Some Features of the Spatial Organization of the Central Nucleus of the Inferior Colliculus of the Cat [1]

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ABSTRACT A series of neuroanatomical and neurophysiological experiments have been conducted within the central nucleus of the inferior colliculus (ICC) of the cat in order to determine some features of the spatial organization of the nucleus. Results from these experiments have demonstrated: (1) the origins of the auditory brain stem afferents to ICC and the topography of those projections in relation to the cochleotopic organization of ICC; (2) the segregation of at least some of those brain stem projections within ICC; and (3) ICC neurons with similar response properties (response properties which are often similar or identical to those of neurons in brain stem auditory nuclei) are often clustered within the nucleus. These results provide evidence that the laminated division of the ICC probably consists of anatomically, physiologically, and functionally distinct subdivisions and that some aspects of auditory sensation may be encoded or represented separately (i.e., in spatially distinct "regions") within the nucleus.

The spatial features of the anatomical and physiological organization of the central nucleus of the inferior colliculus are not well understood. Microelectrode studies have demonstrated that there is a systematic representation of the auditory sensory epithelium within the central nucleus (ICC) in the cat (Rose et al., '63; Merzenich and Reid, '74; Aitkin et al., '75), and anatomical studies have defined a "laminar" pattern of organization that is the apparent structural foundation of that physiological order (Morest, '64a,b; Rockel and Jones, '73a). Beyond this fundamental information, little else is known regarding the spatial distribution of brainstem auditory afferents within the central nucleus, or how information conveyed by those afferents is processed within the three dimensions of the nucleus.

The primary auditory information that ultimately provides input to the ICC is first distributed *via* fibers of the VIIIth nerve to the cell groups of the three main divisions of the cochlear nuclear complex (the anteroventral, posteroventral, and dorsal cochlear nuclei) (Lorente de Nó, '33; Rose et al., '59). Axons from definable cell "fields" of these subdivisions innervate specific brain stem auditory nuclei (e.g., Warr, '66, '69, '72; Osen, '69b; van Noort, '69). Some of these nuclei (e.g., the medial superior olive) receive binaural input (e.g., Stotler, '53; Guinan et al., '72), while others (e.g., the ventral nucleus of the lateral lemniscus) are primarily monaural (e.g., Warr, '66, '69, '72; van Noort, '69; Aitkin et al., '70). By virtue of the distribution of primary information to the very different populations of neurons in the cochlear nuclear complex and the specific redistribution of that information to particular brain stem nuclei, different aspects of auditory sensation are apparently encoded from the common input delivered *via* the auditory nerve. Thus, each of a large number of brainstem nuclei or cell fields abstracts different information from this common input, as reflected by the very different response properties of neurons in these different nuclei.

The ascending information from nearly all of these brain stem auditory nuclei in the cat (including the cochlear nuclear complex) ultimately terminates in the central nucleus of the inferior colliculus (Papez, '30; Woollard

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and Harpman, '39-'40; Stotler, '53; Osen, '72; van Noort, '69; Warr, '66, '69, '72; Fernandez and Karapas, '67; Goldberg and Moore, '67; Brunso-Bechtold and Thompson, '76; Adams, '75). Thus, a large number of inputs from these structures converge on the central nucleus, is somehow processed within its cochleotopic and laminar framework, and is then relayed to the medial geniculate body. Little experimental evidence exists to suggest how input from these various projecting brainstem nuclei is distributed or how the very different information from these sources is processed therein. Within the cochleotopic and laminar framework of the central nucleus, it would seem that other rules of order must exist.

A series of neurophysiological and neuroanatomical experiments were conducted in the central nucleus of the inferior colliculus of the cat to determine how input from these nuclei might be distributed within this structure. By using a combined neurophysiological-neuroanatomical approach, the distribution of neurons with different response properties could be determined, and that distribution related to the anatomical organization of the nucleus and its ascending inputs. Some of the implications of these findings in regard to the processing of auditory information in the midbrain will be discussed.

A preliminary report of these findings has been presented earlier (Aitkin et al., '76).

METHODS

A. *Physiological techniques*

Preparation

Adult cats with no obvious signs of ear infection were initially anesthetized by an intraperitoneal injection of sodium pentobarbital (40 mg/kg), and tracheal and venous cannulae introduced. A surgical level of anesthesia was maintained throughout the experiment by supplementary injections of barbiturates. Body temperature was maintained at approximately 37°C. After placing the animal in a head holder, a midline scalp incision was made. The skin and muscles were reflected and the pinnae resected to permit insertion of flexible sound tubes into each transected external auditory meatus.

For dorsal-to-ventral microelectrode approaches, a craniotomy was performed over occipital cortex and the dura excised. With the use of an operating microscope, the overlying cortex was aspirated by gentle suction until the dorsal surface of the inferior colliculus (IC) could be clearly visualized. A small portion of the bony tentorium cerebelli was removed to completely expose the dorsal colliculular surface. For horizontal penetrations, the craniotomy was extended further ventrally and laterally. Most of the bony tentorium was removed and about one-half of the cerebellum aspirated. Once the appropriate surface of the colliculus was exposed, it was photographed. An enlarged (10 ×) print (with a 0.5-mm grid superimposed) was made on which all microelectrode penetrations were recorded by cross reference to the surface vasculature (as viewed through the operating microscope).

Single neurons were isolated with electrolytically-etched glass-coated platinum-iridium microelectrodes with platinum black tips (ca. 3.5 microns in diameter). Electrodes were introduced into the colliculus by use of a hydraulic microdrive (Kopf) controlled by a stepping motor. The microdrive was attached to a micrometer drive on the H bar of a stereotaxic apparatus (Baltimore Instruments). The colliculus was covered by mineral oil warmed to body temperature, or on a few occasions, with a 3% agar solution (in normal saline). In any single experiment, all microelectrode penetrations were parallel or nearly parallel to one another.

Electrode penetrations were often marked by direct current lesions (15 μmps, 10 seconds) to help in reconstruction of microelectrode tracks. At the conclusion of an experiment, the animal was sacrificed by an overdose of barbiturate, and the cranium was opened widely. The brain was fixed by immersion in formal-saline for four to eight weeks. Frozen sections (50 μ) were cut parallel to penetrations in the frontal or sagittal plane. All sections were mounted and stained with cresyl violet. Virtually all units reported in this study were localized to the ICC. Reconstructions of electrode tracks were facilitated by reference to penetration sites recorded on the photograph.

Stimulation and recording

Tonal stimuli were generated by an oscillator (GR 1309 A) and shaped into trapezoidal tone pips with rise-fall times of 5 msec by an electronic switch (Ludwig, '70). Signals were then fed through two attenuators which provided independent control of the stimulus intensity (in 1 dB steps) to each ear. A passive delay network (Ad-Yu 820F) was interposed

between the oscillator and one tone switch to introduce interaural time differences in the stimuli delivered to the two ears. Stimulus duration and repetition rates were controlled by a series of programmable timers. Stimuli were usually 250 msec in duration; stimulus frequencies were monitored by a frequency meter.

Stimuli were delivered via equal-length tubes coupled to a matched pair of audiometric drivers (Telex Model 61470-07, 10 ohms). The tubes were sealed into each transected external auditory meatus by low melting point wax. The output of each driver was calibrated prior to these experiments using a probe microphone (1/4 inch B & K condenser microphone) and waveform analyser (GR Model 1900 A). The frequency response of these speakers was relatively flat up to 13 kHz, but dropped off over higher frequency ranges. All stimulus levels are given in dB attenuation (dBA) *re* 1 volt RMS input to the drivers, as monitored on an AC voltmeter. All experiments were conducted in an IAC soundproof room.

Signals from isolated neurons were fed to a high-impedance, unity-gain preamplifier, and then to a high-gain amplifier located outside of the IAC room. The spike recording was displayed on an oscilloscope and amplified into a loudspeaker; neural activity could then be monitored both aurally and visually.

For experiments in which the distributions of neuronal response classes in ICC were studied (RESULTS), data were collected in the following manner. A neuron was isolated and its best frequency (the frequency at which the neuron responded at lowest threshold) to contralateral tonal stimulation determined.[4] In all illustrations, best frequencies were translated to the corresponding cochlear place with use of the frequency-position function of Greenwood ('74).[5] Spontaneous activity, if present, was noted. The neural response (net excitation or net inhibition) and response pattern (onset or sustained; see RESULTS) to contralateral and ipsilateral monaural best frequency stimulation (usually 20-30 dB above threshold) were recorded. Binaural interactions, if present, were then assessed. Using best frequency tonal stimulation, the majority of binaural neurons was obviously most sensitive to either (1) interaural time differences, (2) interaural intensity differences, or (3) to the level of the binaural stimulus (but not obviously sensitive to interaural time or intensity differences). Nearly all binaural neurons could be categorized into these classes (RESULTS). The neurons of this last class were excited by stimulation of either or both ears; most of these neurons were termed "excitatory-excitatory" (or "E/E") cells. Neural response rates and discharge patterns to binaural best frequency stimulation were also recorded. For interaural time-sensitive neurons, interaural time differences which covered the behavioral range (± 250 μsec; Rose et al., '66) were systematically introduced in 25 or 50 μsec steps; the interaural time difference at which the discharge rate was maximal or minimal was noted. After obtaining these data, the microelectrode was slowly advanced until another neuron was isolated, and the same procedure was repeated.

