

The Topographic Organization of Corticocollicular Projections From Physiologically Identified Loci in the AI, AII, and Anterior Auditory Cortical Fields of the Cat

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ABSTRACT The connections of the three auditory fields AI, AII, and the anterior auditory field (AAF) with the inferior colliculus (IC) were studied using anterograde tracing techniques. Microinjections of tracers were placed at physiologically identified loci after these fields had been functionally mapped using microelectrode recording techniques. This methodology ensured that the injections were well within the borders of each cortical field that was studied and enabled the elucidation of the topographies of the projections of AI and AAF onto the IC with respect to their cochleotopic organizations.

The projection of loci in AI to the caudal aspect of the IC was in the form of sheets of terminals in the dorsomedial division of the central nucleus bilaterally and the pericentral nucleus ipsilaterally. The topography of projection with respect to the cochleotopic organization of AI appeared to be in register with the described cochleotopic organization of the central nucleus and the pericentral nucleus.

The sheets of labeled terminals in the dorsomedial division of the central nucleus that resulted from the projection of single loci in AI were of the proper orientation to be continuous with the morphological laminae described in the ventrolateral division of the central nucleus. These sheets of corticocollicular terminals also paralleled the dorsomedial aspect of the physiologically defined "isofrequency contours" of the central nucleus.

Single injections placed in AAF produced autoradiographic label in the IC that was of the same basic pattern and systematic topography as the labeling recorded with AI injections; however, it was much weaker. The projection from AII was to the lateral (ipsilateral) and medial (bilateral) aspects of the pericentral nucleus.

Numerous investigators have described projections from the auditory cortex to the inferior colliculus (IC) after cortical lesions in the cat, using the anterograde degeneration techniques (Massopust and Ordy, '62; Rasmussen, '64; Rockel and Jones, '73 a; Cooper and Young, '76). Given the limitations in precision of the degeneration methods, these studies did elucidate general features of the three dimensional patterns of projections from cortical loci.

An important limitation of these studies pertained to the placements of the lesions in the auditory cortex with respect to its internal organization. In general, the lesions were assigned to particular auditory cortical fields according to the cortical sulcal patterns and the evoked potential maps of Rose and Wool-

sey ('49) and Woolsey ('60). Recent investigations have indicated that the locations of auditory cortical fields vary significantly with respect to the sulcal patterns from cat to cat (Merzenich et al., '75, '77; Knight, '77). In fact, the form of the sulcal patterns themselves vary greatly among cats. Moreover, the boundaries, shapes, sizes, and numbers of the cortical fields of the evoked potential maps have been revised using more refined techniques (Merzenich et al., '77; Imig and Reale, '77). Thus, there is a need to determine more accurately the sources of these corticocollicular projections employing current knowledge of the organization of the auditory cortex.

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In the experiments described in this report, microelectrode recording techniques were used to map the locations of one or more of three auditory cortical fields in individual cats prior to the injection of anatomical tracers. This approach ensured that the injections and the spreads of tracers were well within the boundaries of identified cortical fields. Moreover, the use of microelectrode recording techniques allowed a definition of the topographies of the projections with respect to the functional (cochleotopic) organizations in AI and AAF; all injections were introduced at sites of representation of known frequencies and at specified locations along "isofrequency contours" within these cortical field maps.

The major finding of these experiments was that the corticotectal projection from AI onto the dorsomedial division of the ICC (described by others) was precisely topographically ordered as a function of the best frequency site of injection in AI, and was in register with the cochleotopic order of the ICC. This investigation also revealed that the pericentral nucleus received systematically topographic (and also apparently cochleotopic) projections from AI. Differences in the destinations and the forms of terminal arrays of corticotectal projections from AI, AII, and AAF were observed.

METHODS

The corticotectal projections of AI, AII, and AAF were investigated by placing microinjections of tritiated amino acids at physiologically defined loci in these fields. The results presented here were obtained from experiments performed in 37 hemispheres of 26 cats. Sixteen experiments were performed in AI, 10 in AII, and 11 in AAF. As part of another study of the thalamocortical connections of AI, AII, and AAF (Andersen et al., '80a), horseradish peroxidase was also injected in 26 of these hemispheres. The methods employed in these experiments have been described by Andersen et al. ('80a) and will be only briefly outlined here.

Recording

Recordings were performed under ketamine anesthesia. Stimuli were delivered via a hollow flexible tube sealed into the contralateral external auditory meatus and into a chamber in which a calibrated audiometric driver was sealed. Stimuli were trapezoidal tone pips with rise and fall times of 5 msec. The stimuli were 0.2 sec in duration and had repetition rates of 0.8 to 1.0 stimulations per second. The "best frequency" of a unit or unit cluster was determined by defining the frequency at which the unit responded at the lowest sound pres-

sure level. AI and AAF were distinguished by the orientations of their tonotopic organizations; they have mirror-image rostrocaudal tonotopic sequences (see Knight, '77). AII, which is located ventral to AI, was readily distinguished by the much broader "tuning curves" of its neurons relative to the sharply tuned AI neurons. In other words, AII neurons responded with about the same thresholds over a broad range of frequencies that often spanned several octaves.

Injection of tracers

Anatomical tracers were injected in the cortex only after microelectrode recording maps were made of the cortical surface, which determined the locations of the cortical fields, the approximate boundaries of the field to be injected, and, for AI and AAF, the approximate axes of the "isofrequency contours." The pressure injections were made at physiologically defined loci through 1 or 5 μ l Hamilton syringes with 27 or 31 gauge needles. The needles were often affixed with a glass micropipette. Injections were made into the middle layers of cortex (500–1,000 μ depth), and injection volumes ranged from 0.05 to 0.5 μ l, with 0.15 to 0.2 μ l the most common volumes of injection.

For anterograde tracing 0.1 ml of 4,5 ³H-leucine (61 Ci/mole, 0.5 mCi/ml) was desiccated and redissolved in 5 μ l of sterile saline. The final label concentration was 10 μ Ci/ μ l. For retrograde tracing, saturated solutions of HRP (Sigma type VI) were prepared in 5 μ l of sterile saline. For injections of both tracers together, the HRP was dissolved in the leucine solution (Colwell, '75; Trojanowski and Jacobson, '75).

The *effective* spread of the tritiated leucine for each injection was defined as the diameter of the volume of cortical tissue that transported sufficient label to the inferior colliculus to be visualized with the parameters of the autoradiographic method used in that experiment. The effective spread of the tritiated leucine at the injection sites was usually difficult to assess on the basis of the examination of the injection site alone. However, it was possible to estimate the effective spread of the tritiated amino acid for AI injections by examining the autoradiographic labeling in the dorsomedial division of the central nucleus of the inferior colliculus (ICC-dm). As will be shown in the results, the topography of this projection with respect to the cochleotopic organization of AI conformed to the cochleotopic organization of the central nucleus. The width of each projection lamina in the ICC was measured and converted into the best frequen-

cy range it spanned, using the "recording depth vs best frequency" ICC data of Merzenich and Reid ('74). Each frequency range was then compared with the "best frequency vs distance on the cortical surface" graphs of Merzenich et al. ('75). These data were consistent with an effective spread of tracer at the injection site not greater than 0.5 to 1.5 mm in diameter for small (0.1–0.2 μ l) injections. (It was usually about 0.5 mm in diameter.) These measurements were further confirmed in those cases where two injections were made at different positions in the cochleotopic representation in AI (see Figs. 3, 4). In these cases, two distinct bands of label were recorded in ICC-dm when the injections were placed little more than 1 mm apart in the cortical field.

