Chapter 2

Auditory Forebrain Organization

Thalamocortical and Corticothalamic Connections in the Cat

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1. Introduction

Studies conducted over the past five years have led (1) to a redefinition of the boundaries of auditory cortical fields in cats; (2) to a new understanding of the geometry and sources of input to given cortical fields; and (3) to a much more topographically refined definition of the destinations of projections originating in given auditory cortical fields. This new understanding of auditory thalamocortical and corticothalamic organization has been derived from

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unit mapping studies and from results of combined (anterograde and retrograde) tracer injections in a physiological-anatomical study during which injections of tracer materials were introduced at functionally defined auditory field sites.

1.1. Redefinition of Auditory Cortical Fields in the Cat

Before discussing auditory thalamocortical and corticothalamic connections in the cat, it is necessary briefly to review our current understanding of the basic organization of auditory cortical fields and of medial geniculate body subdivisions. Microelectrode unit mapping studies have led to a picture of auditory field boundaries illustrated in Fig. 2.1. (1, 3, 14, 15) (also see Imig et al., chapter 1 this volume). Physiological mapping results were in general consistent with earlier results of Woolsey and colleagues (30–33). Boundaries of fields are drawn somewhat differently, with the appreciation in these unit mapping studies that there are reversals (not discontinuities) in representational sequences across all borders of adjoining topographic fields.

1.2. Internal Organization of Auditory Cortical Fields

We now recognize that there are at least four large "cochleotopic" (or "tonotopic") auditory cortical fields in cats, with a large region ventral to A I having no evident topography. This conclusion was predated by a similar conclusion in earlier studies using evoked response techniques (30–33). Within all identified topographically organized fields, there is a rerepresentation of the cochlear sensory epithelium across one field dimension (13, 14, 17, 18; also see Imig et al., chapter 1, this volume; see Figs. 2.1, 2.2). This pattern of organization was earlier described in detail for A I and a more anterior field, by Tunturi in the dog (27, 28). It was also manifested by the banded patterns of arrays of evoked response within A I, recorded by Woolsey and Walzl (33).

Imig and colleagues (5, 11, 12) provided initial evidence that this isorepresentational axis of A I is divisible into binaural subunits (which they called "binaural columns"), within which column-specific binaural neural response properties are recorded. Recent studies in this laboratory (19) along with anatomical–physiological studies of Brugge and Imig (5) have indicated that these "columns" in the higher frequency aspect of A I are actually bands, extending across A I roughly orthogonal to the axis of representation of frequency, and that there are bands in alternating
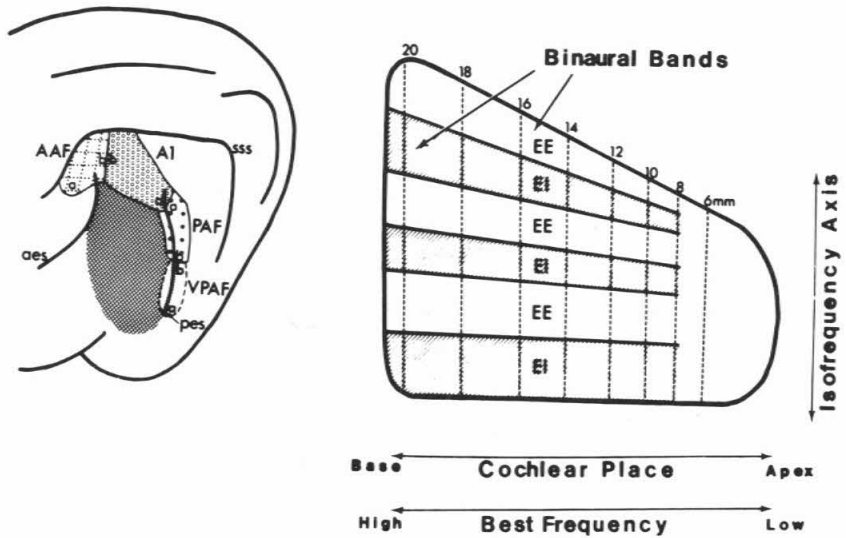
Cat Auditory Fields Internal Organization of A1

FIG. 2.1. Left: Cat auditory cortical fields (after Merzenich et al., 15). AAF = anterior auditory field; A I = primary auditory field; PAF = posterior auditory field; VPAF = ventral posterior auditory field. These four fields are strictly cochleotopically (tonotopically) organized (also see Imig et al., Chapter 1, this volume), with reversals in representation across the cochlear base (b) along the AAF–A I and PAF–VPAF boundaries, and across the cochlear apex (a) along the A I–PAF border. The cross-hatched region is an auditory responsive zone in which no cochleotopic order has yet been defined. Aes, anterior ectosylvian sulcus; pes, posterior ectosylvian sulcus; sss, suprasylvian sulcus.

