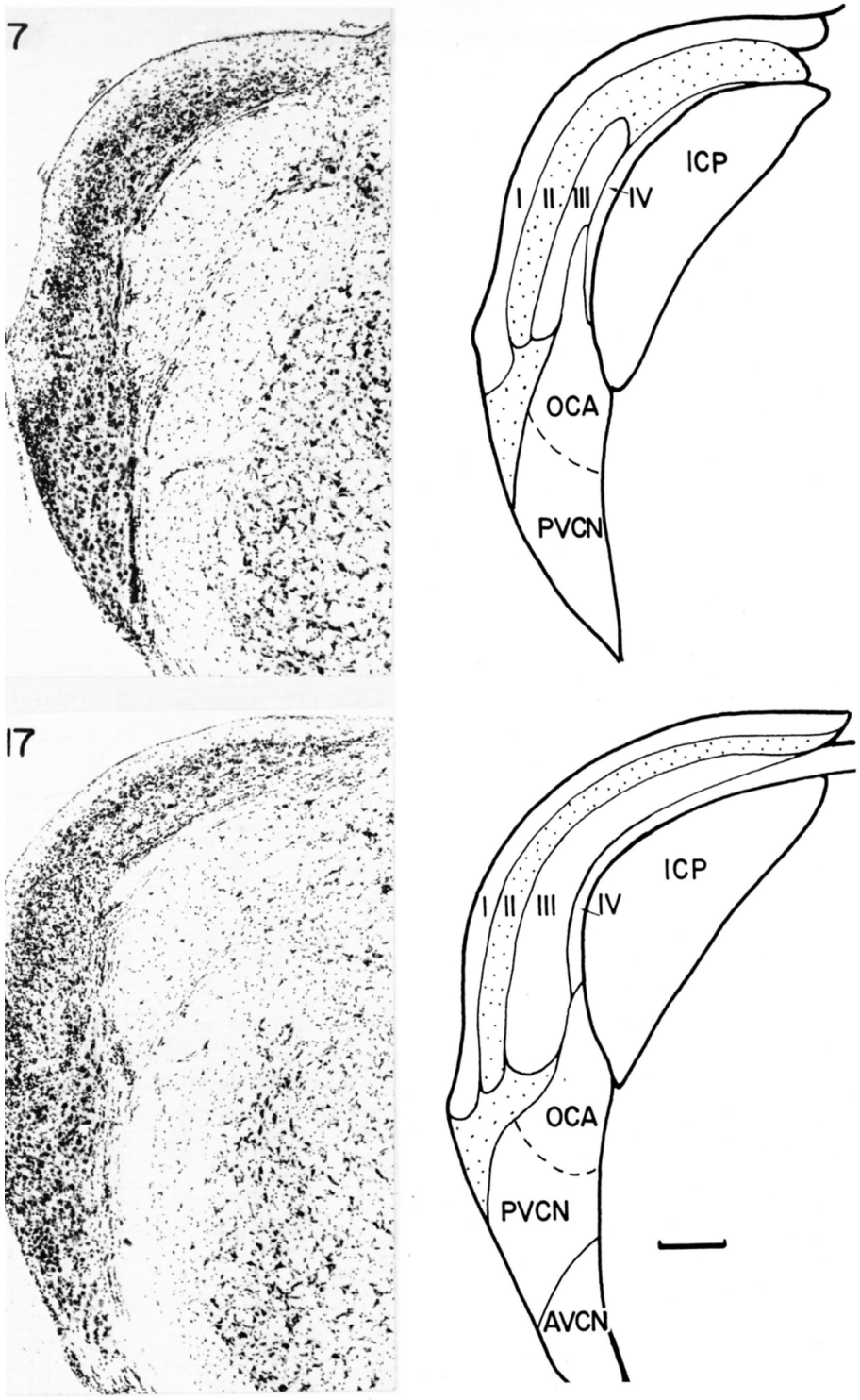

Figure 7-37