B. *Anatomical techniques*

Neuroanatomical experiments were conducted in 18 cats to define the origins of brain stem afferents to the ICC and to directly relate these projections to the anatomical (laminar) and physiological (cochleotopic) organization of the nucleus. In these studies, the retrograde axonal transport of horseradish peroxidase (HRP) was employed to define the origins and topography of ICC inputs. HRP was injected at physiologically defined loci within the ICC. In all of these studies, with the exception of certain procedures described below, the preparation, stimulation, and recording methods were identical to those used in the physiological studies.

Preparation

Animal preparation and IC exposure were as described above, with the exception that skin and muscles overlying the cranial opening were not resected. Microelectrodes were advanced into the ICC in a dorsorostral to ventrocaudal direction, and the best frequencies (represented cochlear place) of single units and unit clusters (to contralateral stimulation) determined with the use of tonal stimuli. After an adequate map of the "tonotopic" (or "cochleotopic") organization of ICC was obtained, the microelectrode was replaced by a 10-μl Hamilton microsyringe with a varnished 28-gauge needle, containing several

[4] It has been argued that the best frequencies of ICC neurons to contralateral and ipsilateral stimulation are very similar if not identical (Erulkar, '69).

[5] $f = 418.6(10^{0.0954x} - 1)$, where f is the stimulus frequency in Hertz and x is the cochlear distance, in mm from the apex, of the maximum amplitude of the traveling wave envelope.

microliters of a nearly saturated solution of HRP (approximately 40% in saline).

The microsyringe was lowered into the central nucleus at the same orientation used for microelectrode recording, and evoked multiunit activity was monitored using the tip of the varnished needle as a recording electrode. A good correlation was usually found between the best frequency (or represented cochlear place) previously determined for a particular depth and that recorded with the insulated microsyringe needle. Between 0.1 and 0.5 μl of the tracer was injected at a given locus and the needle left in position for 15 to 30 minutes. After removal of the microsyringe, the muscle and skin overlying the cranial opening were sutured and the animal allowed to recover from the anesthetic.

Histological procedures

Twenty-four to forty-two hours after the time of injection, cats were anesthetized with sodium pentobarbital and perfused through the heart with 0.9% heparinized saline (37°C) followed by 0.2 M phosphate-buffered (pH 7.6) 2% paraformaldehyde (4°C). The brain was removed, placed in cold fixative for two to five hours, then transferred through a graded series of phosphate-buffered sucrose (4°C) for eight hours.

Frontal sections from the medial geniculate body through the cochlear nucleus were cut on a freezing microtome in repeating 90 μ-30 μ-30 μ series. Sections were reacted with 3,3'-diaminobenzidine (DAB) solution in Trizma buffer, to which a few drops of 30% H_2O_2 had been added (the method of Graham and Karnovsky, '66, as modified by Ralston and Sharp, '73). After 10 to 20 minutes in DAB, sections were washed with three changes of Trizma buffer and mounted on gelatinized slides. The tissue was then dried, dehydrated, cleared, coverslipped, and examined directly for the HRP reaction product.

Neurons of the brain stem auditory nuclei often developed a diffuse, pale-brown coloration, presumably due to endogenous enzymes which reacted with DAB (Wong-Riley, '76). Cells containing the dark-brown, granular HRP reaction product were easily distinguished from these lightly-stained, agranular neurons. However, after a section is counterstained and viewed under light microscopy, the stained Nissl substance in endogenously labeled, pale-brown cells can appear similar to HRP granules. In order to avoid confusion, all HRP cell counts were therefore made in non-counterstained material. Certain sections were subsequently counterstained with cresylecht violet and the cytoarchitectonic boundaries of the brain stem nuclei (which were usually sharp in non-counterstained material because of the endogenous reactions to DAB) were reconstructed.

In each experiment, the distributions of granule-labeled neurons in each nucleus were plotted from thick (90 μ) sections by the combined use of a Zeiss Photomicroscope II in the transmitted light mode and a Bausch and Lomb microprojector. The location of every labeled neuron was recorded on scale drawings of brain stem auditory nuclei. From these observations and drawings, the numbers of cells containing granules were counted and plotted as a function of their locations within nuclei. Since each thick section in which neurons were counted was separated from the next by two 30-μ sections, no neurons could be counted twice.

RESULTS

A. *Anatomical studies*

Origins of brain stem afferents to the central nucleus

By use of the retrograde axonal transport of HRP, these experiments have defined the origins of the brain stem auditory afferents to the ICC. HRP-labeled neurons were localized in over ten brain stem auditory nuclei following injections of the enzyme into the central nucleus. In the largest-volume injection cases, neurons within all of these major projecting nuclei contained the retrogradely transported label. As described in detail below, neurons in only a limited number of these nuclei were labeled with reaction product in smaller-volume injection cases; in each of these smaller injection experiments, the nuclei in which the HRP-labeled neurons were localized varied from experiment to experiment, depending upon the location of the injection site within the ICC.

Six successful injection cases are illustrated. The nuclei labeled following the two largest injections in this series were identical, and the projections defined were generally consistent with results in the earlier, brief reports of Adams ('75) and Brunso-Bechtold and Thompson ('76). These results are illustrated by case 76-26 (figs. 1, 2). The majority of labeled neurons was located bilaterally in the

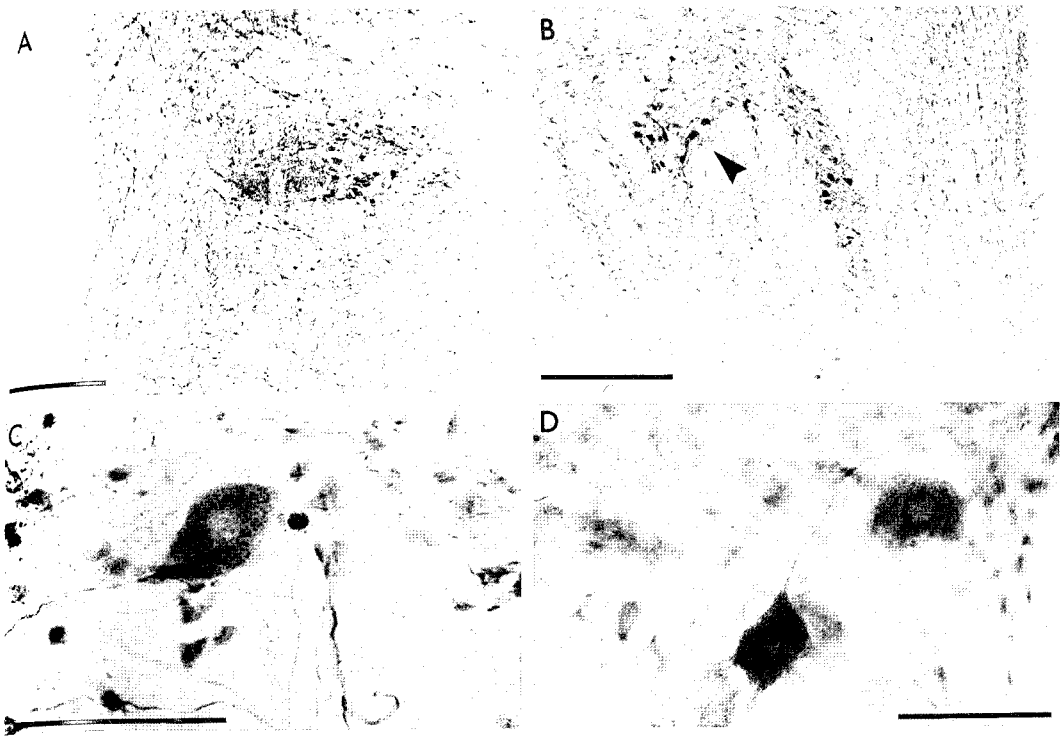

Fig. 1 HRP-labeled neurons in the ipsilateral (A,C) and contralateral (B,D) Dorsal Nuclei of the Lateral Lemnisci (DNLL). Neuron in C was localized to a 30-μ section adjacent to the 90-μ section shown in A. Note that the orientation of the neuron's soma is perpendicular to the HRP-labeled lateral lemniscal axons (vertical in this photograph) coursing through the ipsilateral DNLL. Neurons in D were taken from the 90-μ section shown in B (arrowhead). Calibration bars are 500 μ for A and B, 50 μ for C and D. Case 76-26.

dorsal nucleus of the lateral lemniscus (DNLL) and the lateral superior olive (LSO), ipsilaterally in the ventral nucleus of the lateral lemniscus (VNLL) and medial superior olive (MSO), and contralaterally in the three major divisions of the cochlear nuclear complex (CN). Scattered HRP-neurons were also observed in the ipsilateral ventral and lateral periolivary nuclei (PON) and CN (all 3 divisions), in the contralateral IC, and (in this case only) bilaterally near the facial nucleus.

Photomicrographs of HRP-labelling representative of this experimental series were taken from the nuclei of the lateral lemniscus. Densely labeled neurons were found bilaterally in the DNLL (fig. 1) and ipsilaterally in the VNLL (fig. 2). HRP-labelled neurons in the DNLL were clustered in "islands," and prominently labeled axons of the lateral lemniscus were often seen coursing at right angles to the somas of the labeled neurons on the ipsilateral side (fig. 1C). Unlabeled cells lay in close proximity but did not intermingle with each cluster of labeled neurons.