Right: Schematic illustration of the internal organization of A I. See text for description. Numbers represent cochlear isorepresentational lines (mm from apex). Redrawn from Merzenich et al. (15).

sequence, in which neurons have predominantly excitatory– excitatory (EE) response properties (driven responses to simultaneous stimulation of two ears are greater than those to either ear alone) and, in the alternate bands, excitatory–inhibitory (EI) response properties (stimulation of one ear drives the neuron, while the other ear inhibits the driven responses) (5, 19). There is growing evidence (in studies now underway in our laboratory) for band-specific differences in neural response properties in alert cats. It appears that these A I subunits of like sign (EI or EE "bands") have different (possibly different individual) functional significance and may represent end-processing regions for parallel subdivisions of the auditory projection system of the cat (16, 19).
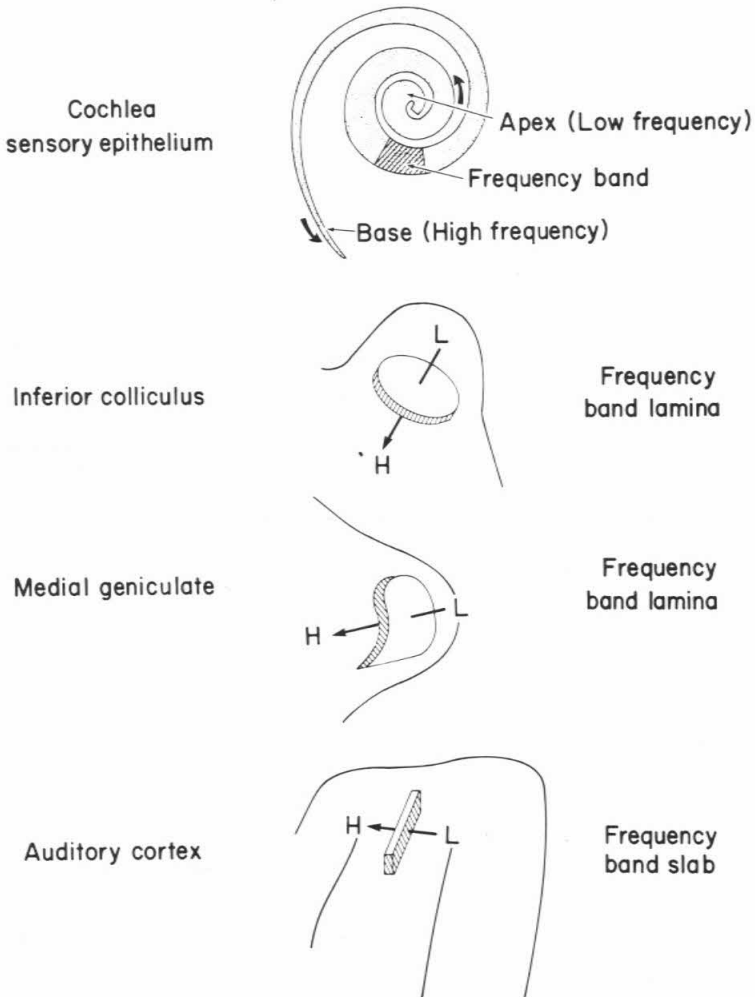
FIG. 2.2 Representation of the cochlear sensory epithelium within "main line" auditory nuclei and cortical fields. Any sector of the cochlea is represented across a relatively flat sheet of neurons that extends across the central nucleus of the inferior colliculus from edge to edge; across a folded sheet of neurons in the lateral part of the ventral division of the MGB; and across a roughly straight slab of neurons within A I (as well as in AAF, PAF, and VPAF). Representationally, there is a rerepresentation of any given cochlear locus across one dimension of A I, and across two dimensions of the central nucleus of the inferior colliculus and lateral ventral MGB. A representational dimension is lost via convergence from MGB neuronal sheets to A I isofrequency (isorepresentational) lines (see 14–16, 18).