Anatomical procedures

Postoperative survival periods were either short (2 days) or long (8–18 days). For long survival cases, all recording and injection procedures were performed under sterile conditions. Following the postoperative period, animals were perfused intracardially with 0.2 M phosphate buffered (pH 7.6) 2.5% paraformaldehyde solution. Ninety or 100 μ frozen sections were processed for HRP according to the protocol of LaVail et al. ('73). Adjacent 30 or 50 μ sections were processed for autoradiography according to Cowan et al. ('72). Some 30 or 50 μ sections were generally processed for both HRP and autoradiography according to Colwell ('75). Exposure times for the autoradiograms were 3–4.5 months.

Data analysis

Sections were examined under bright field and dark field illumination with a Zeiss Photomicroscope III or a low power Olympus Photomicroscope. Low power dark field photomicrographs were made of autoradiograms using a Nikon Ultraphot mounted over a Sage (model 281) stereo light box. Photomicrographs were made with Kodak High Contrast Ortho Process 4 \times 5 sheet film or with Kodak Panatomic X 35 mm film. All line drawings of autoradiographic labeling were made from tracings of photomicrographs, coupled with visual inspection of the sections under the microscope. Terminal labeling was assumed in areas where the ARG label was homogeneous and dense after short survival times (2 days). Fiber labeling was assumed when the autoradiographic labeling was in the form of many thin, individual lines. (The fiber pattern of autoradiographic labeling was more often seen after longer survival periods of 8–18 days.)

Parcellation of the inferior colliculus

The inferior colliculus (IC) has been divided, on the basis of cell morphology and connections, into three nuclei (Ramon y Cajal, '55; Morest, '64, '66a,b; Geniec and Morest, '71; Rockel and Jones, '73a,b). The largest nucleus is the central nucleus (ICC); it is almost encircled by the other nuclei. The names "internuclear rind," "roof nucleus," or pericentral nucleus (Ramon y Cajal, '55; Berman, '68; Rockel and Jones, '73a,b) have been used to describe a sheetlike structure that overlies much of the dorsomedial, dorsal, dorsolateral, and caudal surfaces of the ICC. The external nucleus (Ramon y Cajal, '55; Berman, '68; Rockel and Jones, '73a,b) or pericollicular tegmentum (Geniec and Morest, '71) covers the anterior and lateral surfaces of the ICC. The partition of the inferior colliculus into a central nucleus (ICC), pericentral nucleus (ICP), and external nucleus (ICX), according to the descriptions of Ramon y Cajal ('55), Berman ('68), and Rockel and Jones ('73a, b), will be used here. Figure 1 demonstrates these divisions in the frontal plane through the middle of the IC.

The ICC of the cat has been subdivided into a dorsomedial region and a ventrolateral region on the basis of morphology and connections (Rockel and Jones, '73a; Van Noort, '69). The ventrolateral division is morphologically laminated. This structure is defined by the parallel orientation of the dendrites and axons within the nucleus (Morest, '64; Geniec and Morest, '71; Rockel and Jones, '73a; Fitz-Patrick, '75), and the parallel orientation of the long axes of the perikaryon of certain cell classes (Rockel and Jones, '73a). The dorsomedial region contains large cells with long, radiating dendritic fields. The structure in this region does not appear to be laminated (Rockel and Jones, '73a).

RESULTS

No HRP labeling in the IC after cortical injections

Injections of HRP into AI, AII, and AAF never produced retrograde labeling in the IC or in any other mesencephalic structure. It thus appears that the described projections from the thalamus are the only direct, ascending auditory sensory projections to these three cortical fields in the cat. Since the direct connections of the IC with AI, AII, and AAF are only corticofugal, all the results to be discussed below were obtained by anterograde tracing of labeled proteins resulting from tritiated amino acid microinjections into these three cortical fields.

AI corticotectal projection

After single injections of 3H-l-leucine into AI in cases with short survival times (2 days), the label only appeared in the caudal half of the inferior colliculi. The autoradiographic label was seen bilaterally in the dorsomedial divisions (ICC-dm) of the central nuclei (ICC) and ipsilaterally in the pericentral nucleus (ICP). The autoradiographic label in both the ICC-dm and ICP was distributed to form continuous sheets, tilted down laterally (see Fig. 1). With longer survival times (8-18 days), autoradiographic label within other regions of the mesencephalon was seen. Most, but probably not all, of this labeling was of cortical efferent fibers. Most of these labeled fibers appeared to be destined for the terminal regions in ICC-dm and ICP and for the ipsilateral pontine nuclei.

Path of fibers to the caudal IC after AI injections

The long-survival anterograde tracing experiments revealed the path of the fibers projecting into the inferior colliculi. Four successful long survival experiments were performed. In all four cases, the results were virtually identical.

Labeled corticotectal fibers passed through the MGB and were scattered diffusely throughout the ipsilateral brachium of the inferior colliculus (BIC); no restricted topography of the fiber path was evident within the BIC. There

was terminal labeling in the nucleus of the brachium of the inferior colliculus, medial and adjacent to the brachium.

Some labeled fibers were always seen (in frontal sections) extending up from the BIC to pass between the superficial and intermediate layers of the ipsilateral superior colliculus at its most caudal and lateral extent. However, terminal field labeling was not seen within the superior colliculus. These fibers appeared to follow a caudomedially directed course to enter the rostral aspect of the collicular commissure (CC).

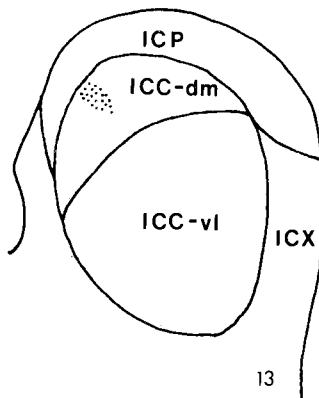
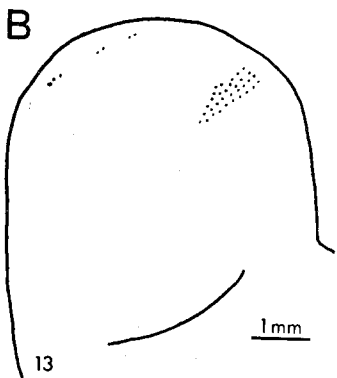
Light terminal label was seen in the rostral pole of the IC in the region of the rostral aspect of the external nucleus (ICX). The path of fibers from the brachium of the inferior colliculus to this region was not evident. This labeled field extended quite far anteriorly, lateral to the periaqueductal gray and medial to the nucleus of the brachium of the inferior colliculus. In the most anterior aspect of this terminal field, label may have extended into the midbrain tegmentum rostral to the ICX.