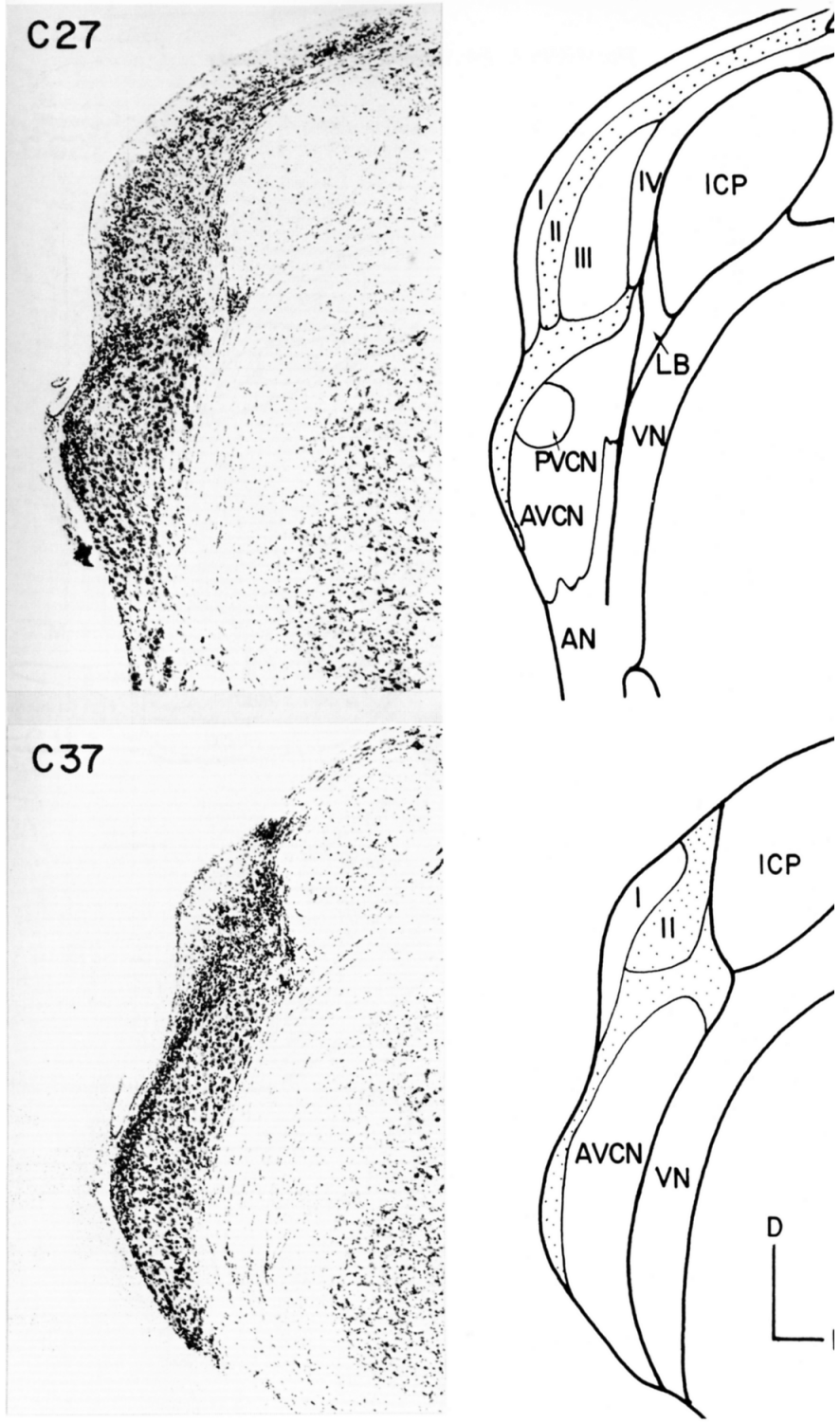

Figure 7-38

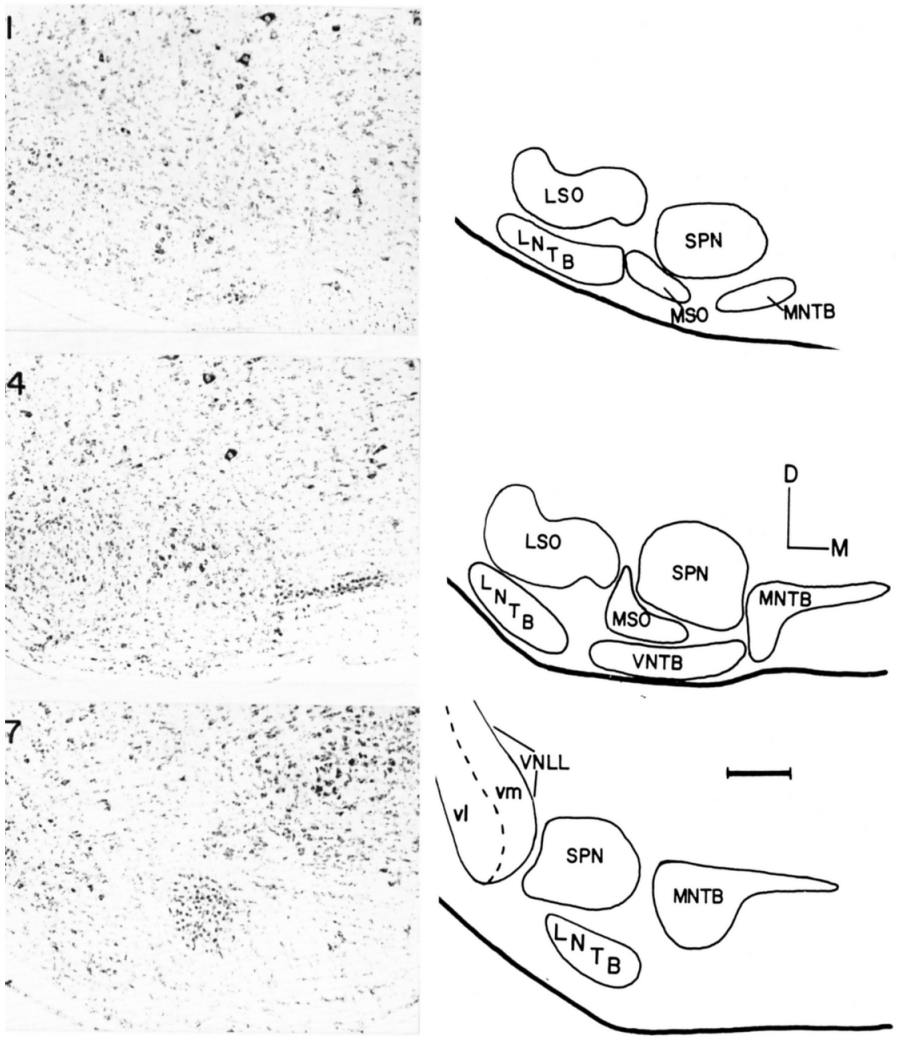