The VNLL apparently consists of two divisions. One of these divisions is slender and elongated and is vertically oriented along the main body of the ascending fibers of the lateral lemniscus (fig. 2A). A more ventral division of VNLL is situated medial to the ascending lemniscal fibers and consists of an ovoidal cluster of cells (fig. 2B). Neuroanatomical (van Noort, '69; Warr, '66, '69) and electrophysiological (Aitkin et al., '70; Guinan et al., '72) evidence suggest that these two VNLL divisions are functionally different; the arrays of HRP-labelled neurons within each division (following ICC injections) were also very different. HRP-labeled neurons in the vertically oriented, dorsal part of "VNLL" were organized in bands that generally traversed the entire medial-to-lateral dimension of that division (fig. 2A). Labeled neurons within a "band" or "streak" were typically

bitufted or spindle-shaped, with their dendrites oriented normal to the fibers of the lateral lemniscus (figs. 2C,D). Unlabeled and labeled neurons were intermingled within any given band. By contrast, HRP-neurons within the more ventral division of the nucleus were restricted within a single, dense cluster, and there, labeled neurons were generally multipolar or star-shaped (figs. 2B,E).

Within the superior olivary complex, HRP-labeled neurons were found in the ipsilateral MSO and PON and, bilaterally, in the LSO. The distributions of HRP-labeled neurons in those (and other) nuclei systematically changed as a function of the best frequency of the injection site (see below). No label was ever found in the neurons of the MNTB or in the contralateral MSO.

Neurons in all three divisions of both CN complexes contained HRP granules, but far heavier labeling was evident in the contralateral CN. In the contralateral dorsal cochlear nucleus (DCN), fusiform cells and a few giant cells were labeled, but no reaction product was observed in neurons within the superficial lamina. In the posteroventral cochlear nucleus (PVCN), octopus cells, multipolar cells, and globular cells contained granules of reaction product. In the anteroventral cochlear nucleus (AVCN), including the large spherical cell field and the lateral cap area of Osen ('69a,b), many small neurons were labeled with HRP reaction product. However, the large and small spherical cells in AVCN, easily characterized in HRP sections counterstained with cresylecht violet, were not labeled.

In addition to these major projections, small numbers of labeled neurons were found in the ipsilateral ventral and lateral periolivary cell groups. As indicated above, scattered HRP neurons were also seen in the three divisions of the ipsilateral CN complex. A small number of labeled neurons was observed in the contralateral ICC, distributed widely through its mass. Finally, a small group of cells situated immediately ventral to the medial division of the facial motor nucleus and at the lateral margin of the pyramidal tract contained HRP reaction product. This group of neurons appeared to be located within the nucleus reticularis paragiganticocellularis lateralis of Taber ('61), and were situated bilaterally. Labeling in these neurons was only observed in this case (76-26), but all experimental brains were not cut through the complete rostro-caudal extent of the facial nucleus.

In summary, these HRP-studies have defined the various origins of the brain stem auditory afferents to the ICC. They are generally consistent with results of other HRP studies in the cat. Thus, major brain stem auditory projections to the ICC originate bilaterally in the DNLL and LSO, contralaterally in the CN, and ipsilaterally in the VNLL and MSO. Other less prominent projections arise in the ipsilateral PON and CN, and from the contralateral IC.

Topography of brain stem projections to the central nucleus

The topography of defined brain stem projections could be directly related to the known physiological (i.e., cochleotopic) organization of the ICC and brain stem auditory nuclei. Within the major projecting nuclei (particularly evident in the MSO, LSO, and the contralateral CN), the location of the HRP-labeled neurons systematically shifted as a function of the represented cochlear place (best frequency) at the injection site. This is demonstrated by two illustrated large volume injection cases (76-26, 76-28), since all of the major projecting nuclei were labeled in these cases, and the injection sites represented different sectors of the cochlea.

Superior olivary complex

Following the injection at a 2 kHz (8 mm from the cochlear apex) best frequency locus in the dorsal aspect of ICC (76-26) labeled neurons were located in the dorsal-medial tip of the ipsilateral MSO and, bilaterally, in the dorsal-lateral tip of the LSO (fig. 3, top half). After an injection into a 9 kHz (14.2 mm from the cochlear apex) best frequency locus, more ventral in the ICC (76-28), the cluster of HRP-labeled neurons in these nuclei were displaced to a more ventro-lateral position in the MSO and to a more ventral position in the LSO (fig. 3, bottom half). Both the locations of HRP-labeled neurons within the MSO and LSO and the recorded best frequencies at the injection sites corresponded closely with the known tonotopic organization of those structures (Guinan et al., '72). Note that a smaller cluster of HRP-cells was situated more ventrally in the MSO and LSO of 76-26, presumably a result of the spread of HRP to a more ventral (i.e., higher frequency) region of the ICC.

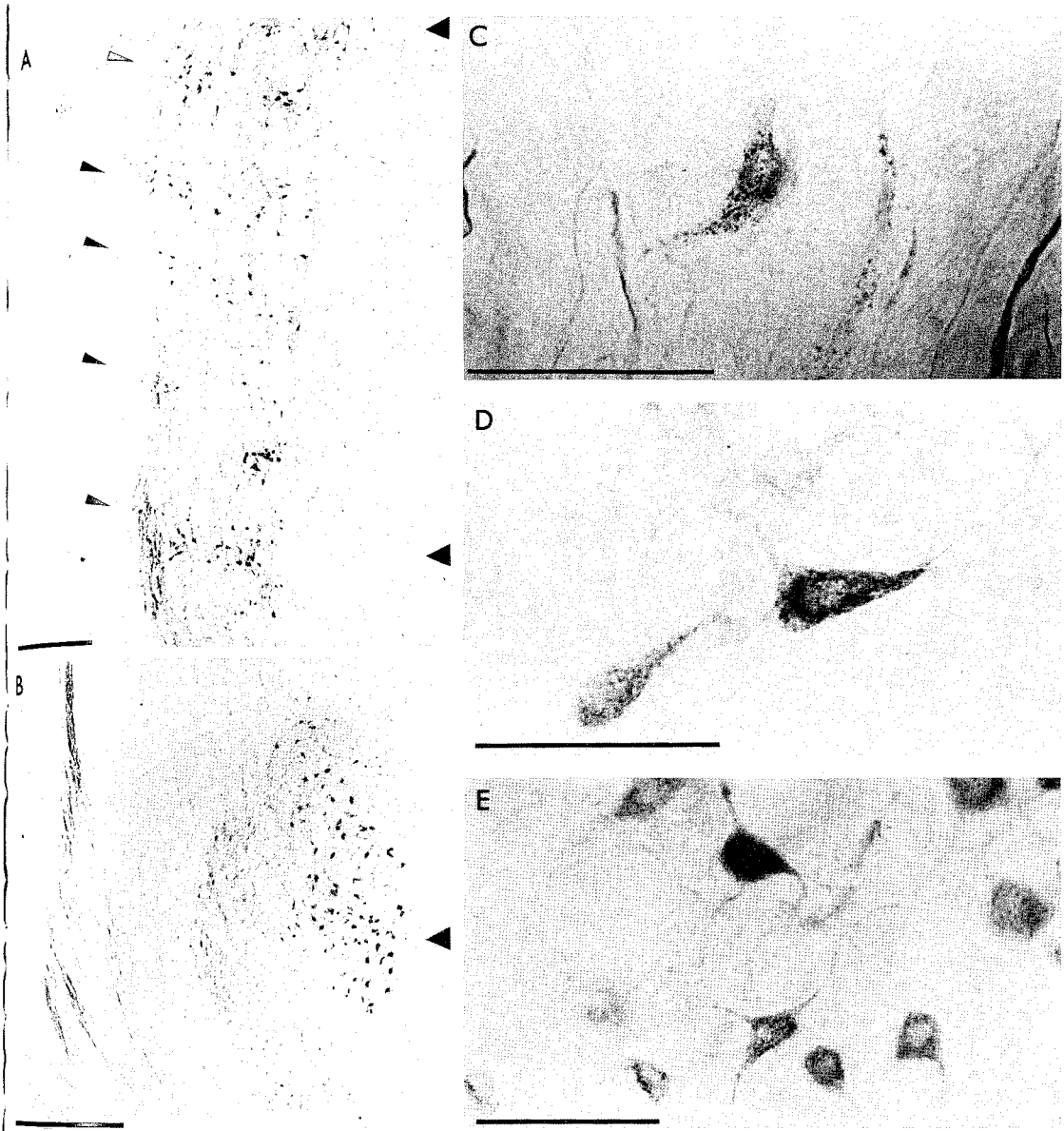

Fig. 2 HRP-labeled neurons in the ipsilateral Ventral Nucleus of the Lateral Lemniscus (VNLL). Note the "bands" of labeled neurons (small arrowheads in A) that cross the lateral-to-medial dimensions of the lateral "streak" of VNLL. C and D are neurons located in the most dorsal (C) and ventral (D) bands (large arrowheads in A). Neurons labeled in the more ventral divisions of VNLL were clustered in its more medial aspects (B). Note the diffuse, endogenous staining that serves to delimit the borders of the nucleus in this unstained section. Neurons in E were taken from the 90-μ section shown in B (arrowhead). Calibration bars are 500 μ for A and B, 50 μ for C, D, and E. Case 76-26.

