Patterns of Sensory Intermodality Relationships in the Cerebral Cortex of the Rat

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ABSTRACT

Patterns of connections underlying cross-modality integration were studied by injecting distinguishable, retrograde tracers (Fluoro-Gold and diamidino yellow) in pairwise manner into different sensory representations (visual, somatosensory, and auditory) in the cerebral cortex of the rat.

In agreement with previous single tracer studies, our results indicate that the central core of sensory areas receives projections mainly from a set of association areas located in a ringlike fashion along the margin of the cortical mantle. The visual cortex received projections from areas 48/49, area 29d, posterior agranular medial cortex (AGm), area 11, area 13, and area 35. All these areas were also connected to the auditory cortex with the exception of areas 29d and AGm. However, lateral to area 29d and posterior AGm, a band of neurons projecting to the auditory cortex was present. Somatosensory cortex was connected mainly with the more anterior aspect of the hemisphere, which included primary motor area, area 11, and area 13.

The patterns of intermodality relationships revealed in the present study were of two main categories. In the anterior and lateral areas, an intermingling of cells projecting to different sensory modalities was observed. In contrast, in areas located along the medial aspect of the hemisphere, cells connected to different sensory modality representations tended to be segregated from each other. Postsubicular cortex (areas 48/49) contained both intermingled and segregated groups of cells. The incidence of clearly identified double-labeled cells concurrently projecting to two different sensory representations was extremely rare. These patterns may form a substrate for different levels of cross-modal sensory integration in the rat cortex.

Key words: auditory, somatosensory, visual, connections, association cortex

The integration of different sensory inputs in the brain is a necessary stage before behavior can be executed. However, this aspect of sensory processing is still poorly understood. One approach to the problem in recent years was to identify candidate areas that might subserve cross-modality integration. Several physiological and anatomical studies (e.g., Jones and Powell, '70; Benevento et al., '77; Bruce et al., '81; Pandya and Yeterian, '85; Goldman-Rakic, '88) have suggested such "polysensory" areas in the cerebral cortex of different mammalian species.

In the rat, tract tracing studies have also implicated a number of areas as possible candidates for cross-modality integration by virtue of their connections with different sensory modality representations. Overall, these association areas appear to be arranged in a peripheral ring, which includes most of the limbic cortex and part of the frontal cortex of the rat. Thus on the medial margin of the hemisphere, posterior and anterior cingulate cortices were reported to be connected to the visual cortex, whereas a neighboring band in area 18b contained auditory projections (Vogt and Miller, '83; Miller and Vogt, '84a; Torrealba et al., '84). More anteriorly, the posterior medial part of the agranular medial cortex (AGm) of Donoghue and Wise ('82) was shown to receive projections from visual, somatosensory, and auditory cortices (Miller and Vogt, '84a; Reep et al., '84; Torrealba et al., '84). This area partially overlaps area 8 of Vogt and Miller ('83).

At the frontal pole, area 11 was reported to be connected to the visual cortex (Vogt and Miller, '83; Miller and Vogt, '84a) but connections to other sensory areas were not described. On the lateral side of the hemisphere, the perirhinal areas 13 and 35 (Miller and Vogt, '84a) were found to be connected to visual, auditory, and somatosensory cortices (Deacon et al., '83; Guldin and Markowitsch...
Finally, at the posterior tip of the cortex, connections to visual areas were found with parts of the postsubicular and parasubicular cortices (areas 48 and 49, respectively, Vogt and Miller, '83). However, we were unable to find further information about the connection of these sensory areas with other peripheral areas.

In all these studies, the polysensory potential of these areas was inferred indirectly by pooling results across different cases. Thus it is still not clear whether in areas considered to be polysensory, there is a precise overlap of connections to different sensory representations or whether interdigitation of unisensory columns might exist. Alternatively, in areas considered to be unisensory, is there a sharp transition from one sensory modality to another, or do these areas contain broad overlap zones that might also subserve intermodality integration? Finally, an interesting question pertains to the nature of feedback connections from polysensory areas: Do neurons projecting from such areas remain segregated by modality or do they bifurcate to innervate directly two different sensory areas?