Figure 7-39

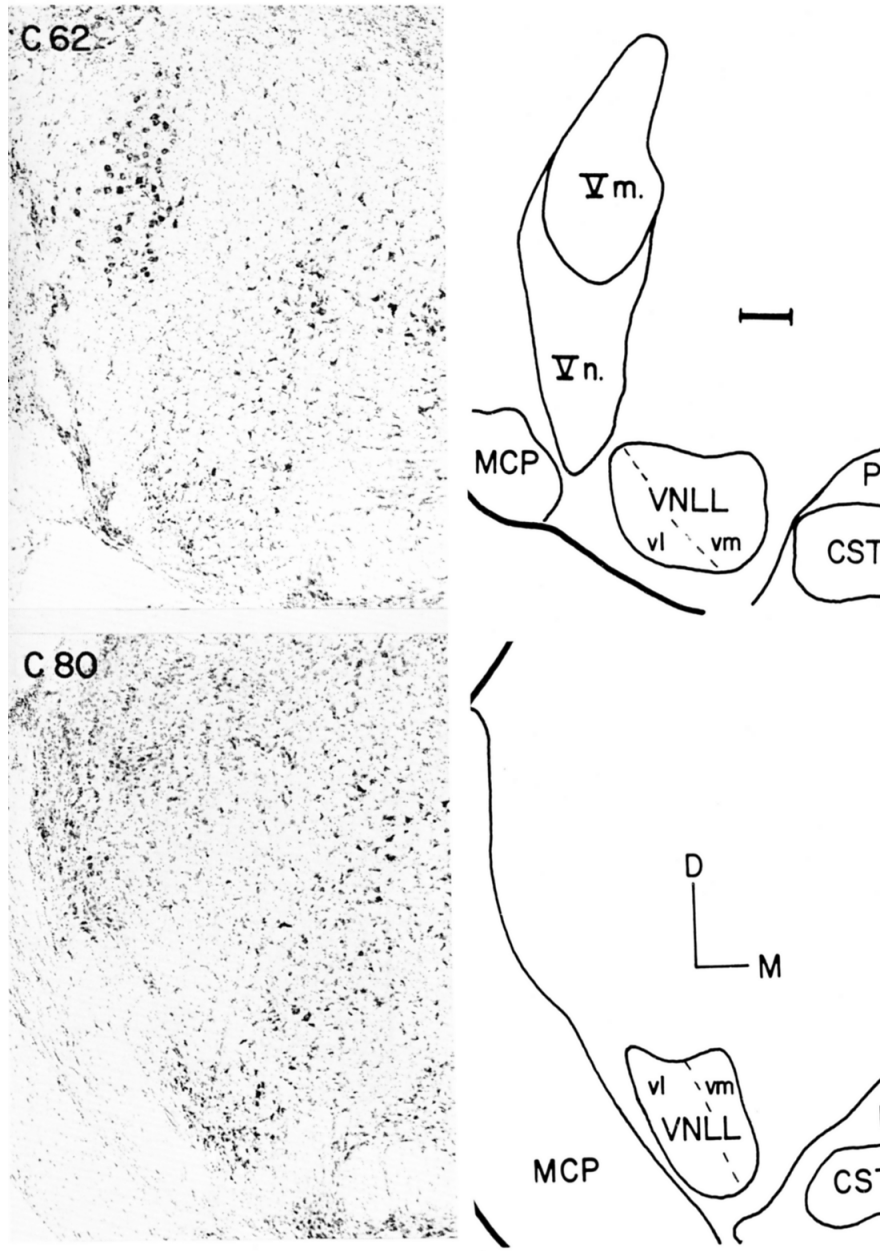