For all injection cases in which the MSO and LSO were labeled by the retrograde tracer, the HRP cells were distributed along the entire rostral-caudal extent of the nucleus (see histograms, fig. 3), forming a slab-like array of neurons. The width of this array (in frontal section) within each nucleus varied in different cases as a function of the volume of

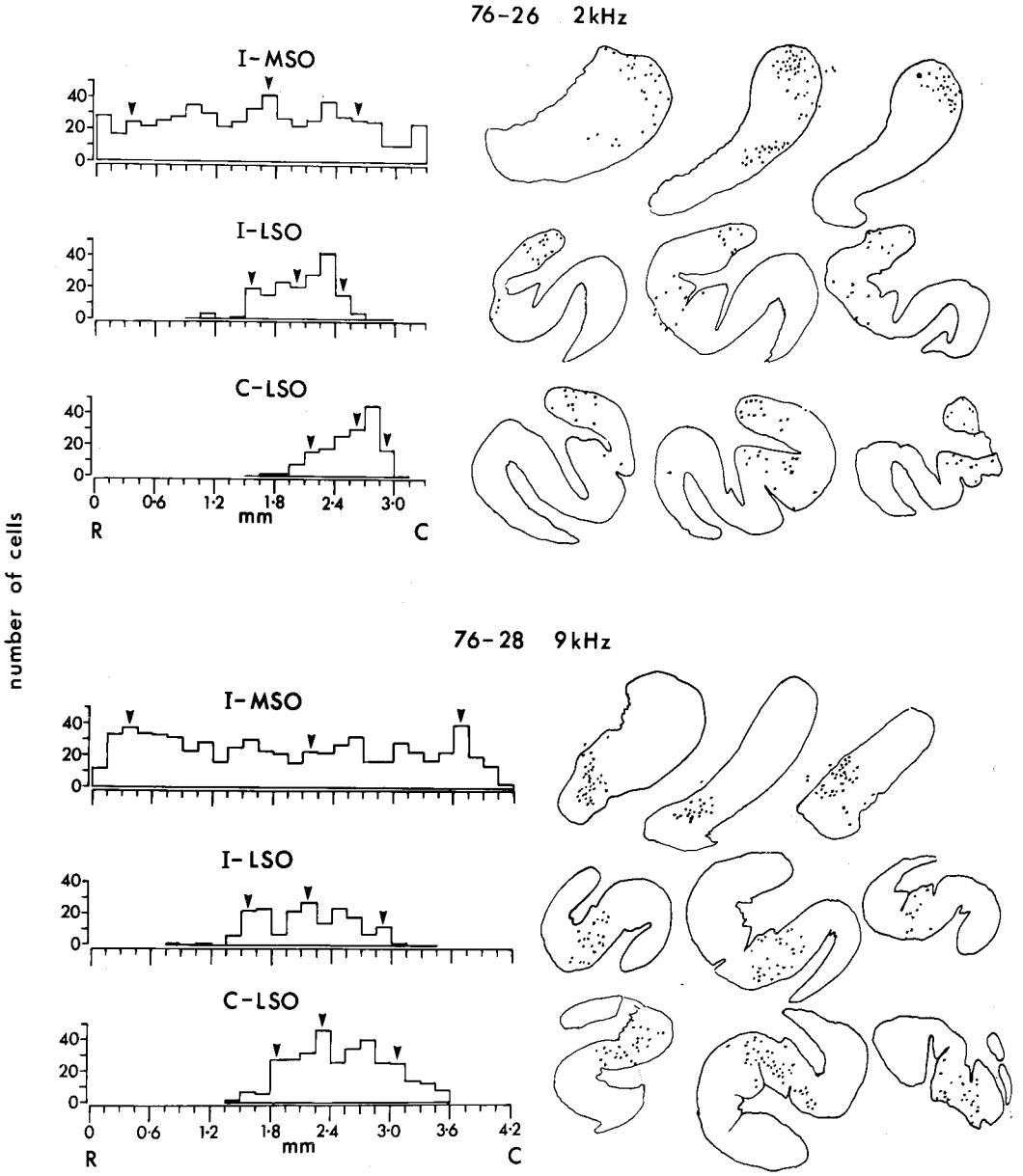

Fig. 3 *Right hand side:* outline drawings of 90-μ frontal sections through the ipsilateral (I) MSO and both ipsilateral (I) and contralateral (C) LSO's for cases 76-26 and 76-28. Each dot in this and other similar illustrations represents a single HRP-labeled neuron. Best frequency at the ICC injection site was 2 kHz for case 76-26, 9 kHz for case 76-28. *Left hand side:* histograms of the number of labeled neurons in each 90-μ section (ordinate) as a function of the location of the section along the rostral (R) to caudal (C) extent of the superior olivary nuclei, in mm (abscissa). Arrowheads above each histogram correspond to the locations of each outline drawing to the right of that histogram. Note that the number of neurons counted does not include HRP-labeled neurons present in the interleaved 30-μ sections.

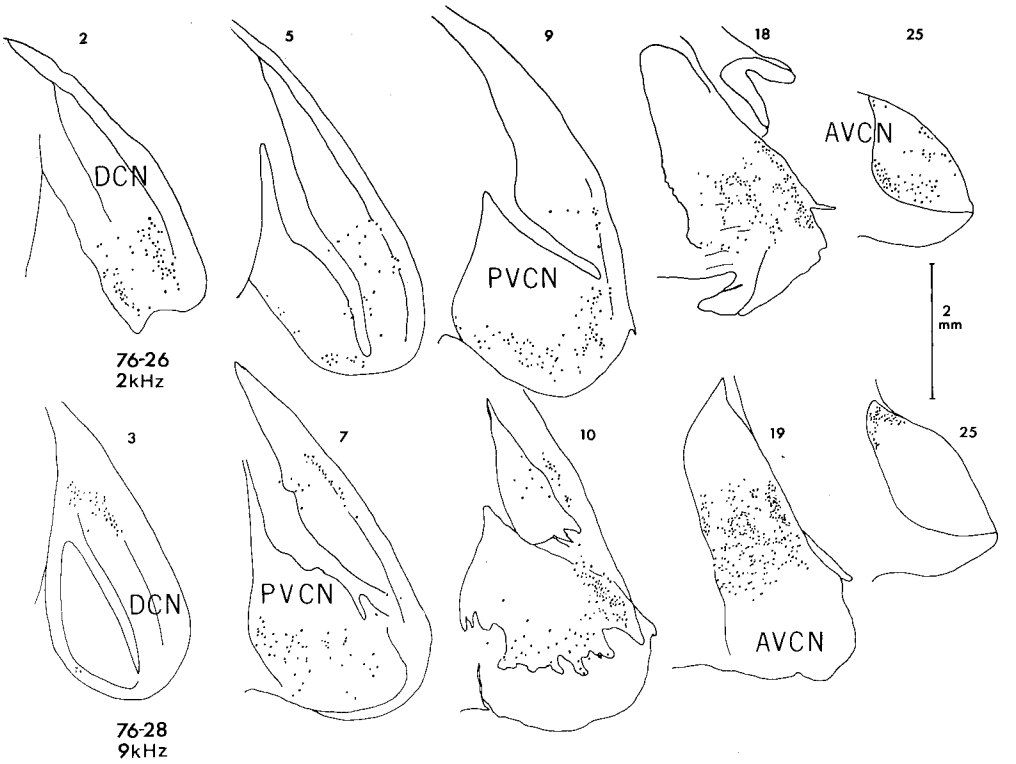

Fig. 4 Outline drawings of frontal sections through the contralateral cochlear nuclei of cases 76-26 (upper row) and 76-28 (lower row), arranged from caudal to rostral (left to right). Section separation given by the number multiplied by 150 μ.

the tracer injected, but the length of the projecting "slab" covered the rostral-caudal extent of the nucleus, regardless of the size of the injection. Larger injections resulted in a fairly wide array of labeled neurons (fig. 3: 76-26, 76-28); the array was much narrower with smaller injections. In the smallest volume injection case in which neurons in the MSO and LSO were labeled, only a very few HRP-labeled neurons were present in each 90-μ section, but they were evenly distributed along the entire length of each nucleus. Results in all other cases were consistent with these topographical findings.

Cochlear nucleus

In the contralateral CN, the distribution of the tracer could also be directly related to the represented cochlear place at the injection site. Figure 4 compares again the patterns of HRP-labeled neurons following the largest low best frequency injection (76-26, 2kHz, 8.0 mm) and the largest high best frequency injection (76-28, 9kHz, 14.2 mm). The lower best frequency injection (76-26) led to transport of HRP by neurons (primarily fusiform cells and a few giant cells in the deep lamina) localized ventro-caudally in DCN (fig. 4, Sections 2, 5). HRP granules were localized ventro-medially in octopus cells, (fig. 4, Section 2) and in multipolar cells (fig. 4, Sections 5, 9) of PVCN. Many globular cells and some marginal cells were also labeled (fig. 4, Section 18). In the AVCN, small neurons containing HRP granules were scattered throughout the rostral portion of the nucleus (fig. 4, Section 25), including the area described as the large spherical cell field by Osen ('69a,b). (Note that in all cases in AVCN labeling, the large spherical cells did not appear to be labeled.)