To answer these questions directly, we employed a double-label tracing paradigm, which enabled us to relate, within the same case, the organization of connections of two different sensory areas. Our results show that within the set of the peripheral association areas, two patterns of neuronal labeling were present. In areas located on the medial margin of the hemisphere, the neurons projecting to different unimodal cortical areas occupied separate but neighboring territories. In contrast, in lateral and anterior areas, neurons linked to different unimodal sensory areas were intermingled within the same territory. These different neuronal arrangements may relate to the role of the peripheral areas in cross-modality interactions.

METHODS

The experimental paradigm employed in this study involved injections of two distinguishable tracers into different sensory representations in the cerebral cortex of the rat. This approach enabled exact analysis of the relative distribution of neurons projecting to different targets in the same animal. Below is a detailed description of the methodology employed.

### Abbreviations

| A1 | primary auditory cortex |
| AC | anterior cingulate cortex |
| AGm | agranular medial cortex |
| AP | anterior pretectal nucleus |
| BLA | anterior basolateral amygdaloid nucleus |
| DLG | dorsal lateral geniculate nucleus |
| Ent | entorhinal cortex |
| L | lateral |
| LD | lateral dorsal nucleus |
| LP | lateral posterior nucleus |
| M1 | primary motor cortex |
| MG | medial geniculate nucleus |
| Pir | piriform cortex |
| Po | posterior nuclei group |
| R | rostral |
| S1 | primary somatosensory cortex |
| S2 | secondary somatosensory cortex |
| V1 | primary visual cortex |
| VL | ventral lateral nucleus |
| VPL | ventral posterolateral nucleus |

### Tracer injections

A total of 36 adult hooded rats was used in this study. The rats were anesthetized with Nembutal (40 mg/kg) supplemented with ketamine (Vetalor, doses of 5 mg i.m.). Two separate injections of the fluorescent tracers Fluoro-Gold (FG, Fluorochrome, Englewood, Co., Schmued and Fallon, '86) and diamidino yellow dihydrochloride (DY, Keizer et al., '83) were placed in different sensory areas in the right cortical hemisphere by using stereotactic coordinates. FG was injected iontophotographically through glass pipettes (4% in 0.1 M sodium acetate buffer pH 3.3, 40–70 μm tip diameter) by pulses of 5 μA, 7 sec on 7 sec off, direct current for 15 minutes. DY was pressure injected through a Hamilton syringe attached to a glass pipette (0.1–0.15 μl of 2% DY aqueous solution). After a week of recovery, the rats were reanesthetized and a large flap of bone overlying the left hemisphere was removed, exposing major portions of the parietal and occipital cortices and smaller portions of the fronto and temporal cortices. Twenty-five to 35 injections of horseradish peroxidase (HRP, each injection 0.25–0.35 μl, 10–20% solution) were evenly placed over the exposed cortex for staining of the callous connections (Olavarria and Montero, '84, Malach, '88).

### Histology

Two days after injections of HRP, the rats were deeply anesthetized with 10% chloral hydrate, perfused with a brief wash of 0.1 M phosphate-buffered saline (PBS), followed by 4% paraformaldehyde containing 5% sucrose in PBS solution. Six brains were prepared for coronal sectioning, which included gelatin embedding of the brain and postfixation overnight in a 4% paraformaldehyde solution containing 30% sucrose in phosphate buffer. In the other 30 cases, the right cortex was flattened between two glass slides (Welker and Woolsey, '74; Olavarria and Montero, '84; Malach, '88) and postfixed overnight in 4% paraformaldehyde, 20% sucrose PBS solution. Sections were cut on a freezing microtome at 60 μm for coronal sections, 40 μm for tangential sections of the flattened cortices. Five out of six sections from cases sectioned in the coronal plane were collected for histological and neuroanatomical analysis. This included Nissl stain, acetylcholinesterase (AchE) histochemistry (Geneser-Jensen and Blackstad, '71), myelin stain (Hutcheson and Weber, '83), HRP reaction with tetramethyl benzidine as a chromogen (Mesulam, '78) according to a modified procedure (Malach, '88), and scanning of the fluorescence labeling, which was done on an otherwise unprocessed section.