Figure 7-40

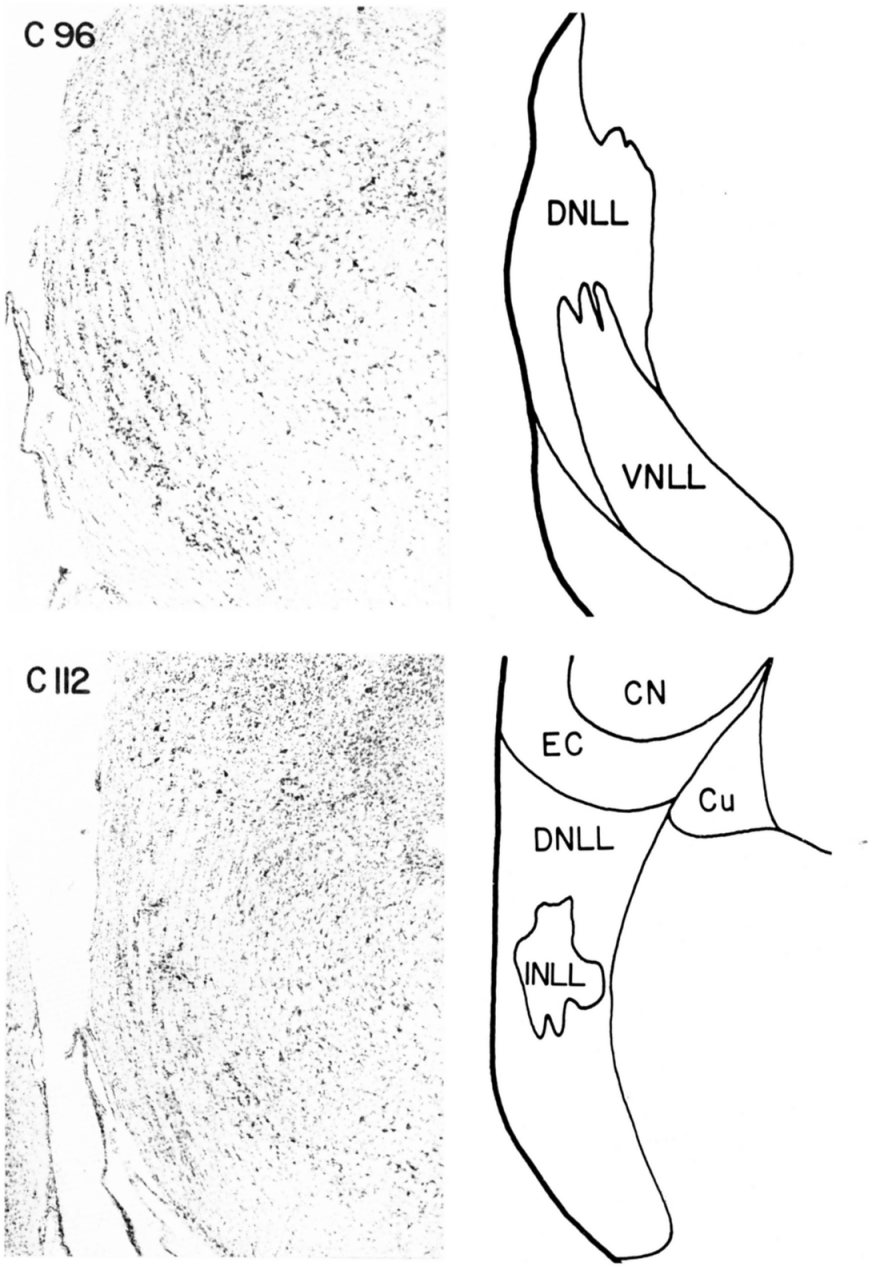

Figure 7-41