1.3 Internal Organization of the Medial Geniculate Body (MGB)

Anatomical results described later are most consistent with definition of MGB subdivisions defined in Golgi studies of the nucleus (20, 21, 24), although they are not consistent in all respects with the details of descriptions of those studies. In subsequent descriptions, the terminology of Morest (20, 21) will be used in describing MGB organization.

2. Basic Approach

The goal of these studies was to define the arrays of thalamic neurons, in three dimensions, projecting to restricted A I loci. Also of interest was the relationship of the projecting neuronal arrays to the patterns of terminals of the descending corticothalamic projections.

Brief physiological mapping studies were conducted to define the approximate locations within A I at which combined injections of anterograde and retrograde tracer were introduced. In these physiological experiments, (a) the approximate boundaries of A I were defined, (b) the orientation of the isorepresentational frequency axes of A I were determined and (c) the "best" frequency positions were identified for single or multiple locus injection sites. Generally, in the multiple injection experiments, a second injection was made either at another location along the same "isofrequency contour" or at a different "best frequency" representational location in the same auditory field.

After 24–40 hour survival periods, animals were perfused with paraformaldehyde and the brains were processed using standard histochemical (DAB) and autoradiographic techniques. These procedures are described in detail in other reports from this laboratory (1–4, 7–8).