At the level of the anterior pole of the ipsilateral central nucleus of the inferior colliculus, many labeled fibers from the BIC passed dorsally and medially. Most of these medially directed fibers descended into the ipsilateral dorsomedial region of the ICC and passed caudally into terminal fields in ICC-dm. Others entered the collicular commissure and could be followed into the contralateral dorsomedial division of the ICC. More caudally,

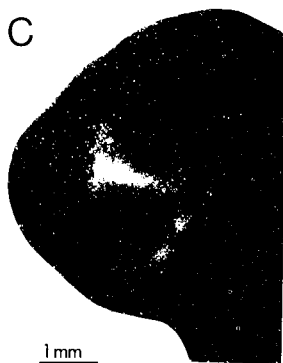
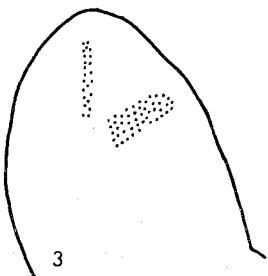
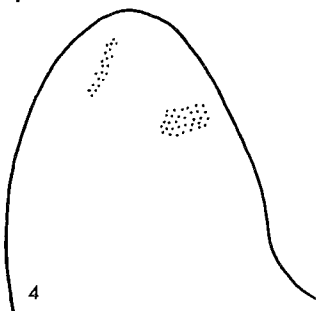
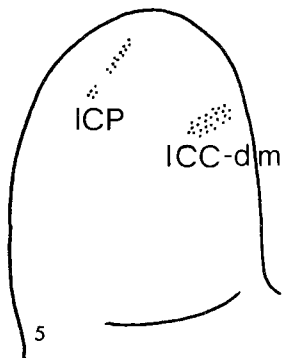
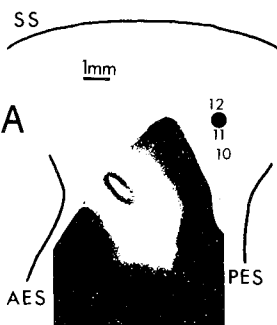
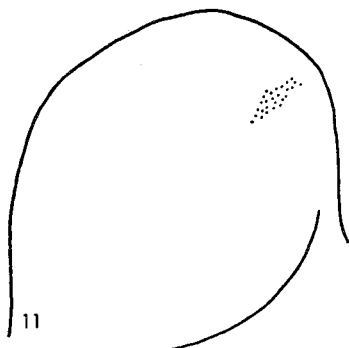
Abbreviations

AI	first auditory field	ICC-vl	ventrolateral division of the ICC
AII	second auditory field	ICP	pericentral nucleus of the IC
AAF	anterior auditory field	ICP-l	lateral aspect of the ICP
AES	anterior ectosylvian sulcus	ICP-m	medial aspect of the ICP
ARG	autoradiography	ICX	external nucleus of the IC
BIC	brachium of the inferior colliculus	M	medial division of the medial geniculate
CC	collicular commissure	PES	posterior ectosylvian sulcus
Dd	deep dorsal nucleus of the medial geniculate	SS	suprasylvian sulcus
HRP	horseradish peroxidase	TAA	tritiated amino acids
IC	inferior colliculus	VI	pars lateralis of the ventral division of the MGB
ICC	central nucleus of the IC	Vo	pars ovoidea of the ventral division of the MGB
ICC-dm	dorsomedial division of the ICC	Vt	transitional zone of the ventral division of the MGB

Fig. 1. A representative example of the projection of a locus in AI to the inferior colliculus. In this experiment, 0.25 μ l of 3H-l-leucine was injected at an 11 kHz locus in AI. A) shows, on the cortical surface, the site of injection within AI and a frontal section darkfield photomicrograph through the center of the injection site. The calibration line represents 1 mm for both the drawing of the cortical surface and the darkfield photograph. B) shows frontal sections through the inferior colliculus. The stippling indicates autoradiographic labeling. The sections are numbered caudal to rostral, in 120 μ steps, beginning at the caudal pole of the inferior colliculus. C) is a darkfield photograph of a frontal section through the MGB and shows the typical pattern of label expected for an AI injection at an 11 kHz locus. (The labeling in the MGB was used as a cross reference to confirm the cortical location of the injection.) The three dimensional structure of the projection to the IC is in the form of two sheets of labeled terminals in ICP and ICC-dm of the ipsilateral IC and a sheet of labeled terminals in ICC-dm of the contralateral IC.



CASE 76-119
AI INJ.; 11 KHZ



these fibers passed into terminal fields in the contralateral ICC-dm. A second group of fibers passed lateral and dorsal to the ipsilateral central nucleus and could be traced caudally into the autoradiographically labeled terminal fields within the pericentral nucleus. In these long survival cases, other laterally situated labeled fibers coursed ventralward in the lateral region of the ipsilateral external nucleus, and more posteriorly, they continued ventrally into the tectopontine tract. Terminal labeling was noted ipsilaterally in a restricted region of the dorsolateral pontine nucleus and in a small pontine cell group intercalated within the pyramidal tract. No terminal fields were observed within the ipsilateral external nucleus. Labeled fibers were noted within the dorsalmost aspect of the ipsilateral cerebral peduncle. These fibers were presumably destined for the ipsilateral pontine nuclei as well (Brodal, '69).

AI projection onto ICP and the dorsomedial division of ICC

With AI injections, terminal fields in ICP and ICC-dm were always apparent in the caudal half of the IC. The most dense labeling occurred in the more caudal regions. The basic pattern of labeling was the same (in all 16 experiments), regardless of the survival times used. (However, terminal labeling appeared relatively more rostrally with progressively longer survival times.) The autoradiographic grains in the ipsilateral ICP and dorsomedial division of the ICC formed sharply defined sheets (see Fig. 1). The contralateral projection to the dorsomedial division also formed a sheet that occupied a similar position and orientation in respect to the ipsilateral ICC-dm projection. This contralateral label was always fainter; indeed, in several cases, it was not evident. Moreover, the contralateral sheet of label in ICC-dm was often wider and shorter than the ipsilateral sheet (see Fig. 1, section 13; and Fig. 2). The orientation of the ICC-dm sheet was dorsomedial to ventrolateral in the frontal plane (see Fig. 1). The tilt

was greater in the more rostral aspect of the projection (see Figs. 3, 4). This orientation appeared to parallel the orientation of the cellular laminae of the adjacent ventrolateral division of the ICC.

Anteriorly, the ICP autoradiographic terminal label also formed a distinct sheet, oriented dorsomedially to ventrolaterally (see Fig. 1). Posteriorly, particularly in the region of the ICP which covers the dorsocaudal surface of the inferior colliculus, the ICP terminal sheet often rotated, so that in frontal sections, it had a nearly vertical orientation (see Fig. 1). The ICC-dm and ICP projections always came into close apposition at their ventrolateral edges in the extreme caudal pole of the IC (see Fig. 1, sec. 3; Fig. 3, secs. 29 and 32; Fig. 4, sec. 16). No projections from the ipsilateral AI cortical field to the contralateral ICP were ever recorded.

Topographic organization of the AI corticotectal projection

The projections to ICC-dm and ICP are both topographically organized with respect to the cochleotopic representational order in the AI cortical field. Injections introduced at the sites of representation of successively more apical (lower frequency) cochlear locations in AI resulted in sheets of autoradiographic label that were located at successively more medial positions in ICP, and in sheets of label that were located in successively more dorsolateral positions in the ICC-dm. There was an apparent frequency reversal in the topographic projection from AI to ICC-dm and ICP along their mutual border, with injections at the AI sites of representation of lowest frequencies projecting along this border.