In the higher best frequency injection of 76-28 (fig. 4, lower row), the labeled array of neurons was more rostral and dorsal in DCN, and

again the reaction product was most prominent in the fusiform cells of the middle lamina (fig. 4, Sections 3, 7, 10). In PVCN, HRP granules were present in small cells and in multipolar cells situated further rostrally and dorsally (fig. 4, Sections 7, 10) than in 76-26. As in the latter experiment, a contingent of labeled neurons occurred as a swathe across AVCN at a mid-rostral-to-caudal level (fig. 4, Section 19), identifiable in this and other high frequency injections as the small spherical cell area (Osen, '69a,b). As in the case of the more rostral AVCN labeling of 76-26, only a fraction of the small cells in this area were labeled. Note that the 9 kHz best frequency injection of 76-28 did not lead to uptake in the rostral aspect of AVCN, except at its dorsorostral tip (fig. 4, lower section 26). Cells in this region were also labeled in other experiments and were presumably analogous to the peripheral cap of marginal cells observed by Osen ('69a,b).

The topography of these connections, most apparent in the fusiform cell layer in the DCN, conforms with the defined tonotopic organization of the CN complex (Rose et al., '59). Thus, for example, a strip of fusiform cells located relatively caudally and ventrally projected to relatively dorsal (low best frequency) regions of ICC, while a more dorsal and rostral strip projected to more ventral (higher best frequency) regions of the ICC. Results in all other cases were consistent with these general findings.

Nuclei of lateral lemniscus

The topographical relationship between the distributions of labeled neurons and the best frequencies at the injection sites were not nearly as apparent in the NLL. The complex and irregular appearance of the clumps of cells composing DNLL made exact comparisons between the regions containing HRP cells in different experiments difficult. However, in general, for lower-frequency injections labeled cells were observed more ventrally in DNLL (e.g., 76-28). This is consistent with the described tonotopic organization of DNLL (Aitkin et al., '70).

Cells in the lateral streak of VNLL (figs. 2A,C,D) were labeled in bands, and although the thickness of the bands varied from experiment to experiment, it was virtually impossible to determine the topographic relationship between cells in this portion of VNLL and the injection site. By contrast, the rounded mass of cells at the ventral extremity of the VNLL consisted of a single, relatively uniform cluster of neurons (figs. 2B,E). Although there was clearly a shift in the main concentration of labeled cells from experiment to experiment, the irregular boundaries of the ventral part of VNLL made any topographical relationships with injection sites difficult to define.

Segregation of brain stem afferents to the central nucleus

As demonstrated above, all brain stem auditory nuclei known to project to the ICC were labeled, following large HRP injections. In each of the smaller volume cases, neurons in only *some* of these nuclei were labeled. These smaller injections were often made at sites in ICC representing similar sectors of the cochlea, but the distributions of HRP-neurons in the brain stem (i.e., the nuclei which were labeled by the tracer) were never identical. Data from these injections indicate that afferent inputs to the ICC from different brain stem auditory nuclei are segregated to at least some extent within the ICC, and that regions or areas within ICC that represent the same cochlear place can receive input from different auditory brain stem nuclei.

Two of these smaller injection cases (76-4, 0.1 μl, 15.4 mm; 76-10, 0.25 μl, 16.4 mm) clearly demonstrate this segregation of ascending afferents to ICC. These injections were both made in high frequency regions of ICC, yet were sufficiently far apart to make it unlikely that major overlap occurred between ascending axonal groups that incorporated and transported HRP in the two cases. The injection of 76-10 was introduced in the extreme posterior aspect of ICC, while the injection site of 76-4 was located centrally in the nucleus. HRP-labeling following the injection in 76-4 was solely restricted to neurons in the ipsilateral MSO, LSO, and PON. In each 90-micron section, only one to four neurons were labeled in each nucleus; neurons clearly contained reaction product, and were restricted to the ventral tip of MSO and medioventral aspect of LSO. The topography of the projection in this experiment was thus similar to that of 76-28 (described earlier), although numbers of labeled cells were far lower. Note that no neurons were labeled within the CN or NLL on either side.

By contrast, over 75% of labeled neurons in experiment 76-10 were within the principal

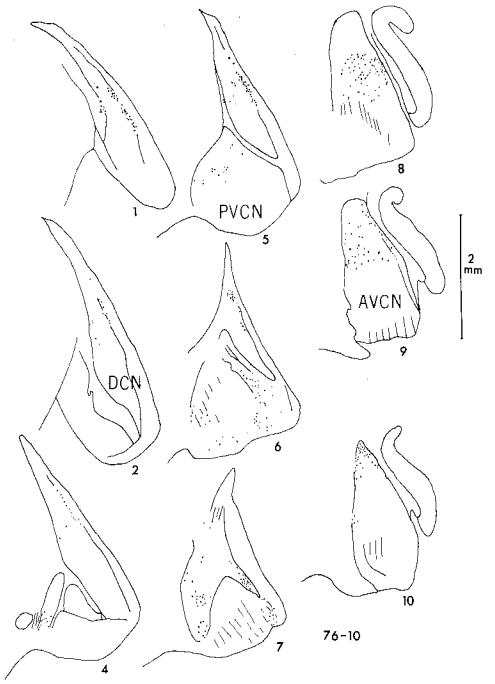

Fig. 5 Outline drawings of the contralateral cochlear nucleus of case 76-10, including DCN (1-6), PVCN (2-7), and AVCN (7-10). Numbers indicate section separation in 300-μ steps. Best frequency at the injection locus was 12 kHz.

divisions of the contralateral CN (fig. 5). There was also labeling of a small number of neurons in the ipsilateral VNLL and PON. In this case, no neurons were labeled in the MSO, LSO, or DNLL of either side. Results from these experiments are compared to four other injection cases in figure 6. For each case, the number of labeled neurons in each nucleus is plotted as a percentage of the total number of HRP-labeled neurons recorded in each experiment (N's in fig. 6). Only neurons in the thick (90 μ) sections were counted. As illustrated, the labeled nuclei and the proportion of HRP-labeled neurons distributed within each major projecting nucleus were very similar following the two largest volume injections (76-26, 72-28; figs. 6C,D) but the results of other (smaller) recorded injection cases differed in detail from these larger volume cases and from each other (figs. 6A,B,E,F).

For example, in 76-10 over 75% of the labeled neurons were localized to the contralateral CN, while in 75-6, less than 5% of the total number of HRP cells were found in the contralateral CN. Over 35% of the labeled neurons were in the contralateral CN in 75-8, and CN contained no HRP cells in 76-4. In fact, over this experimental series, no single nucleus invariably contained labeled neurons. Thus, it is likely that no single nucleus projects to all parts of the ICC.

These results provide anatomical evidence for a segregation of the ascending inputs from brain stem auditory nuclei within the ICC. Larger injections presumably resulted in incorporation and transport of HRP by axons terminating over a large area in ICC, and therefore HRP-labeled neurons were found in all brain stem auditory nuclei projecting to ICC. Following smaller injections, HRP was presumably incorporated by terminals ending in relatively restricted regions of ICC, and therefore labeling was restricted to a limited number of projecting nuclei. As demonstrated earlier, regardless of the size of the injection and the number of nuclei labeled, the topography of the defined projections corresponded with the known cochleotopic organization of the brain stem auditory nuclei. Thus it would appear that there is some form of segregation of afferent inputs in the ICC, and that this segregation constitutes another feature of the anatomical organization (in addition to the laminar organization) of the nucleus.

B. *Physiological studies*

The objective of these experiments was to determine the basic distribution of neurons with different response properties within the ICC, and to relate their distributions to the 3-dimensional cochleotopic organization of the nucleus. These data (reported below) were derived in a series of single unit experiments in cats in which response properties were defined for large numbers of neurons studied within the ICC in each individual animal. In these studies, single neurons were examined in horizontal or dorsoventral microelectrode penetrations that passed through the nucleus.

Response classes of central nucleus neurons

Some of the data from these experiments are summarized in figure 7, in which the number of monaural and binaural ICC neurons studied is shown as a function of the location along the cochlea (distance from the cochlear apex) that they represent (METHODS). The distribution of all binaural and monaural neurons studied in this series is represented in figure 7F. The paucity of neurons repre-