3. Summary of Results

3.1. Geometry of Arrays of Neurons Projecting from the MGB to A I

Arrays of neurons projecting from MGB subdivisions to restricted A I loci are illustrated by example in Figs. 2.3, 2.4. With a moderate sized injection (Fig. 2.3), the array constituted a continuous neuronal sheet that bisected the lateral part of the ventral nucleus,
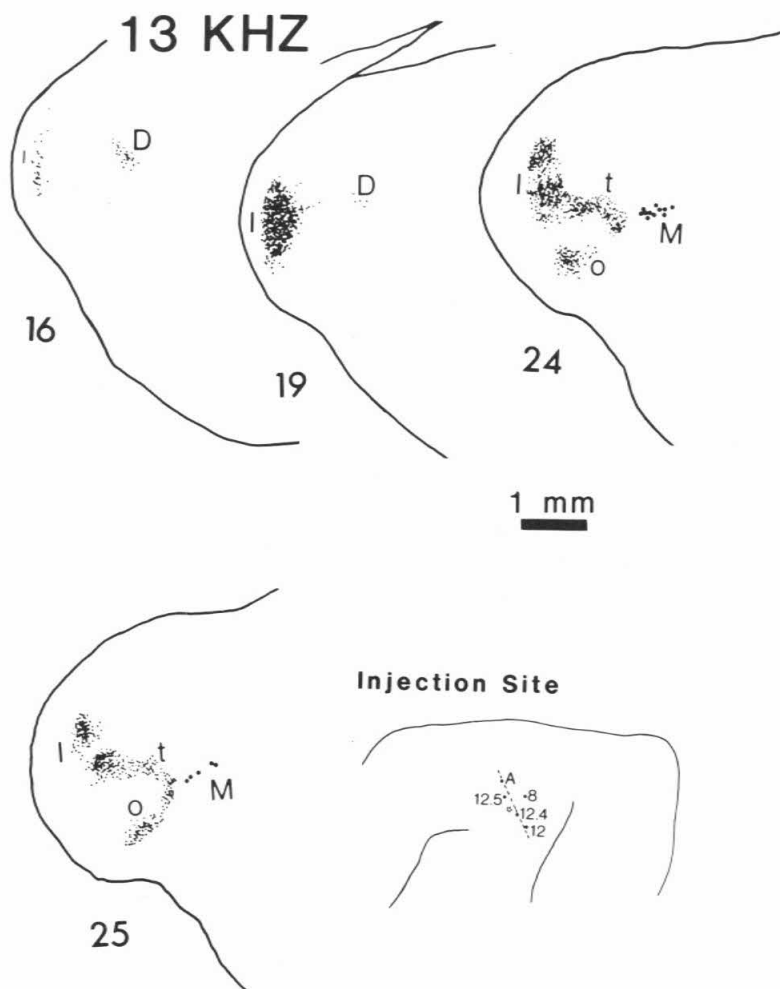
FIG. 2.3. Drawings of sections through the MGB in a cat, illustrating the geometric figure of the complex neuronal array that projects to a 13 kHz representational (horseradish peroxidase injection) site within A I. The HRP injection site is illustrated diagramatically at the lower right. These numbers represent best frequencies defined for neurons within penetrations normal to indicated sites. The approximate isorepresentational axis is indicated by the dashed line. This 0.2 μL injection (and all other illustrated injections) was wholly restricted within A I. Note the complex sheetlike folded array in the lateral (1), transitional (t) and ovoidal (o) parts of the ventral division, as well a projecting column of neurons within the deep part of the dorsal division (D) and a projecting cluster of neurons within the medial division (M). Numbered sections (S) were 150 μm apart. The deep dorsal array extended well rostral to S 16; the ovoidal–lateral arrays in the ventral division extended more than 450 μm caudal to S 25. Note the broken appearance of the array (banded, in three dimensions) in S.24 and 25.
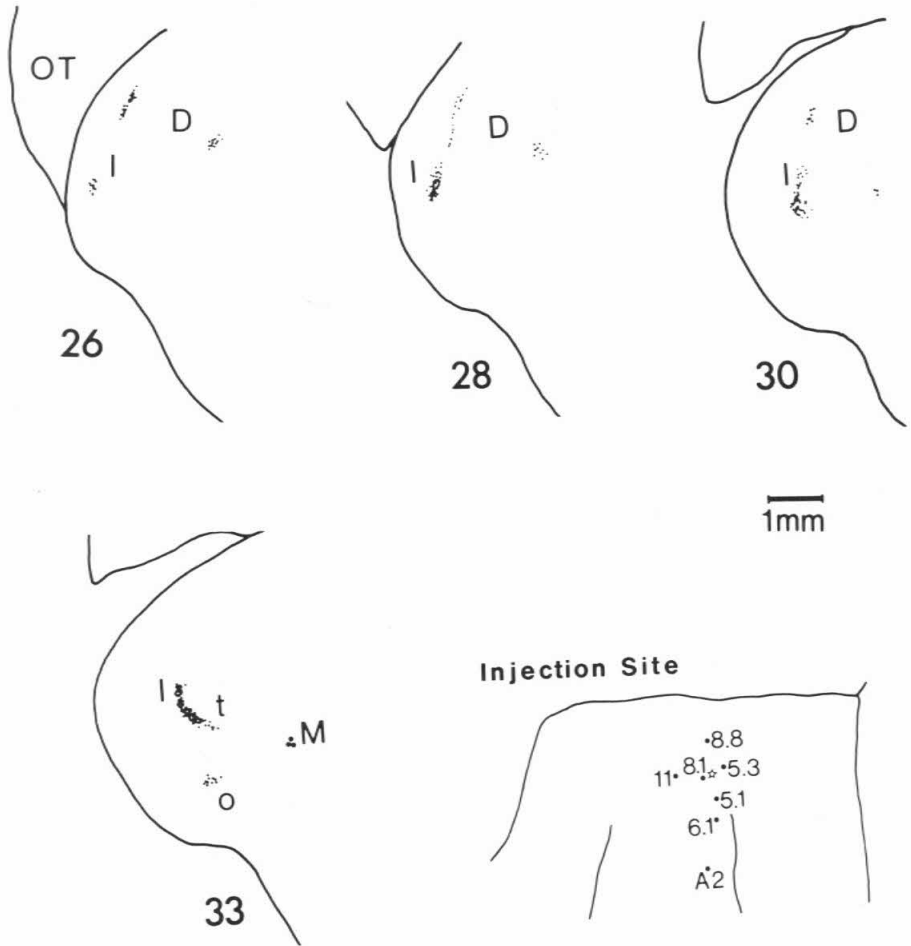
7.5 KHZ

FIG. 2.4. Array of neurons projecting to a 7.5 kHz representational locus (0.1 µl HRP injection, at the site illustrated at lower right). Note the broken (two-column) array in the lateral part of the ventral division (Ss. 26–28) and the restriction of labeled neurons within a very narrow MGB band. Abbreviations and descriptions as in Fig. 2.3. OT, optic tract. Section 26 is most rostral.