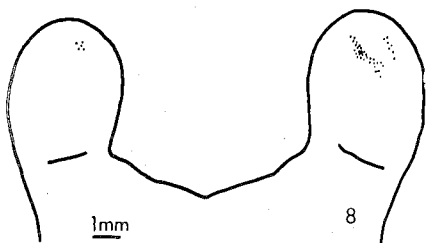
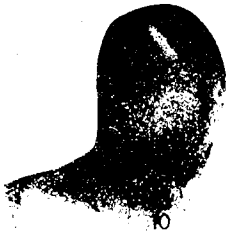
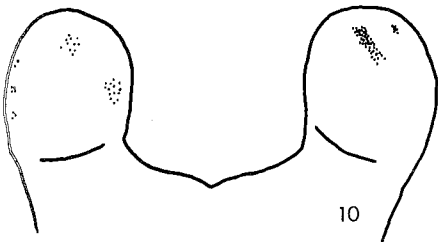
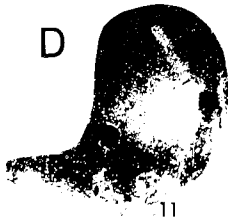
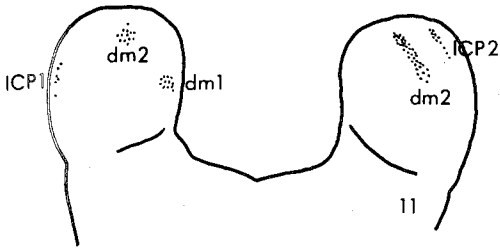
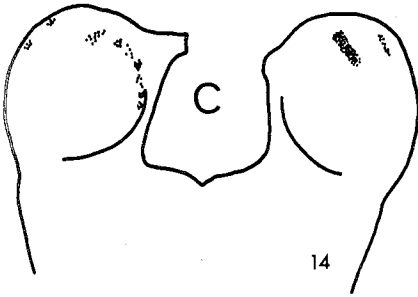
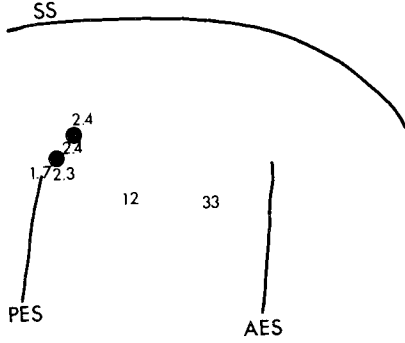
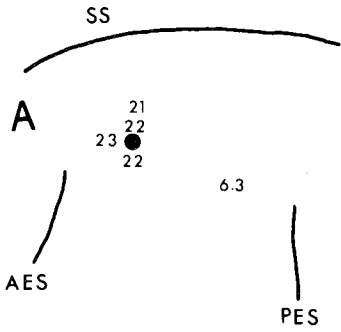
Figure 2 is an example of an experiment that demonstrates the topographic organization of the AI projection into the IC. In this case, injections were placed in the left AI auditory field at a 22 kHz locus and in the right AI at two 2.4 kHz loci. In the right inferior colliculus, a continuous sheet of autoradiographic label was seen that passed

Fig. 2. A representative example of the topographic organization of the corticotectal projection *re* the cochleotopic order of AI. In this experiment, 0.3 μ l of ³H-l-leucine was injected at a 22 kHz locus in the left AI auditory field, and at two positions along a 2.4 kHz isofrequency contour in the right AI. A) shows surface views of the left and right cortical surfaces with the injection sites represented by the black spots. B) is a darkfield photograph of a frontal section through both MGBs. Labeling in the left and right MGBs indicates the topographic organization of the corticothalamic projection onto the ventral division of the MGB, with higher frequency representational sites projecting relatively more dorsomedially. C) shows sections through the two ICs with stippling indicating areas of autoradiographic labeling. The subscripts indicate labeling 1) from the higher frequency place injection, and 2) lower frequency place injection. Section numbering is caudal to rostral, in 200 μ steps, beginning at the caudal pole of the IC. D) shows darkfield photomicrographs of the right IC drawn in C. Notice the topographic organization in ICC-dm and ICP, with the higher frequency representational region of AI projecting relatively more medioventrally in ICC-dm and ventrolaterally in ICP. Also, the general patterns of label are similar for a single locus injection and two injections made along an isofrequency contour.

CASE 76-141

LEFT
AI; 22KHZ INJ.

RIGHT
AI; 2.4 KHZ TWO INJ.



77·45; AI INJECTIONS

1) 18.5 KHZ 2) 2 KHZ

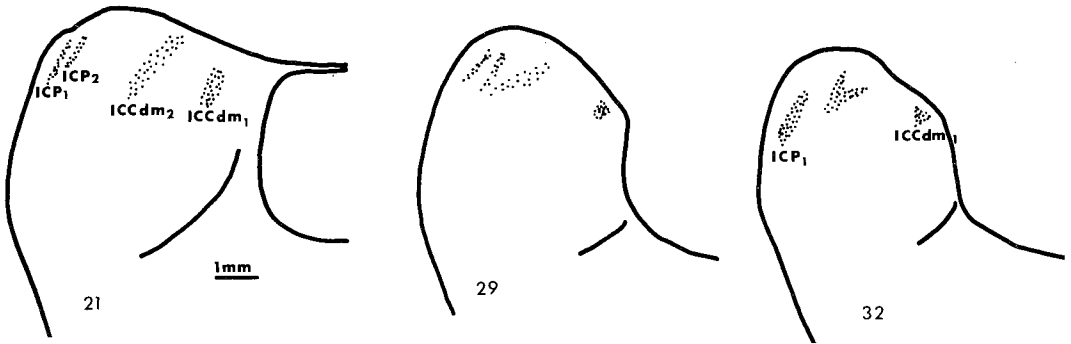


Fig. 3. A representative example of the systematic topography of the AI corticotectal projection onto the IC. Subscripts indicate labeling as a result of injections ($0.5 \mu\text{l}$) at 1) an 18.5 kHz locus in AI, and 2) a 2 kHz locus in AI. Higher frequency positions in AI project to more ventromedial positions in ICC-dm and more lateral positions in ICP. The laminar projections in ICC-dm are longer for relatively lower frequency representational loci in AI (see section 21). The ICP and ICC-dm labeled terminal sheets come into close apposition more rostrally after injections of tritiated amino acids in relatively lower frequency representations of AI (see section 29). Sections numbered rostral to caudal in 30μ steps.

through ICC-dm (dm_2). This labeled sheet resulted from the injections at the 2.4 kHz representation in the right AI. In the left inferior colliculus, there were two foci of label in ICC-dm in sections 10 and 11. The more ventral focus of ARG label (dm_1) resulted from the 22 kHz place of injection in the AI tonotopic representation of the left cortex. The more dorsal focus of ARG label (dm_2) resulted from the injections at the 2.4 kHz representation in the contralateral AI. (Autoradiographic labeling from the 22 kHz locus of injection in the left AI did not appear bilaterally in ICC-dm, as was sometimes the case in short survival experiments.) Examination of these sections demonstrated that the lower frequency injection sites in the right cortex produced more dorsal and lateral autoradiographic label in ICC-dm, as compared with autoradiographic label that resulted from the higher frequency representational site injection in the left cortex. This was particularly apparent in the left inferior colliculus of sections 10 and 11, where the projection from the location of the relatively lower frequency representation of the contralateral AI (dm_2) was directly comparable to the more medial and ventral projection from the location of the relatively higher frequency representation of the ipsilateral AI (dm_1). Examination of these sections also indicated that the projection from the lower frequency representation of the right AI occupied a more dorsal and medial position in the right ICP (ICP_2) than the projection to the left ICP (ICP_1) from the

relatively higher frequency representation of the left AI.

In three experiments, injections were placed at two widely separated locations re the cochleotopic representation in single AI cortical fields. In each experiment, the two injections resulted in two parallel sheets of label in both the ipsilateral and contralateral dorsomedial divisions (see Figs. 3, 4). In both of these illustrated cases, there were also two distinct sheets of label evident at more caudal levels within the ipsilateral ICP (see Figs. 3, 4). These experiments directly demonstrate that there exists a topographic organization of projection into both the ICC-dm and ICP with respect to the cochleotopic organization of AI. These double-injection experiments also demonstrate that the laminar terminal fields in ICC-dm and ICP come into close apposition with one another at successively more rostral levels, with single injections into successively lower best frequency representational sites in AI (see Fig. 3, sec. 29; and Fig. 4, sec. 16).