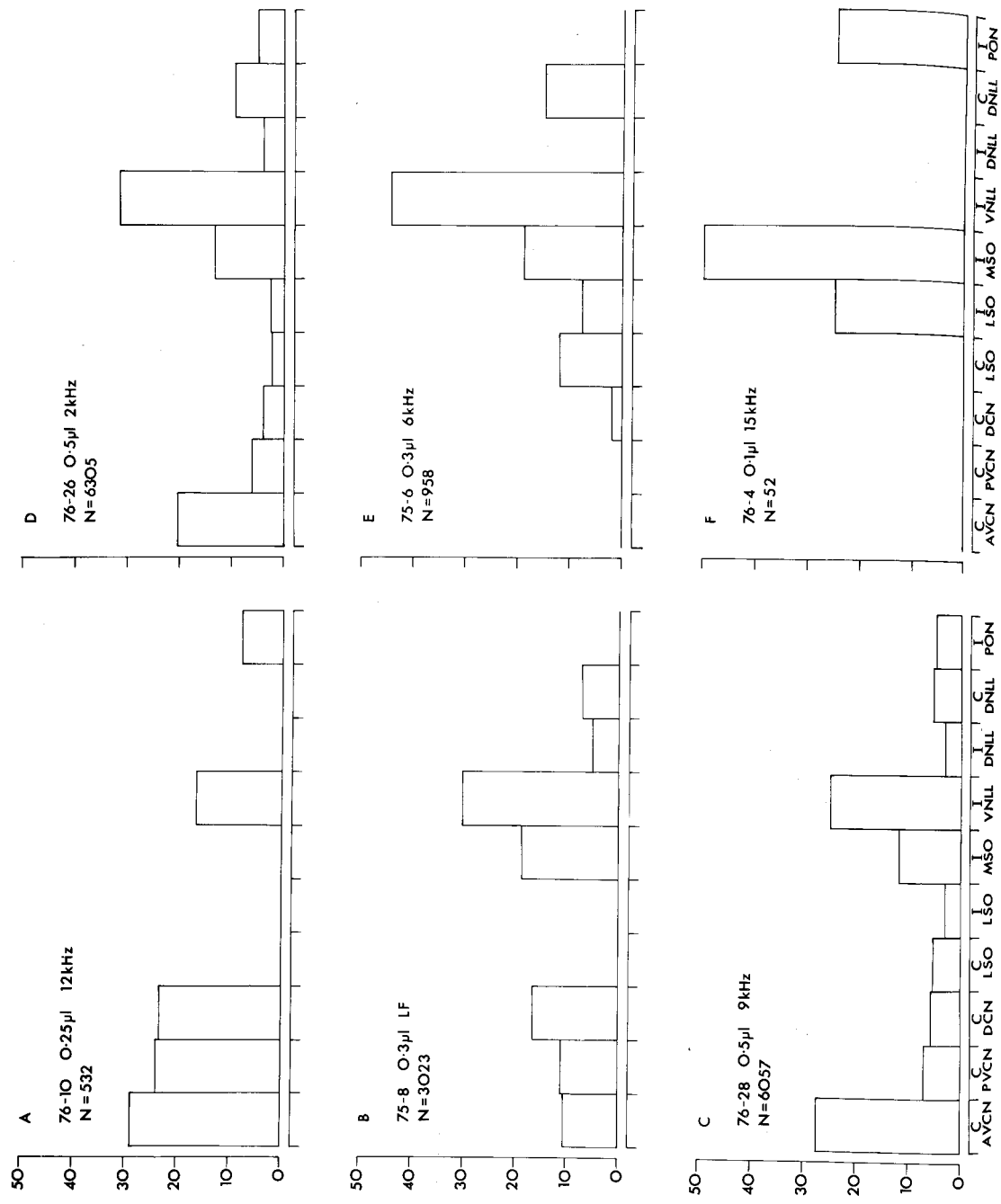
A
76-10 0·25µl 12kHz
N=532
B
75-8 0·3µl LF
N=3023
C
76-28 0·5µl 9kHz
N=6057
D
76-26 0·5µl 2kHz
N=6305
E
75-6 0·3µl 6kHz
N=958
F
76-4 0·1µl 15kHz
N=52
PERCENTAGE
0
10
20
30
40
50
C AVCN
C PVCN
C DCN
C LSO
I LSO
I MSO
I VNLL
I DNLL
C DNLL
I PON

Figure 6

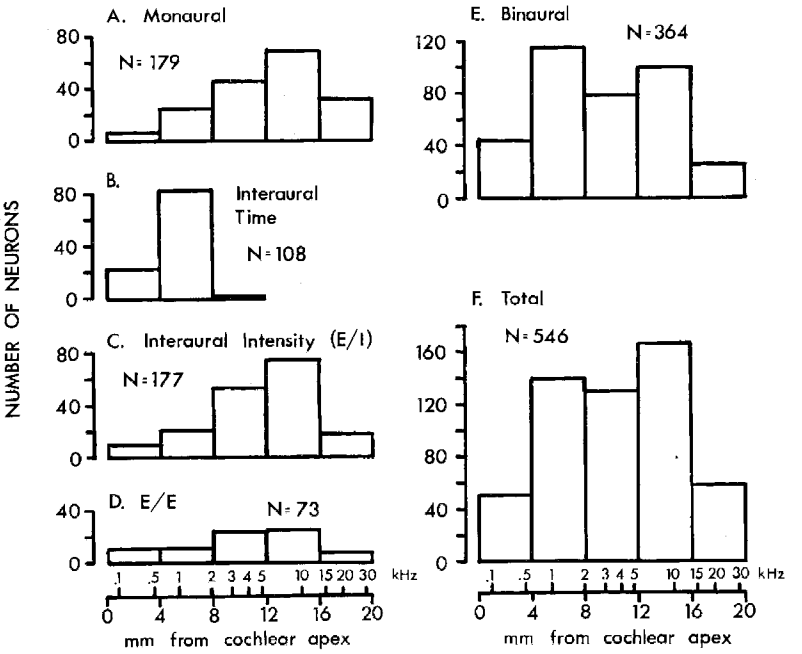

Fig. 7 Numbers of ICC neurons (ordinate) in each response "class" plotted as a function of their represented cochlear place (abscissa), in 4-mm bins. Best frequencies (in kHz) that correspond to the represented cochlear place are listed in these and other figures along the same axis.

senting cochlear sectors further than 16 and less than 4 mm from the apex is probably a consequence of anatomical-surgical limitations that restricted microelectrode placements.

The distribution of monaural and binaural ICC neurons representing different cochlear loci is illustrated in figures 7A and E. Of the 546 classified ICC neurons in these experiments, 179 (33%) were excited or inhibited soley by one ear under the defined stimulus conditions and were therefore classified as monaural. Responses of 364 (67%) ICC neurons were influenced by inputs derived from both ears, and were therefore classified as binaural. Three other ICC units were spontaneously active, and were unaffected by the applied auditory stimulation.

As described in METHODS, it was found that binaural ICC neurons could be conveniently delineated into three major classes by their responses to best frequency tones: (1) neurons whose firing rates varied as a sensitive function of interaural intensity differences; (2) neurons whose firing rate varied as a function of interaural time differences of $\pm$ 250 μsec or less (the behaviorally relevant range in the cat; Rose et al., '66); and (3) neurons whose firing rates primarily varied as a function of the intensity of stimuli delivered to either or both ears, but were not noticeably sensitive to interaural time or intensity differences.

The distribution of these three classes of binaural neurons (as a function of the cochleotopic organization of the ICC) is shown in figures 7B, C, and D. Note that "excitatory-excitatory" binaural neurons ("E/E" neurons) were relatively evenly distributed as a function of represented cochlear place (fig. 7D). Interaural time-sensitive neurons primarily represented the most apical 8 mm of the basilar partition (fig. 7B). By contrast, most (146/177, 82%) interaural intensity-sensitive neurons derived their input from cochlear positions more basal than the 8 mm position (fig. 7C).

The excitatory inputs to ICC neurons de-

Fig. 6 Histograms of the numbers of HRP-labeled neurons in each nucleus (abscissa) expressed as a percentage of total number (N) counted in each of six experiments. Note that percentages and total numbers were taken from neurons counted in the 90 μ (but not the interleaved 30 μ) sections. In each case, the experiment number, injection volume, and best frequency (in kHz) at the injection site in ICC are identified. See text for abbreviations.

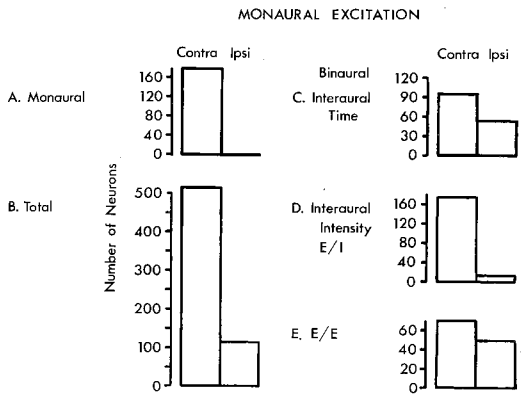

Fig. 8 Numbers of ICC neurons in each response "class" excited by monaural stimulation of either the contralateral ("Contra") or ipsilateral ("Ipsi") ear.

livered from each of the two ears are summarized in figure 8. Most excitatory inputs which drove ICC neurons were ultimately derived from the contralateral ear (fig. 8B). Nearly all monaural neurons, and nearly all binaural neurons sensitive to interaural intensity differences, were excited by stimulation of the contralateral ear (figs. 8A,B). For the vast majority (98%) of neurons sensitive to interaural intensity differences, the contralateral input was excitatory and the ipsilateral input inhibitory.

By contrast, the ipsilateral ear often excited binaural ICC neurons whose firing rates were functions of interaural time differences and those binaural neurons that were not sensitive to differences of interaural time or intensity. While the great majority (86%) of time-sensitive ICC neurons were excited by contralateral stimulation, about one-half were driven by ipsilateral monaural stimulation (fig. 8C). As will be discussed in more detail below, most (81%) of the interaural time-sensitive cells fired maximally with the contralateral stimulus leading.

Nearly all ICC neurons (97%) with E/E response functions (i.e., neurons that were not obviously sensitive to differences in interaural time or intensity) were driven by contralateral stimulation. A majority of these neurons were also excited by tonal stimulation of the ipsilateral ear (fig. 8E). For most of the 73 E/E neurons studied, the discharge rate to binaural stimulation appeared to represent either a summation or a facilitation of the responses to stimulation of either ear alone.

Segregation of neural response classes within the central nucleus

Within ICC, neurons with the same binaural interaction pattern were usually found in close proximity to one another. Although exceptions were common, for neurons representing any given sector of the basilar membrane within ICC, binaural responses changed as a function of location within the nucleus. This was particularly evident in horizontal microelectrode penetrations.