from edge to edge, folded medialward into the transitional part of the lateral division, then, further posteriorly, folded back outward to form a second usually thinner band bisecting the ovoidal part of the ventral nucleus. A topographically separable cell column is seen within the deep part of the dorsal nucleus, extending rostrally into the lateral part of the posterior group. Finally, there is a distinct
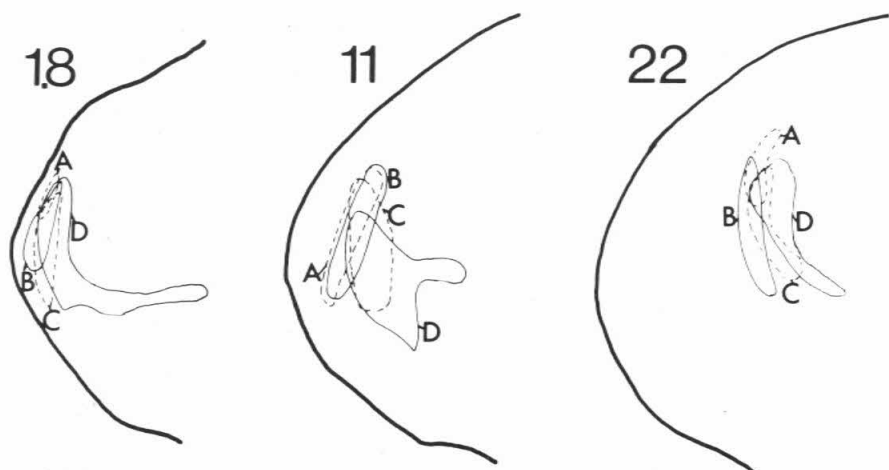
FIG. 2.5. Lines circumscribe all neurons projecting from the lateral ventral MGB at four levels, to 1.8-, 11- and 22-kHz A I representational loci. Section A is at the rostral extreme of the labeled cell array in IV. Section D is at the most rostral level at which the array extends medialward to appose labeled neurons within the medial division. Sections B and C were ⅓rd of the distance and ⅔rds of the distance from A toward D, in all three examples. The lower frequency-destined thalamocortical neurons extended over a somewhat shorter rostrocaudal distance (about 1.2 mm) than did the two higher frequency arrays (which were about 1.5-1.8 mm long) (see ref. 8).

small group of labeled neurons within the medial nucleus of the MGB.

The complexly folded band of labeled cells within the ventral division of the MGB changes systematically as a function of the site of the injection. This shift of array location as a function of A I best frequency locus is illustrated by the outlines of three arrays following injections at different best frequency loci (Fig. 2.5) and by photomicrographs of a double injection (two-frequency) case (Fig. 2.6). Successively lower frequency projection arrays were lateral to and folded within (see Fig. 2.6) the higher best-frequency projection arrays. The lower the best frequency, the shorter the anterioposterior dimension of the array, and the narrower and smaller the proportional size of the ovoidal sector of the array.

The sheet of labeled neurons within the pars ovoideus of the ventral nucleus is flat and not coiled, as might have been expected given the description of a "coiled" cell and axon orientation in this region (20, 21). The arrays in the lateral and transitional sectors of the MGB parallel the axes of Morest's defined cellular and fiber laminae.
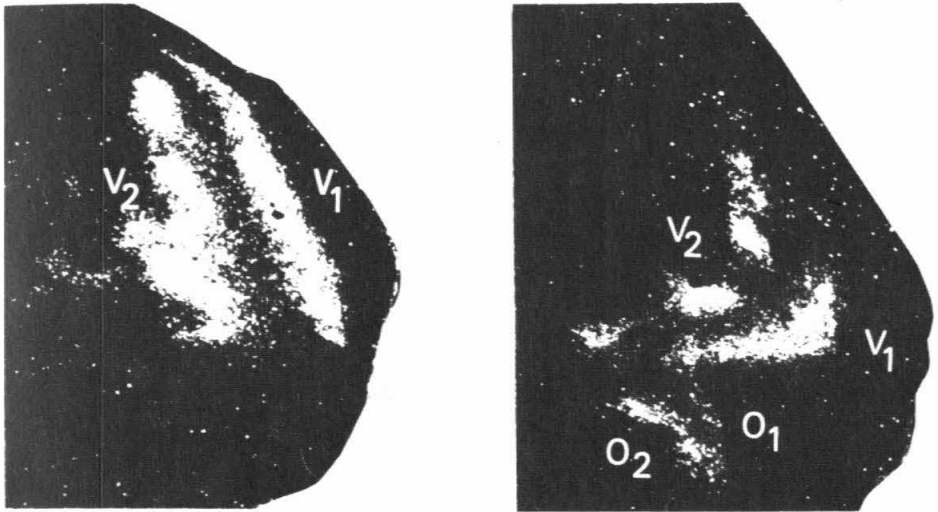
FIG. 2.6. Double array labeled by two small injections into 4.5 and 14 kHz representational loci in A I in an adult cat. The section at the left is from near the middle of the arrays in the lateral part of ventral MGB; the section at the right is from the caudal third of the arrays. The injections in this cat were combined HRP-radioactive leucine cocktails. Photomicrographs are autoradiographs; the HRP-labeled cell distributions very closely paralleled these two corticothalamic arrays (i.e., they closely overlaid projecting neurons; see Colwell and Merzenich, 8). Note the broken distribution of the label for the higher frequency injection (V_2–O_2) with 5 or 6 clear clusters of grains (columns, in three dimensions) evident in the caudal aspect of the projection.