In three other experiments, two, three, and four injections were made along isofrequency contours in AI. In all these cases, the same pattern of projection in the IC was seen as with single injection cases. Multiple injections along the isofrequency contour produced only one sheet of label in the ipsilateral ICP and single sheets in the ipsilateral and contralateral ICC-dm (see Fig. 2, sec. 11, 10 and 8 of row D).

Injections at lower best frequency loci in AI produced bilateral laminae in ICC-dm which

CASE 77-4

AI INJECTIONS: 6 KHZ LAMINA
2 KHZ LOCUS

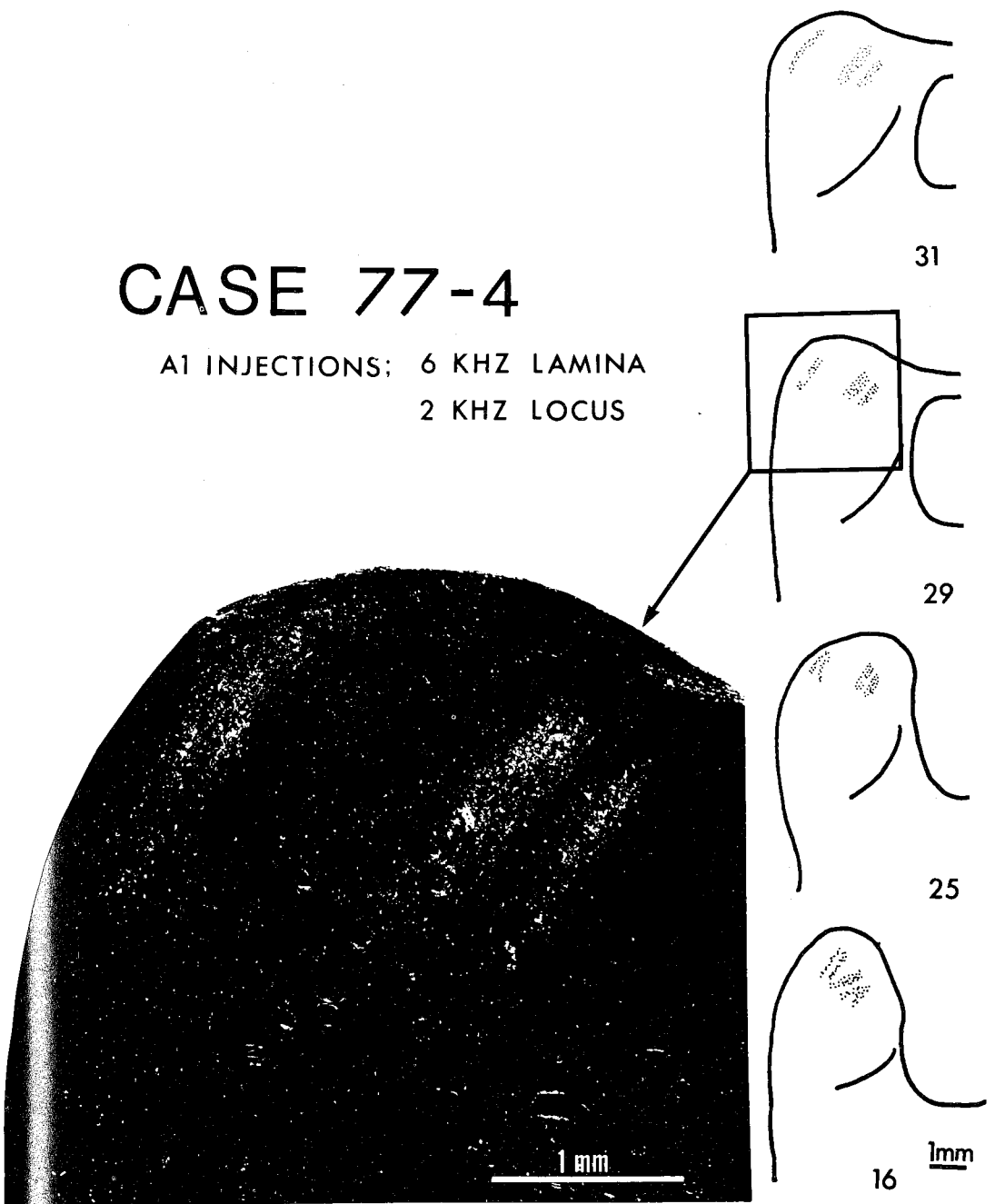


Fig. 4. An example of the topography of the corticotectal projection from AI. In this experiment, injections of 3H-l-proline were made along almost the entire extent of a 6 kHz isofrequency contour and at a 2 kHz locus in AI. On the right are frontal sections through the ICC, with stippling indicating autoradiographic labeling. On the left is a darkfield photomicrograph of one of the drawn sections on the right. Note the two laminae in ICP and ICC-dm. The more medial lamina in ICC-dm and the more lateral lamina in ICP represent the higher frequency place injections in AI. These results again demonstrate the form of the projection from an isofrequency lamina in AI is similar to the form of the projection from a locus in AI.

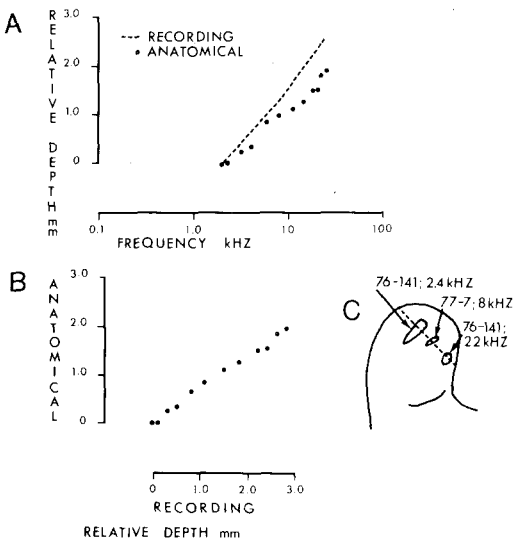


Fig. 5. In this figure, the relative positions of the corticotectal projections in the ICC, as a function of the best frequency positions of the AI injections, are compared with the best frequency-relative position microelectrode recording data obtained from the ICC in the study of Merzenich and Reid ('74). In A) the relative depths of the projections in the ICC are plotted (solid dots) against the best frequency determinations of the cortical injection sites. The relative depths of best frequency determinations from recordings in the ICC are also plotted on the graph (dashed line). These two plots are similar, indicating that the topographic (cochleotopic) order of the projection is in relative register with the cochleotopic organization of the ICC. In B) the relative depths of the anatomical and recording data are plotted against one another. If the two sets of data were exact, they would fall along a line of a 45° angle. Instead, the data points form a straight line that indicates a 30% greater depth for the recording data with each comparison. The proportional variation is consistent with a proportional shrinkage of the tissue during fixation. C) indicates three examples of how the 12 anatomical data points were obtained. The projections to ICC-dm from the same levels in IC were superimposed. Measurements were made from a line approximately perpendicular to the projection laminae. The measurements were made referenced to the lowest frequency place projection from AI.

were longer when viewed in the frontal plane (see Figs. 2, 3). This result is consistent with the suggestion that a larger volume of the dorsomedial division is committed to the representation of the lower frequency regions of the cochlea (FitzPatrick, '75). However, it must be emphasized that injections at all places in the cochleotopic representation of AI produced labeling in the dorsomedial aspect of the central nucleus (presumably, but not unequivocally, restricted to ICC-dm). This finding is consistent with the interpretation that there

is a complete or nearly complete representation of the cochlea within ICC-dm.