Figure 9 illustrates five representative penetrations taken from this series of experiments. In penetrations 1 and 3 of experiments 76-41 and penetrations 1 and 2 of experiment 76-46, neurons isolated had similar best frequencies, presumably indicating that electrodes must have passed approximately parallel to the ICC laminae. In penetration 1 of 76-41, the response properties of 16 ICC neurons were categorized. During this penetration, 12 successively isolated units were sensitive to interaural time differences (filled triangles, leftmost graph). Each time-sensitive unit was driven by monaural contralateral and ipsilateral stimulation (cf. fig. 8C), and responded to suprathreshold best frequency stimulation with a sustained discharge. Eight of these 12 time-sensitive neurons isolated sequentially discharged maximally when the ipsilateral stimulus was leading; three units fired best when the contralateral stimulus was delivered first; and one unit responded maximally when no interaural time differences were introduced. In this entire experimental series, only 13 time-sensitive neurons (of a total of 108) were studied that discharged maximally when the ipsilateral stimulus was leading, and eight of those neurons were isolated in this penetration within 1500 microns of one another. A sequence of ten time-sensitive neurons was also encountered over approximately 1,500 microns in penetration 1 of 76-46. All interaural time-sensitive units isolated in this penetration responded maximally to ipsilateral time delays, and eight of those ten units responded to suprathreshold best frequency stimulation only at the onset of the binaural stimulus.

Neurons studied in penetration 3 of 76-41 and penetration 2 of 76-46 derived their input from approximately the same sector of the basilar membrane (about 15-16 mm from the cochlear apex). There was no obvious segregation or grouping of response classes in the first

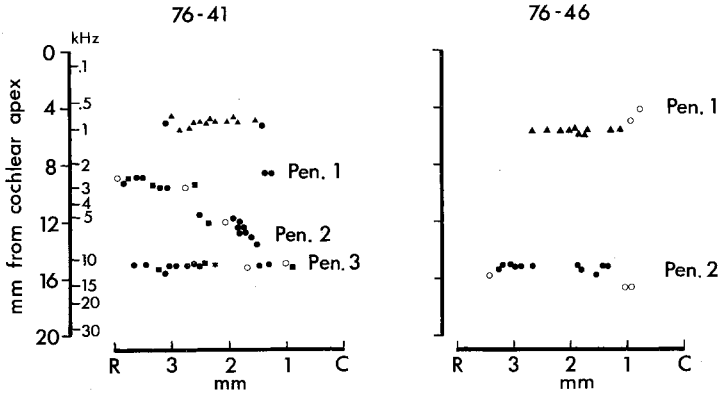

Fig. 9 Illustrations plot the represented cochlear place of each isolated neuron as a function of the neuron's location (in mm) relative to the caudal (C) surface of the IC (abscissa). R is rostral. In figures 11-14, open circles represent monaural neurons and closed symbols represent binaural neurons. Closed symbols represent the following binaural response "classes": circles, interaural intensity-difference ("E/I") neurons; triangles, interaural time-sensitive neurons; squares, binaural "E/E" neurons; stars, binaural neurons that could not be categorized in any of these other response "classes."

seven neurons isolated in penetration 3 of 76-41. Neurons with binaural (filled symbols: fig. 9) and monaural (open circles) properties were intermingled, and one spontaneously active unit (asterisk) was unaffected by auditory stimuli. However, eight of the next nine neurons isolated successively in this penetration were sensitive to interaural intensity differences. All eight were driven by the contralateral ear and inhibited by the ipsilateral ear (cf. fig. 8D). In penetration 2 of 76-46, 11 neurons sensitive to interaural intensity differences were isolated consecutively; again, all were driven by the contralateral ear and inhibited by the ipsilateral ear. The first eight of these interaural intensity-sensitive neurons responded throughout the duration of the best frequency stimulating tone, while the three most rostral studied binaural neurons responded only at the stimulus onset.

Penetration 2 of 76-41 apparently did not parallel ICC laminae, as neurons examined in this microelectrode track represented cochlear loci covering approximately a 4-mm segment of the basilar partition. The first eight units studied were isolated within 500 microns of one another. All were sensitive to interaural intensity differences, and each was driven by the contralateral ear and inhibited by the ipsilateral ear (cf. fig. 8D). Seven of those eight interaural "intensity difference" neurons fired throughout the duration of the stimulus. A variety of response functions was

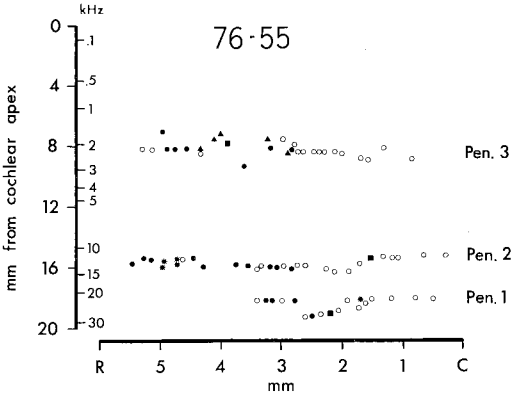

Fig. 10 Represented cochlear place of ICC neurons isolated within three horizontal penetrations in experiment 76-55, plotted as a function of their location (in mm) from the caudal surface of the IC. Penetrations 1 and 3 were 1,100 μ medial and 900 μ lateral to penetration 2, respectively. These penetrations were made oblique to the sagittal plane, accounting for the unusual length of each track within ICC.

seen in the neurons examined from that point on, and although no obvious order was present, most neurons were influenced by binaural interactions.

Most neurons isolated in the caudal aspect of ICC in three horizontal penetrations in experiment 76-55 were monaural (fig. 10). Penetration 1 covered approximately 3,000 microns along the rostral-caudal dimension of

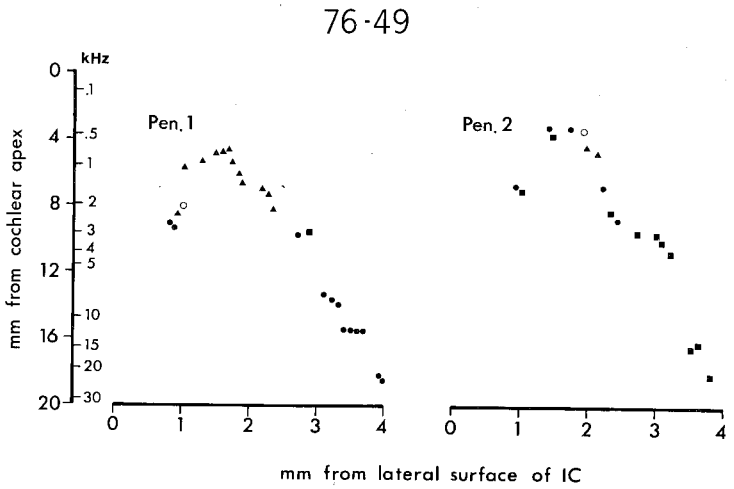

Fig. 11 Represented cochlear place of ICC neurons isolated within two penetrations in experiment 76-49, plotted as a function of their location (in mm) from the lateral surface of the IC. Penetration 2 was 350 μ rostral to penetration 1.

ICC, and 12 of the 18 ICC neurons isolated were monaural, and fired only at the onset of a contralateral stimulus. All other neurons studied in this microelectrode track also responded only at the stimulus onset, with the exception of one spontaneously active unit that was unaffected by auditory stimulation (asterisk).

In penetration 2, 12 of the first 14 neurons isolated over the caudal 2,800 microns of the ICC were only excited by contralateral monaural stimulation. More rostrally, 16 neurons were isolated, 13 of which were binaural. The responses of ten of these binaural units was a function of interaural intensity differences. In penetration 3, all neurons isolated in the more posterior aspect of ICC were also monaural and driven by the contralateral ear.

The response classes of ICC neurons also appeared to be grouped, to some extent, along the lateral-to-medial dimension of the nucleus. Figure 11 illustrates data obtained from an experiment in which the electrode was introduced into the lateral surface of the IC in a horizontal plane. Here the represented cochlear place of studied neurons is plotted as a function of distance from the lateral surface. In each penetration the cochlear place represented by each isolated neuron gradually moved toward the apex, and then reversed and continued to progress more basally. The general form of each curve is compatible with the orientation of the ICC laminae in the cat as defined by Golgi studies (Rockel and Jones, '73a), and if each curve is inverted, their shapes closely approximate the contours of ICC laminae (cf. figs. 5 and 22, Rockel and Jones, '73a).

Note that although in each penetration a similar sequence of neurons was isolated that represented nearly identical cochlear positions relative to the lateral-medial distance in the ICC, the classes of neurons studied in these two penetrations were quite different. In penetration 1, 12 of the first 15 neurons studied in the more lateral aspect of the nucleus were sensitive to interaural time differences (filled triangles). Nearly all (11/12) of these delay-sensitive cells fired in a sustained pattern to best frequency tone pips. Ten of the next 11 neurons isolated in the more medial aspect of the nucleus were sensitive to interaural intensity differences (filled circles). In penetration 2, the response properties of neurons representing the most apical 8 mm of the cochlea were mixed. Firing rates of eight of the nine neurons isolated within the most medial 1,700 microns of this penetration were functions of binaural intensity levels. None of these eight neurons were sensitive to interaural time or intensity differences, and all were driven by monaural stimulation of either ear (cf. fig. 8E). It is likely that these neurons were located within the dorso-medial division of the ICC (Rockel and Jones, '73a).