The location of cell columns in the deep dorsal and medial divisions also shifted systematically as a function of the cortical best frequency locus of the injection site. There appears to be a reversal in best-frequency representational sequence across the boundaries between the lateral part of the ventral nucleus and the deep part of the dorsal nucleus, with highest frequencies represented along their mutual border. Another apparent reversal was evident along the border of the lateral transitional and ovoidal parts of the ventral division, with lowest frequencies represented on this border [see Colwell and Merzenich (8) for further details].

3.2. Banding of the MGB Ventral Division Projection

With injections that spread across the cortex more than about a millimeter, a *continuous*, folded sheet of projecting neurons was almost invariably observed within the ventral division. However,
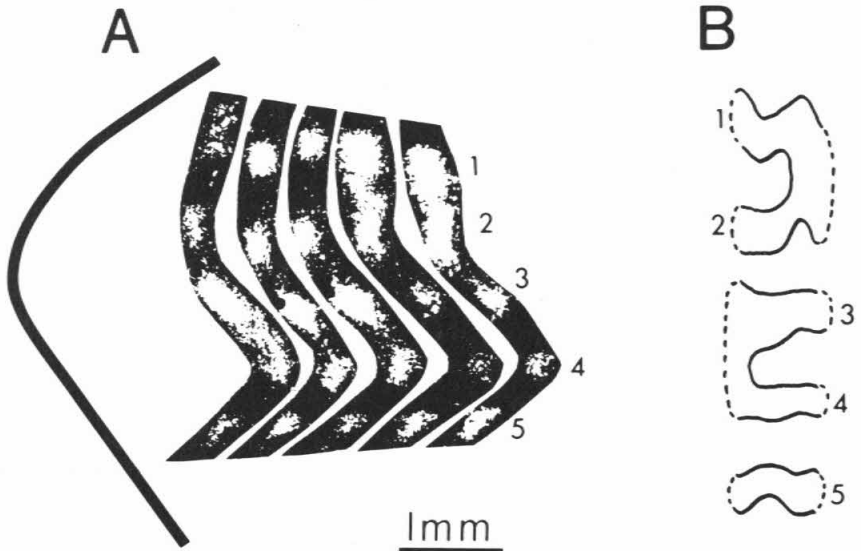
FIG. 2.7. Banding of the corticothalamic array, illustrated by example with another small-injection case into higher frequency A I. In the caudal aspect of the array, five clear bands of grains are evident, extending over about a 1 mm region. The broken label from five adjacent sections through this zone are shown apposed in the reconstruction at the left (A). This sector of the corticothalamic array is reconstructed to scale (from a lateral view) in B. These stubby bands were evident in all smaller injection higher-frequency A I representational site studies, in both corticothalamic terminal and thalamocortical neuronal arrays (see Figs. 2.3, 2.4, 2.6 for other examples). With larger injections, corticothalamic and thalamic arrays in the lateral–transitional parts of the ventral nucleus were usually continuous. Adapted from Andersen (1).

with smaller injections (especially at higher best frequency cortical representational loci), *discontinuous, banded* arrays were commonly recorded. An example is illustrated in Fig. 2.7. It is possible that these banded arrays of neurons (and corticothalamic terminals) represent a segregation of thalamic projections to the "binaural bands" of A I. That is, "binaural bands" might also exist within the ventral division of the MGB. This banding in the ventral division is further manifested by results of tracer injection studies in the ICC, in which restricted injections resulted in banded terminal arrays in the efferent projection to the MGB (2). With small cortical injections introduced at low frequency representational loci, again, the projecting MGB arrays were not discontinuous.