A comparison was made between the locations of the ICC-dm label arrays resulting from injections of tracer at several different positions in the cochleotopic representation in AI and the cochleotopic organization of the ICC (Merzenich and Reid, '74). The relative positions of the sheetlike terminal arrays of the cortical projections onto the ICC for 12 different frequency-site locations in the tonotopic map in AI have been plotted as a function of relative depth in Figure 5. To derive these values, each projection was photographed at the same level in the ipsilateral inferior colliculus (at approximately the junction of the middle and caudal thirds), and a tracing was made of the inferior colliculus and the projection. These tracings were combined onto one IC as shown in the inset of Figure 5 for three of these experiments. The distances between the centers of these parallel laminar projections and the center of the lowest best frequency place projection (2 kHz) were measured along an axis approximately perpendicular to the laminae (the dotted line in the inset). The axis of the microelectrode penetrations in the experiments of Merzenich and Reid ('74) were also approximately perpendicular to the isofrequency contours of the ICC.

On the graph in A of Figure 5, the ICC relative depth vs. best frequency recording data of Merzenich and Reid ('74) is represented by the dashed line. The dots represent the relative depth of the autoradiographically labeled terminal arrays in the ICC, plotted as a function of the best frequency representational sites of the tracer injections in AI. This graph shows that the topographic organization of the AI terminal projection laminae in the ICC is very similar to the cochleotopic organization of the isofrequency contours within the ICC. However, the anatomical points consistently fall on the short side in terms of relative depth in the ICC when compared to the depth of the homotypic best frequency determinations in the ICC.

In the graph in B of Figure 5, the relative anatomical depths of the projections in the ICC have been plotted against the relative depths of the ICC recording data for homotypic best frequencies in AI and the ICC. The fact that this plot is roughly linear demonstrates that the two sets of data vary in a proportional fashion, with the anatomical projection depths being about 30% less at all frequencies. This proportional compression is consistent with

the interpretation that the variation is due to a proportional shrinkage of the tissue, resulting from perfusion fixation, staining, and the additional processing of the tissue required for autoradiography (Bleier, '61; Karten and Hodoss, '67). Thus, the cochleotopic organization of the ICC and the cochleotopic organization of the AI projection onto the ICC appear to be in register along the axis perpendicular to the isofrequency contours.

Fiber projection of AII onto the tectum

Long survival experiments demonstrated that the corticotectal fibers from AII follow a path similar to those from AI. Fibers pass caudal to the MGB in the brachium of the inferior colliculus. Labeled fibers were scattered diffusely throughout the brachium. There was very light label over the nucleus of the brachium of the inferior colliculus.

At the rostral pole of the inferior colliculus, fibers passed dorsomedially from the brachium. Some entered the collicular commissure and coursed into the contralateral inferior colliculus. In the contralateral IC, these fibers ended in a terminal field just medial and dorsal to the ICC.

However, the bulk of the medially directed fibers passed caudally, in the ipsilateral IC, dorsal and medial to the ICC. This medial projection produced terminal field labeling along most of the rostrocaudal extent of the IC, with this label being heaviest caudally.

The remaining lateral labeled fibers of the ipsilateral IC passed caudally into a continuous terminal field in the lateral and posterior aspects of the ICP. In long survival experiments, some labeled fibers were seen coursing ventrally in the ipsilateral ICX, but no autoradiographically labeled terminal fields were apparent in this region. These labeled fibers continued ventrally into the ipsilateral tectopontine tract and distributed restricted terminal fields to the same ipsilateral pontine nuclei as the AI projection. No label was seen in the ipsilateral ICC or within the contralateral ICC, ICX, or BIC.

Distribution of terminal fields in the IC after AII injections

After single injections of 3H-l-leucine into AII, three sheets of terminal label were seen passing rostrocaudally in the IC. Two sheets were located in the ipsilateral IC: one was located medially and the other laterally (see Fig. 6). A third corresponding medial sheet

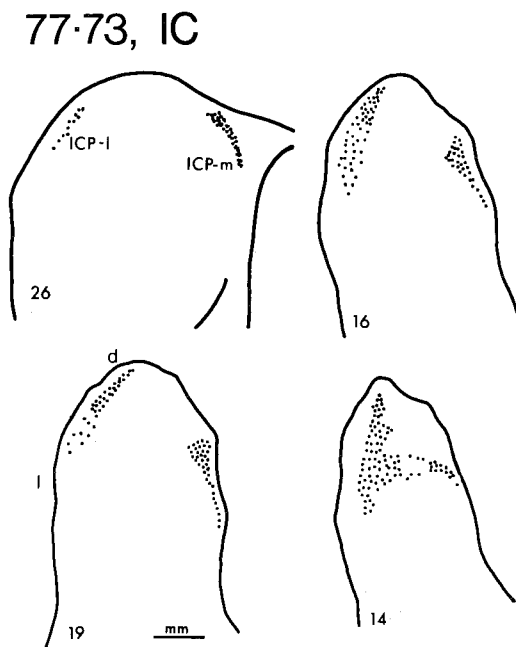


Fig. 6. A representative example of the projection of AII loci onto the IC. In this experiment, an injection of $0.25 \mu\text{l}$ of 3H-l-leucine was made into AII 2 mm from the AI-AII border. Sections are numbered caudal to rostral in 120 μ steps; the caudal pole of the IC begins at section 12. Survival time was 8 days.

was located in the contralateral inferior colliculus.

The ipsilateral and contralateral medial label arrays were most frequently in the form of thin and sometimes irregular sheets located adjacent to the dorsomedial edge of the ICC (see Fig. 6). There appeared to be no label in the adjacent ICC, although the exact border of this nucleus was often difficult to define in these Nissl-stained sections. The ipsilateral and contralateral projections were roughly mirror-symmetric; however, the ipsilateral medial sheet was much more heavily labeled than the contralateral one. Again, contralateral labeling was not recorded in several cases. It is difficult to assign this medial sheet of autoradiographic label to a previously described subdivision of the inferior colliculus. The rostral region of the label could be classified as existing over the lateral margins of the "intercommissural nucleus" (Geniec and Morest, '71). However, most of the labeled sheet was caudal to the commissure of the inferior colliculus and caudal to the "intercom-

missural nucleus." The cells in the region over which label was evident appeared to be smaller, more tightly packed, and slightly lighter staining with Nissl stains than were the cells of the adjacent dorsomedial division of the ICC. Rostrally, these neurons formed a thin layer sandwiched between ICC-dm and the periaqueductal gray. Caudally, these neurons appeared as a thin superficial lamina covering the dorsomedial surface of the ICC-dm and bordering the fourth ventricle. This cell region was continuous dorsally with the dorsal aspect of the ICP and was in a region that is sometimes included in the definition of the ICP (see Rockel and Jones, '73a,b). In this study, this region of label will therefore be called the medial part of the pericentral nucleus of the inferior colliculus (ICP-m). The ipsilateral lateral sheet of the label was located, then, in the lateral part of the ICP (ICP-l) (see Fig. 6). This is the same region which was labeled after AI injections, although the labeling appeared to cover larger areas of this part of the nucleus after AII injections of equivalent size.