DISCUSSION

Cochlear nucleus projections to the ICC; distribution of monaural neurons in the ICC

These anatomical studies have demonstrated that neurons within all three subdivisions of the contralateral CN provide a large number of afferents to the ICC, and that the topography of those projections is directly related to the laminar (cochleotopic) organization of ICC. Seven of the nine morphologically distinct "classes" of CN cells (Osen, '69a,b) appear to project to the ICC. The overwhelming majority of CN neurons, irrespective of their morphological classification, are monaural. During these physiological studies in ICC, 179 neurons were isolated that were predominantly influenced by monaural stimulation; 178 of those neurons responded only to contralateral stimulation. These monaural neurons were often clustered, and appeared to be concentrated in the posterior aspect of ICC.

Restricted HRP injections into the posterior aspect of ICC resulted in labeling that was primarily concentrated in the contralateral CN. Similar HRP-labeling patterns in the brain stem have been reported after injections into ICC of the tree shrew (Jones, '76). These neurophysiological and neuroanatomical results suggest that monaural inputs may predominate and may be partially restricted to particular regions of the ICC, and that the contralateral CN is the major source of the brain stem synaptic input to those regions.

The HRP studies reported here and by Adams ('76) have defined the CN cell types that project to the ICC in the cat, and clarified some questions raised by Osen's ('72) earlier study. Following destruction of the ICC, Osen observed no chromatolysis in the large and small spherical cells of the contralateral AVCN. She suggested that these neurons might send collaterals to the SOC and ICC, and therefore little if any chromatolysis would take place following lesions. Our results have indicated that small neurons located within the large and small spherical cell fields project to ICC, but the spherical cells do not. This is also consistent with recent electrophysiological studies (Bourk, '76), which have shown that large spherical cells are not antidromically excited by stimulation of the contralateral IC.

Finally, in a number of the experiments reported above, a small number of scattered HRP-labeled neurons were localized to the ipsilateral CN. In physiological recordings from over five hundred ICC neurons, only one monaural unit was driven solely by the ipsilateral ear.

NLL projections to the ICC; response properties of ICC and NLL neurons

These HRP results have shown that the NLL provide a major share of the input to ICC. Previous anatomical (Stotler, '53; van Noort, '69) and physiological (Aitkin et al., '70; Brugge et al., '70) studies have demonstrated that DNLL is primarily a binaural nuclear complex and the results presented above clearly demonstrate that each DNLL provides major inputs to both ICC's. Thus the large majority of these synaptic inputs to ICC neurons must be transmitting binaural information to the ICC neurons on which they synapse. These HRP results have revealed that the projections from the two DNLL are not distributed throughout the entire ICC, and suggest that at least some of the projections from each DNLL remain segregated from one another within the ICC, although overlap between the two projection systems might occur.

Aitkin et al. ('70) reported that nearly 90% of DNLL neurons were binaural, and responded with sustained discharge patterns to best frequency tones. Low best frequency DNLL neurons were commonly sensitive to interaural time differences. The responses of higher best frequency neurons typically were functions of interaural intensity differences, and these neurons were driven by the contralateral ear and inhibited by the ipsilateral ear. Two similar populations of neurons were observed within the ICC in the present study. However, the described HRP injections were not small or restricted enough to enable any correlations to be made between the DNLL projections to ICC and the recording sites within ICC at which groups of neurons with these specific response properties were found.

During the electrophysiological experiments in ICC, virtually no neurons sensitive to interaural time or intensity differences were observed with response properties corresponding to those of contralateral DNLL neurons. By contrast, neurons with response properties mimicking ipsilateral DNLL neurons were common. These neurophysiological results suggest, then, that the inputs from contralateral DNLL neurons responding to interaural time or intensity differences are com-

bined with inputs from other brain stem sources on ICC neurons. In any event, contralateral "DNLL-like" responses are in some way masked by neural processing in the ICC.

The VNLL usually contributed a significant proportion (averaging 30%) of the neurons projecting to ICC injection loci. In contrast to DNLL, the VNLL is less homogeneous in structure, connections, and electrophysiology. In these anatomical studies, two different labeling patterns were observed within VNLL following HRP injections into ICC, suggesting that there are two VNLL nuclei.

The orientation of ascending inputs to the lateral streak of VNLL (Warr, '66, '69, '72; Fernandez and Karapas, '67; van Noort, '69) appear to parallel the orientation and distribution of the HRP-labeled neurons described in these studies. van Noort ('69) has claimed that the SOC supplies afferent fibers to neurons of the lateral streak of VNLL, but not the ventral cluster of neurons. This ventral group of neurons receives most of its projections from the contralateral PVCN and the ipsilateral AVCN (Warr, '66, '69; van Noort, '69). Aitkin and colleagues ('70) have demonstrated that most neurons in the lateral streak are binaural, and that most neurons in the ventral cluster are monaural. In view of the differences in the structure, connections and electrophysiology, it appears that the two divisions of "VNLL" should be regarded as distinct auditory brain stem nuclei, as van Noort ('69) and Guinan et al. ('72) have suggested. When these earlier anatomical and physiological data are assessed in relation to the projections defined in this study, it would appear that neurons of the ventral cluster of the VNLL primarily deliver monaural auditory information to ICC, while the neurons in the more dorsal, lateral streak of VNLL primarily deliver binaural information.

SOC projections to the ICC; response properties of ICC and SOC neurons

The anatomical data presented above have demonstrated that the ipsilateral MSO and LSO and contralateral LSO send major projections to ICC. The LSO is a binaural nucleus; virtually all of its neurons are driven by the ipsilateral ear and inhibited by the contralateral ear (and hence are sensitive to interaural intensity differences), and discharge in sustained firing patterns to tonal stimulation (Tsuchitani and Boudreau, '67; Boudreau and Tsuchitani, '68). Neurons in the MSO are also predominantly binaural, are driven by monaural stimulation of either ear, and respond in sustained firing patterns to tonal stimulation (Guinan et al., '72; Goldberg and Brown, '69). The discharge rates of those few neurons studied were often functions of interaural time differences (Hall, '65; Goldberg and Brown, '69).

In the study reported here, a large population of ICC neurons with response characteristics similar to ipsilateral MSO and contralateral LSO neurons were isolated within ICC in close proximity to one another (e.g., penetrations 1 and 2 of 76-41, fig. 9). Neuroanatomical evidence indicates that the SOC does not project to the entire ICC and that at least some portion of the projections of each MSO and LSO remain segregated within ICC (e.g., figs. 6B,C,F), although overlap between any or all might occur. Furthermore, inputs from the two LSOs are apparently not perfectly coincident.

As indicated above, many ICC neurons have response properties similar to ipsilateral MSO and contralateral LSO neurons. However, virtually *no* neurons respond as if they were driven solely by the ipsilateral LSO (i.e., ipsilateral excitation, contralateral inhibition). The fact that few if any ICC neurons have "ipsilateral LSO-like" responses provides preliminary evidence that this ipsilateral LSO input (like the contralateral DNLL input) plays some modulatory role in the processing of auditory information within the ICC.

Spatial organization of the ICC

Data derived in these studies have provided evidence that the brain stem afferents to ICC neurons change within the three dimensions of the nucleus and that the response properties of ICC neurons also change within the confines of the structure. Golgi studies of the cat inferior colliculus (Rockel and Jones, '73a; Morest, '66) indicate that the ICC is not a homogeneous structure. Morest ('66) has distinguished three major subdivisions (pars lateralis, medialis, and centralis) in his conceptualization of the central nucleus, each with a distinctive neuropil. D. Jones (personal communication) has evidence that the central nucleus of the tree shrew may be subdivisible on the basis of cytoarchitecture, and recent studies on the endogeneous peroxidatic activity of ICC neurons in the cat (Wong-Riley, Merzenich, and P. Jones, personal communication) also suggest that the ICC might consist of a number of subdivisions. Thus it appears

that the large laminated division of the ICC of the cat cannot be regarded as a uniform structure on anatomical or physiological grounds. Evidence presented here and in these other cited studies indicates that the ICC probably consists of a number of subdivisions. Although the techniques utilized in these experiments did not provide sufficient resolution to permit a schematic reconstruction of the ICC, it is clear that these subdivisions must be integrated within the laminar, cochleotopic organization of the ICC, and thus constitute another basic feature of the anatomical and physiological organization of the nucleus. These subdivisions may be related to the segregation of brain stem afferents described here, but a definition of that relationship must await application of more refined experimental techniques.

Implications on the role of the ICC in the processing of auditory information

The response characteristics of auditory neurons have been presumptively related to the auditory sensation(s) they might encode (e.g., Boudreau and Tsuchitani, '68; Goldberg and Brown, '68, '69; Rose et al., '66). Physiological data presented above have demonstrated that neurons that could encode different aspects of sound sensation may be segregated within ICC, and have provided some physiological evidence that *different aspects of auditory sensation might be encoded or represented separately within the nucleus.* This information appears to be processed in parallel within ICC, and this processing appears to be directly related to the segregation of afferents described. Other neuroanatomical and neurophysiological data reported here (particularly with regard to ICC inputs from the ipsilateral LSO and the contralateral DNLL) indicate that auditory information carried by some brain stem afferents must converge with other inputs on ICC neurons; in any event, response properties of neurons in these brain stem nuclei are not characteristic of any significant neuronal populations in the ICC of the anesthetized cat.

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