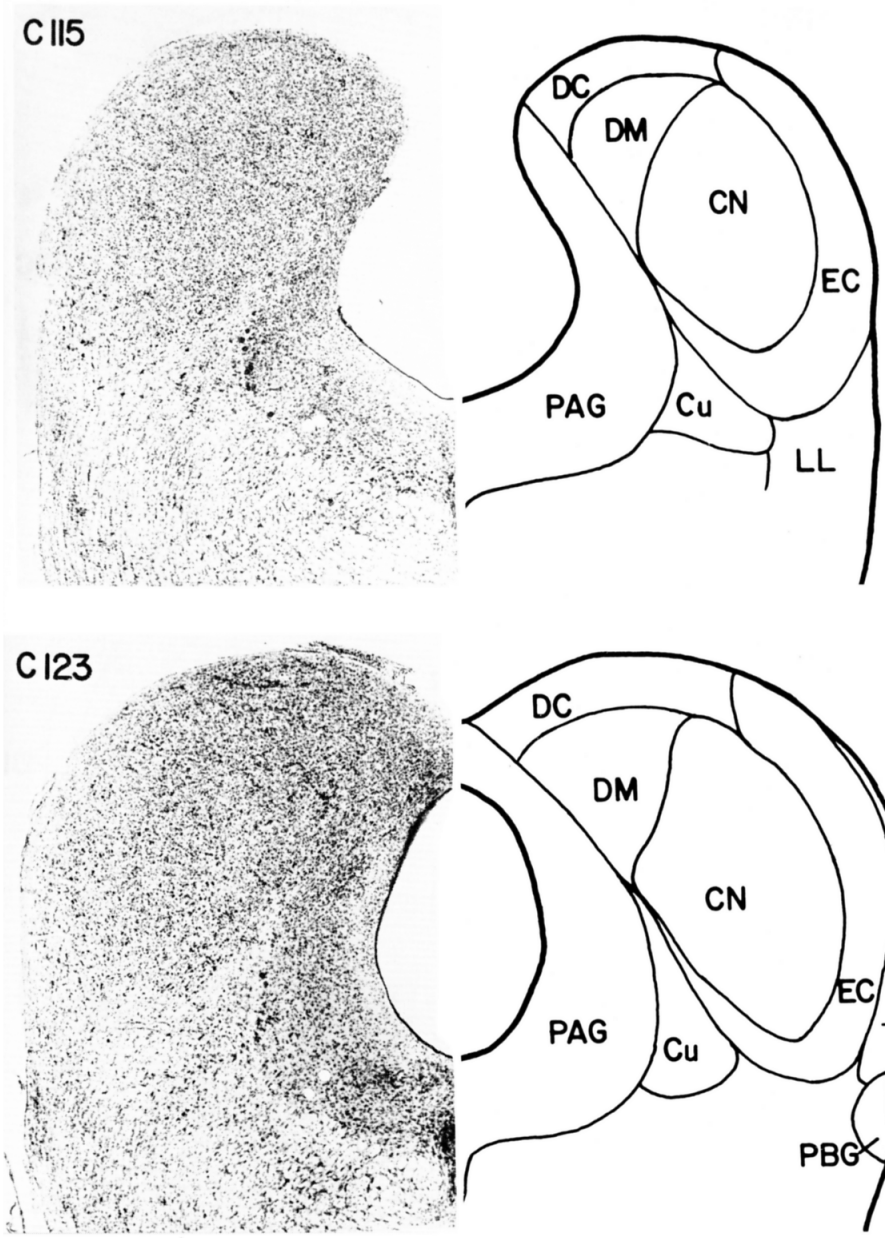

Figure 7-42