3.3. Descending Corticothalamic Projections from A I to the MGB.

There is a remarkably detailed reciprocal projection from the neurons of each A I locus back into the complex arrays of neurons in the MGB projecting to those loci (8). In fact, given problems in correlating material developed by the two histochemical methods, the pattern details of the two projections are very remarkably similar.

3.4. Interconnections of MGB Nuclei with Other Cortical Fields

Extensive studies of connections of the MGB with another large topographic auditory cortical field in the cat, the anterior field (AAF; see Fig. 2.1), have revealed that it derives its input from the same four principal MGB (IV, OV, M, D) sources as A I. The projection arrays of these two cortical fields also have similar geometric patterns. The principal difference is in the relative numbers of neurons in each subdivision of the MGB that project to each field. AAF receives its strongest projection from the deep dorsal division. (1, 3).

The connections of A II are primarily with nuclei that do not project to A I or AAF (the caudal aspect of the dorsal division, the ventral lateral nucleus and the medial division) (1, 3). These data and studies by other investigators are consistent with the interpretation that there are two largely parallel auditory projection pathways (1, 3; also see 6, 9), projecting to cochleotopically and noncochleotopically organized regions of auditory cortex in the cat.

4. Conclusions

The results of these studies are basically consistent with those of other investigators (esp. 10, 22, 23, 25, 26, 29) using techniques not involving false label through damage to fibers of passage, i.e., with results of studies, in which injections or lesions were in A I. Differences in interpretation of the MGB sources of neurons projecting to different cortical fields are believed to result from differences in the definition of (or in failure to define) the actual locations and boundaries of auditory cortical fields in those other studies.

The locations and boundaries of these relatively small cortical fields are inconstant (17, 18), largely because the dorsomedial ter-

mination zones of the anterior and posterior ectosylvian sulci are highly variable. Thus, physiological or cytoarchitectonic definition of injection or lesion sites (the latter is very difficult) is requisite for straightforward interpretation of such studies.

From these experimental data, the following basic conclusions about the organization of interconnections of the auditory cortex and thalamus can be drawn:

1. Complex arrays of neurons extending across four MGB subdivisions project to restricted A I loci. There is a remarkable convergence in the MGB-A I projection, from complex sheets and columns and clusters of MGB neurons to small A I sites.

2. These tracing studies provide evidence for the existence of repeating subunits in cortex, since injections in which tracer spreads over only a fraction of A I result in a continuous sheet of labeled neurons that bisect the nuclei of the MGB (i.e., extends across the nuclei from edge to edge). Thus, the *same* MGB neuronal figure must project to different (repeating) sectors along A I isorepresentational lines. This conclusion is also supported by the observation that a second injection along an isofrequency line does not add dimensionally to the projection array. We might hypothesize that at higher frequency A I representational loci, this repeating subunit is an adjacent pair of EE and EI bands.

3. Results with smaller injections indicate: (a) There is a banded structural organization of the ventral nucleus of the MGB, with the bands oriented orthogonal to isofrequency contours; and (b) that a given A I binaural band receives input from a *series* of MGB ventral nucleus bands. Again, this constitutes a remarkably complex pattern of convergence.

4. MGB "bands" appear to be established via a banded segregation of input from different response-specific sectors of the ICC to the MGB.

5. There is a remarkable reciprocity of connections between A I and MGB subdivisions.

6. MGB interconnections with another topographic cortical field in the cat, the anterior auditory field, are just as complex as with A I. The same four principal nuclear subdivisions (1V, OV, M, D) are reciprocally interconnected with this field.

The basic information processing significance of these complex connections is still unknown and they constitute a great practical problem for auditory neuroscientists. The detailed relationship with (and function of) A I (and MGB) functional subfields, their brain stem and ICC and MGB sources and the sources of different cortical band-specific inputs are all under intensive investigation. These studies are leading to an increasing understanding of the functional organization of the higher levels of this very complexly organized information handling system.

Acknowledgments

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