In the posterior pole of the IC, the sheet of label in ICP-l of the ipsilateral IC often had a nearly vertical orientation. At this caudal level, the label in ICP-m commonly arched across the dorsal surface of the ICC and merged with the ICP-l component of label (see Fig. 6, sec. 14). Caudal to the ICC, where frontal sections only contained the ICP, terminal label and labeled fibers were seen scattered throughout the ICP. The intensity of labeling in the IC after AII injections was always weaker than after AI injections.

AAF corticotectal projections

Injections of anterograde tracer into AAF produced a pattern of label in the inferior colliculus that was similar to that produced with AI injections, except that the AAF projection was much weaker than the AI projection. In fact, of 11 injection cases in AAF which produced a prominent pattern of labeling in the MGB typical of AAF injections, only four of these cases resulted in labeling in the IC.

In two experiments, two injections of tracer were placed at cochleotopically dissimilar positions in AAF. In both cases, these injections resulted in two laminae of label in the ipsilateral ICC-dm. The laminae were in approximately the same positions in ICC-dm that would have been occupied by label had the injections been placed instead in cochleotopically homotypic regions of AI.

No projections to the superior colliculus from AI, AII, or AAF

In 36 experiments, the entire rostral to caudal extent of the superior colliculus was examined for autoradiographic labeling after injections of tritiated amino acids into the auditory cortex. In all, 16 experiments involved AI injections, 10 involved AII injections, and 11 involved AAF injections. In these 36 cases (including five long survival experiments), no apparent terminal labeling was ever seen in the superior colliculus. This apparent lack of a projection from AI, AAF, or AII onto the superior colliculus was a surprising result, since auditory responses are commonly recorded in the deeper layers of the superior colliculus and are often assumed to be a result of a convergence of visual and auditory corticotectal projections. Of course, other auditory cortical fields (not investigated in these experiments) may project onto the superior colliculus.

DISCUSSION

The corticotectal projections from AI loci terminate in the inferior colliculus in the form of distinct sheets of terminals in the dorsomedial division of the central nucleus and in the pericentral nucleus (see Fig. 7). Although there was autoradiographic label in the region of the external nucleus, it appeared to be only of fibers passing through the nucleus. Only the projection to the ICC-dm is bilateral, and it is less intense (and indeed not always evident) on the contralateral side.

Injections into AII produced a sheet of label in the lateral region of the ICP and a second thin sheet of label in the medial aspect of ICP. Whereas the lateral label was definitely of the appearance equated with terminal fields, the medial labeling may have been of fibers passing to the posterior surface of the ICP. No label appeared to be present in the central nucleus after AII injections. Only the labeling in the medial aspect of the ICP was bilateral.

Injections into AAF rarely produced labeling in the IC. When labeling did occur, it was of the same basic pattern as seen after AI injections, although much lighter. It is possible that this labeling is a result of transsynaptic transport from the ipsilateral AI, as it has been shown that AAF projects in a restricted fashion to cochleotopically homotypic locations in AI (Imig and Reale '77). In any case, the projection from AI to the inferior colliculus appears to be the strongest of the corticotectal projections defined using these methods.

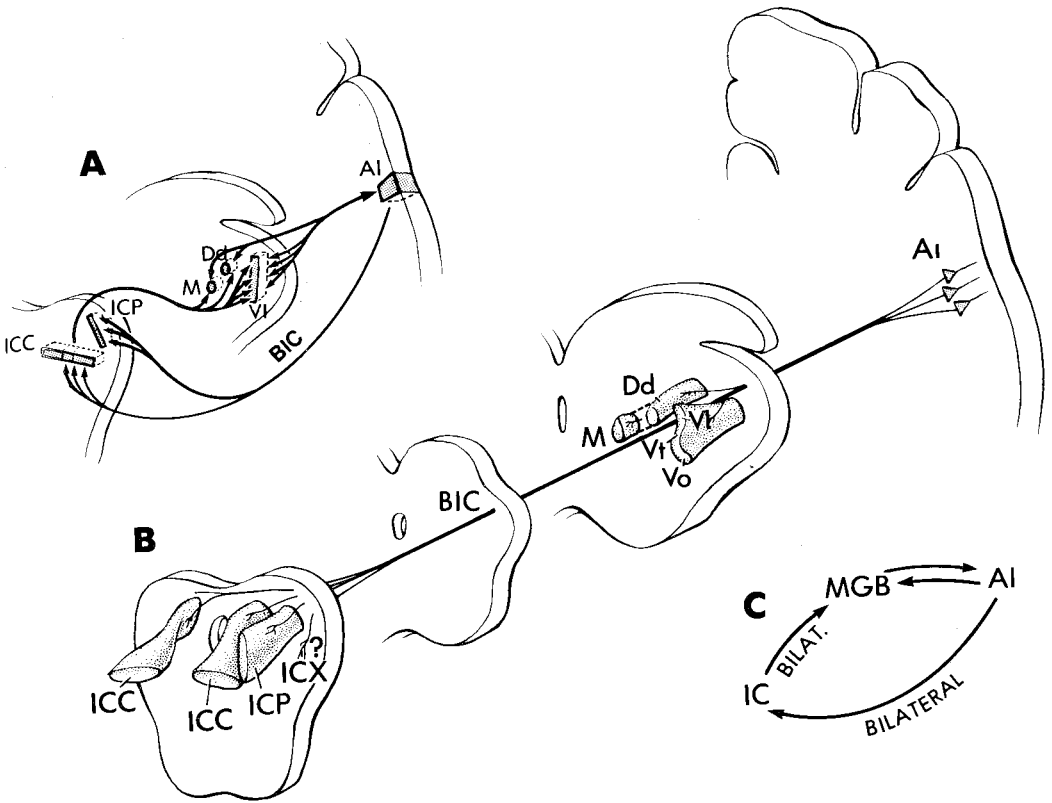


Fig. 7. A schematic representation of the connections between the IC, MGB, and AI. A) indicates that a locus in the ICC diverges to the medial (M), deep dorsal (Dd), and ventral (pars lateralis, VI) divisions of the MGB. A cochleotopically homotypic locus in AI has the same overlapping pattern of connections, both corticothalamic and thalamocortical, with the MGB. AI also projects to the dorsomedial aspect of the ICC along a presumably cochleotopically homotypic isofrequency contour subtending the ICC and a presumably cochleotopically homotypic isofrequency contour in ICP. B) represents the three dimensional form of the projection of a locus in AI onto the IC and MGB. The projection onto the IC is in the form of sheets of terminals in ICC-dm (ICC) and ICP. The projection onto the MGB is in the form of a column of terminals extending through Dd and M, and a sheet of terminals extending through the ventral division. This sheet is folded caudally and includes pars lateralis (VI), pars ovoidea (Vo), and the "transitional zone" (Vt). This pattern of the labeled terminals is the same as the pattern of neurons in the MGB that project onto the same cortical locus. C) shows the very gross pattern of connections between the IC, MGB, and AI. The MGB receives bilateral projections from the IC and is reciprocally connected to the ipsilateral AI. AI projects bilaterally to the IC, and the IC is thus indirectly, reciprocally connected to AI through its connections with the MGB.

Relation to previous studies

The corticotectal projection has been previously studied in the cat by tracing anterograde degeneration following lesions in the auditory cortex (Massopust and Ordy, '62; Rasmussen, '64; Kusama et al., '66; Diamond et al., '69; Rockel and Jones, '73a; Cooper and Young, '76). Generally, these lesions included several auditory fields. The pattern of projection that was consistently reported was similar to the composite of the patterns of AI (or AAF) and

AII projections reported here. The corticotectal projection was reported to be bilateral (Rasmussen, '64; Kusama et al., '66; Diamond et al., '69; Rockel and Jones, '73a; Cooper and Young, '76). Ipsilaterally, degeneration was noted in regions that correspond to the ICP, ICC-dm, and ICX (Massopust and Ordy, '62; Kusama et al., '66; Van Noort, '69; Diamond et al., '69; Rockel and Jones, '73a; Cooper and Young, '76). However, there is some question as to the certainty of the degeneration in ICX being of terminal fields (Diamond et al., '69).