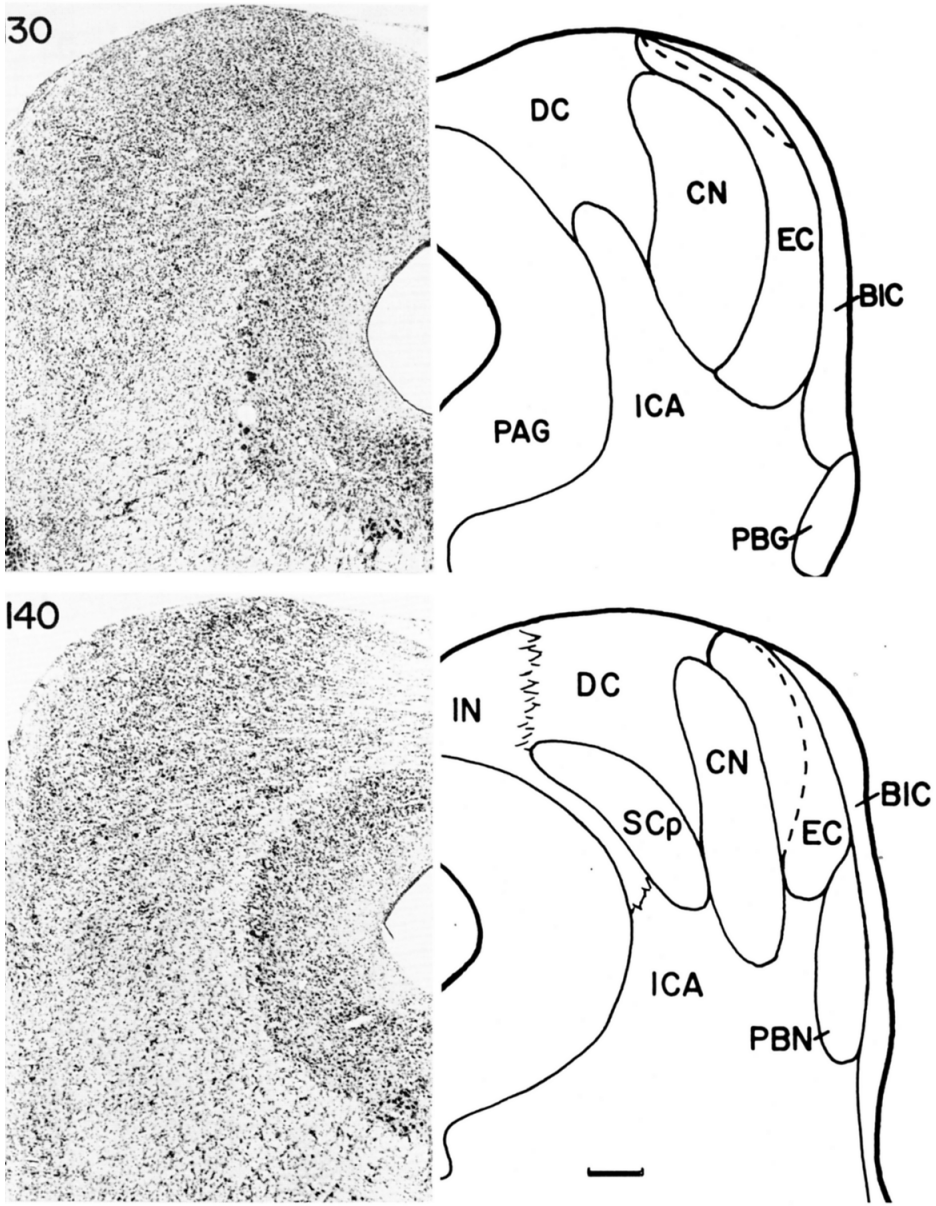

Figure 7-43

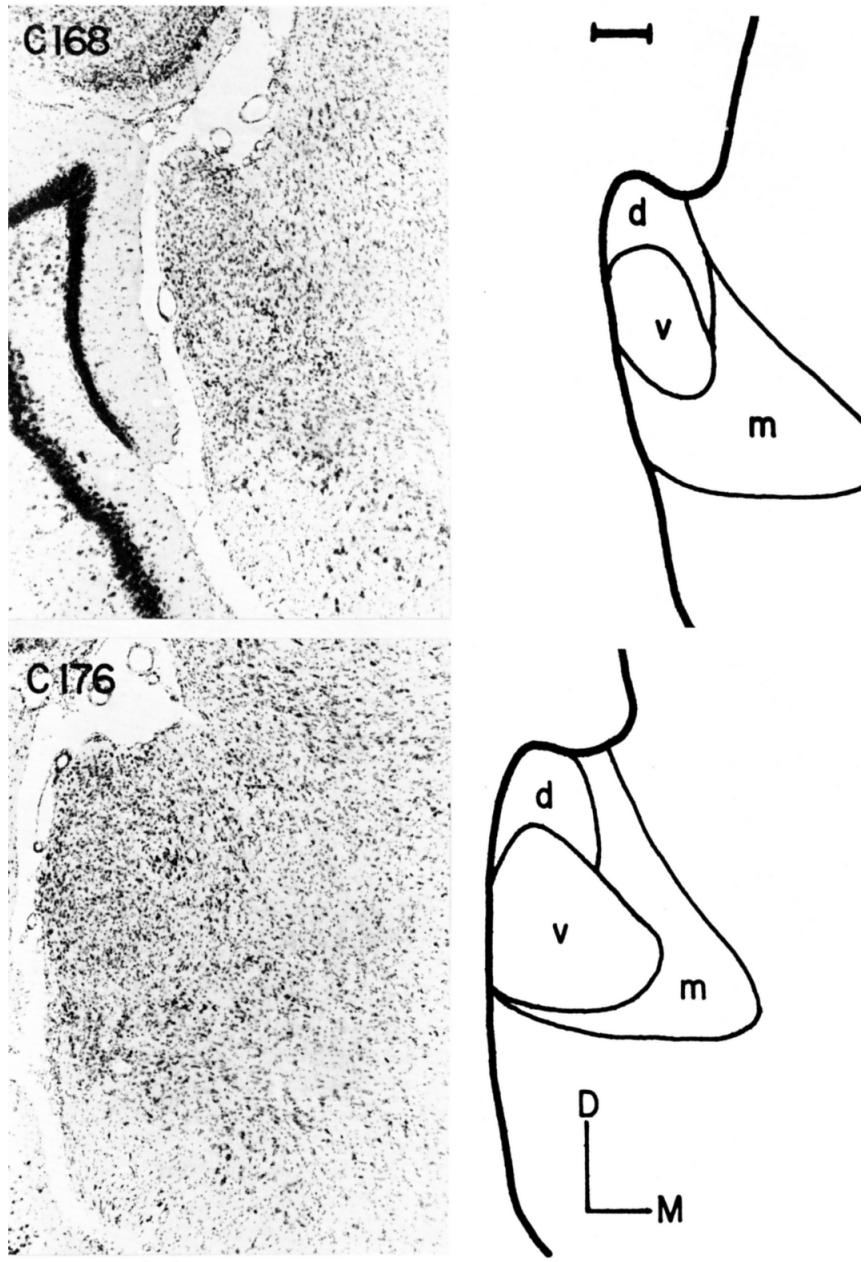