A projection to the contralateral ICC-dm was also reported and noted to be less intense than the ipsilateral projection (Rockel and Jones, '73a).

More restricted lesions were also made in some of these studies. Small lesions, presumably within AI, produced bilateral degeneration in the ICC-dm that was quite restricted (Rockel and Jones, '73a). Diamond et al. ('69) reported that AI lesions produced laminar degeneration in the ICC-dm with fibers oriented in rows coursing dorsomedially to ventrolaterally. Lesions to the insular-temporal region produced a pattern of degeneration in the IC similar to the AII pattern of projection seen in the present study. Thus, in terms of the subdivisions of the ICC which receive projections from the auditory cortex, the data reported here are consistent with these previous, but less specific, degeneration studies.

No apparent inferior colliculus to cortex projections

The HRP injections into AI, AII, and AAF never produced HRP labeled cells in the inferior colliculus. Although it is not entirely satisfactory to argue from the basis of this negative evidence, these findings suggest that there are no direct projections from the inferior colliculus to these auditory cortical fields.

There also may not be a geniculotectal projection. It is of interest that the corticotectal fibers reach the inferior colliculus by passing through the medial geniculate body. Ades ('41), using the Marchi method, made lesions of the MGB and noted degenerating fibers entering the inferior colliculus. Van Noort ('69) also made lesions of the MGB and reported anterograde degeneration in the IC that was of the same pattern as resulted from cortical lesions. However, the lesions in these studies may have interrupted the corticotectal fibers passing through the MGB. In recent experiments, HRP injections made in the ICC did not produce HRP-labeled cells in the MGB, although lower brainstem auditory nuclei projecting to the IC were always labeled (Roth et al., '78; Andersen et al., '80b).

The major connections between the inferior colliculus, medial geniculate body, and the three auditory cortical fields AI, AII, and AAF appear to be the following: 1) a bilateral projection from the inferior colliculus onto the medial geniculate (Woollard and Harpman, '40; Moore and Goldberg, '63; Powell and Hatton, '69; Van Noort, '69; Jones and Powell, '71; Kudo and Niimi, '78; and Andersen et al., '78);

2) reciprocal ipsilateral only connections between the medial geniculate and AI, AII, and AAF (Colwell and Merzenich, '80; Andersen et al., '80a); and 3) bilateral projections from AI, AII, and probably AAF back onto the inferior colliculus (see Fig. 7).

Cochleotopic organization of connections

There were systematic topographies in the projections from AI (and apparently AAF) onto the dorsomedial division of the ICC and from AI to ICP. The topographic arrangements of these projections were consistent with a cochleotopic organization of the connections. These results, taken in conjunction with the results of tectothalamic and thalamocortical tracing studies (Andersen et al., '78; Colwell and Merzenich, '80; Andersen et al., '80a) indicate that a cochleotopic order of connections is maintained throughout the IC-MGB-AI-IC loop (see Fig. 7a).

Divergent form of the projections

The three dimensional sheet form of the terminal arrays of the corticotectal projections from loci in the auditory cortex is of special interest (see Fig. 7). There are locus-to-sheet projections from AI (and presumably AAF, if the labeling after AAF injections is not transynaptic) onto ICC-dm, and locus-to-sheet projections from AI, AII, and presumably AAF onto the ICP. The orientation of the ICC sheets parallels that of the "isofrequency contours" of the ICC (Merzenich and Reid, '74), which clearly extend through both the ventrolateral and dorsomedial divisions of the nucleus. That these corticocollicular projections are only to the dorsal aspects of these sheets and not to their ventral aspects implies that there is a functional segregation along these isofrequency contours in the ICC. The isofrequency contours of the ICC have been shown to be approximately of the same orientation, in three dimensions, as the laminar structure of the cell processes within the ventrolateral division of the ICC (Morest, '64; Rockel and Jones, '73a; Merzenich and Reid, '74; FitzPatrick, '75). Since the sheets of corticotectal terminals restricted to ICC-dm are apparently in register with the three dimensional cochleotopic organization in the ICC, these terminal arrays are probably continuous with the clearly defined morphological laminae in ICC-vl.

The locus-to-sheet divergence from AI to ICP also appears to be of proper orientation and topography to be in register with the described cochleotopic organization in ICP

(Rose et al., '63; Merzenich and Reid, '74; Aitkin et al., '75). Although three dimensional recording maps have not been made in the ICP, it is quite probable that the sheets of terminals also coincide with isofrequency contours within the structure.

Convergent structure of the projections

Similar best frequencies are represented along radially aligned slabs in AI (Merzenich et al., '75). Multiple injections along an isofrequency contour in AI produced the same pattern of label in the inferior colliculus as a single injection. Thus, each sector of an isofrequency contour in AI appears to project onto an isofrequency contour in ICC-dm and ICP. Therefore, each locus in ICC-dm or ICP receives a convergent input from a corresponding line of neurons located along a homotypic isofrequency contour in AI. This line of cells probably resides in layer 5 of cortex (see Ravizza et al., '76). Besides this intranuclear convergence, there also appears to be an internuclear convergence. If the light label in ICC-dm after AAF injections is not due to transsynaptic transport, then AI and AAF both converge in their projections onto homotypic isofrequency contours in ICC-dm. Also, AI, AII, and presumably AAF converge in their projections onto the lateral and posterior aspects of ICP.

Descending control

At present, little is known about the function of the descending cortical projection (see Ramon y Cajal, '55; Desmedt, '60; Rasmussen, '64; Howe and Harrison, '74). Electrical stimulation of auditory cortex reduced or abolished auditory-evoked potentials in the IC (Massopust and Ordy, '62; Amato et al., '70). This result suggests that the corticotectal projection is inhibitory. On the other hand, the corticotectal (Rockel and Jones, '73c) terminals form asymmetrical synapses and have spherical synaptic vesicles, and thus, may have an initially excitatory action. However, it is difficult from these data to assess the actual physiological action of these descending pathways, given the difficulties in interpretation of population responses (evoked potentials) and the reservations of inferring function from the morphology of synapses.

In summary, the most important finding of this study is that there exists a topographic and apparently cochleotopic organization of projection from AI cortex into the dorsomedial aspect of the the central nucleus of the inferior

colliculus and the pericentral nucleus of the inferior colliculus. Single loci in AI project as terminal sheets in these IC structures, and these sheets of terminals quite likely conform to homotypic isofrequency contours within the inferior colliculus. AI injections produced the strongest autoradiographic labeling in the inferior colliculus. Injections into AAF produced a similar but lighter pattern of labeling than that seen after AI injections. AII injections produced a diffuse pattern of labeling restricted predominantly to the pericentral nucleus.

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NOTE ADDED IN PROOF

The pericentral nucleus of the inferior colliculus as defined by this study corresponds to the first and second layers of the dorsal cortex of Morest, and the dorsomedial division of the central nucleus corresponds to the third and fourth layers of the dorsal cortex (Morest; personal communication). Each lamina of labeled terminals in the dorsomedial division resulting from single AI injections extends across both layers three and four of Morest's dorsal cortex of the inferior colliculus.

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