Figure 7-44

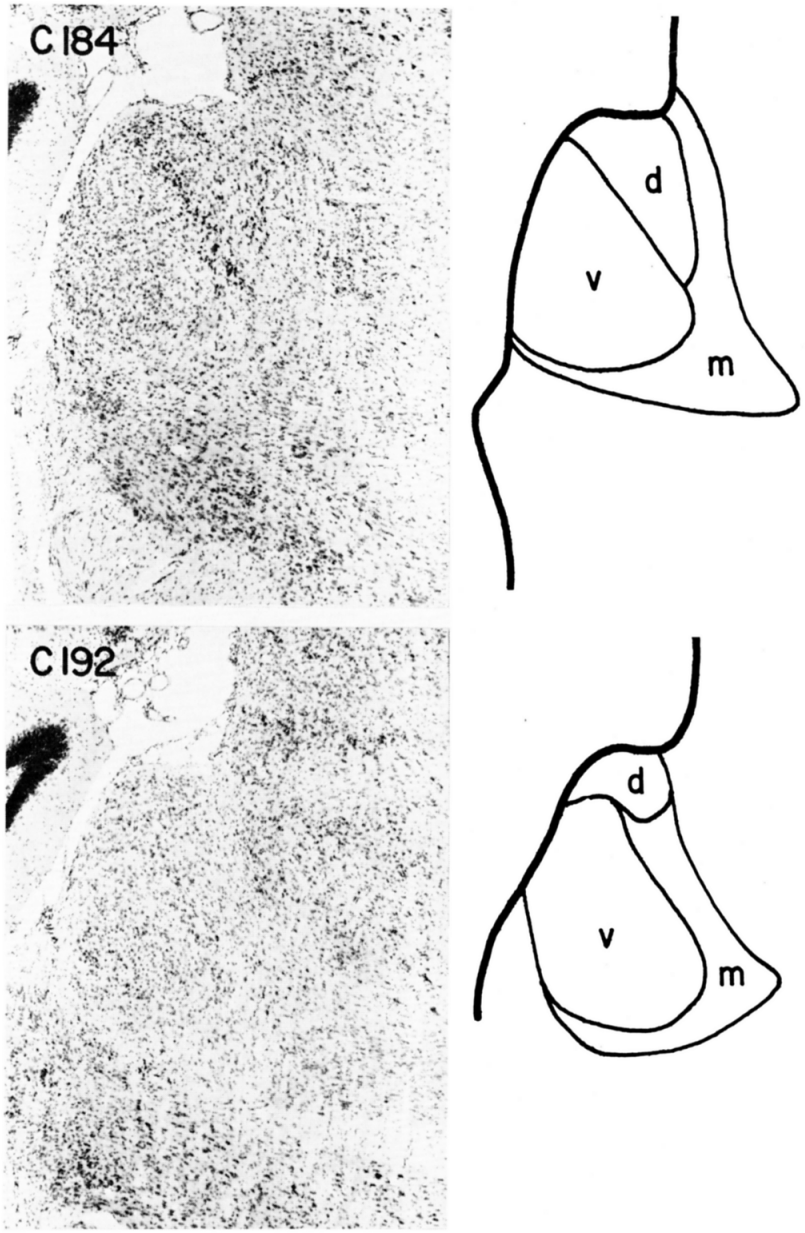

Figure 7-45

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