All tangential sections from the flattened cortices were collected, one out of two sections was kept unprocessed for mapping of fluorescent label. The remaining sections were processed alternately for HRP and Nissl stain. Photographs of coronal and tangential unprocessed sections were taken prior to mounting on Kodak LPD-4 film under brightfield illumination. This procedure reveals myeloarchitectonic patterns in the same sections scanned later for fluorescence (Malach, '89).

Sections were mounted on gelatin-coated slides. Myelin, AchE, and Nissl-stained sections were dehydrated in increasing alcohols, passed through three changes of xylene, and mounted with Permount. HRP stained sections and sections kept for fluorescence scan were rapidly dehydrated in increasing alcohols, passed through xylene, and mounted with Fluoromount.
Data processing

Fluorescent labeling of retrogradely filled cells was viewed with an epifluorescence microscope (Zeiss Universal), with filter setting of 02-UV for FG, 18-blue violet for DY. DY was seen also at 02-UV, but its greenish color and the oval, smooth shape of the labeled nuclei (Keizer et al., '83) were clearly distinguishable from the orange-golden color and starlike granular appearance of the FG labeled cytoplasm and processes (Schmued and Fallon, '86) as can be seen in Figure 7. Double-labeled cells were identified by their golden FG haze, which disappeared under blue violet excitation, surrounding the DY labeled nucleus, which was visible at both wavelengths. Drawings were prepared from coronal sections stained for AchE, Nissl substance, HRP-labeled callosal connections, and myeloarchitecture including vascular landmarks, which served to align the drawings of the patterns of fluorescent-labeled neurons.

To map the distribution of fluorescent-labeled cells, sections were scanned with a computer controlled system. The system consisted of optical rulers attached to the microscope stage, which recorded its x-y coordinates at 1 μm resolution. In addition, a pointer was viewed in the microscope field with the aid of a drawing tube facing a computer screen. By moving the pointer and the microscope stage, the operator could scan the entire section at high power and record the location of fluorescent-labeled cells, as well as vascular and other landmarks, into the computer memory rapidly and accurately. The stored coordinates were translated into a color coded map of the location of the cells in the section. The distribution of fluorescent labeling was subsequently aligned with drawings of cytoarchitectonic and callosal patterns by means of the vascular landmarks.

Definition of cortical areas

Coronal sections. The cortical areas in the coronal sections were delineated according to the Nissl, AchE, myelin stains, and their relation to the pattern of callosal connections. The cytoarchitectonic borders of the visual areas, including the primary visual cortex (V1), area 18a, and area 18b (Krieg, '46b; Miller and Vogt, '84b) were correlated with myelin (Zilles, '85) and AchE stains, as demonstrated in Figure 1, and the pattern of callosal connections (not shown). The borders of the somatosensory cortex (Krieg, '46b; Welker, '71, '76; Welker and Sinha, '72) and the auditory cortex, including the secondary auditory areas (area 22, area 36, area 20), which surround the primary auditory cortex, area A1, (Krieg, '46b; Cipolloni and Peters, '79; Vaughan, '83; Sally and Kelly, ' 88; Roger and Arnault, '89) were distinguished by their cyto- and myeloarchitectonic characteristics. We could not distinguish clearly in our material the borders between area 36 and area 20 (Miller and Vogt, '84a).

Primary motor area (M1) was defined cytoarchitectonically by the appearance of the broad layer V, containing large, dark, Nissl-stained cells. This area corresponds to area AG1 of Donoghue and Wise ('82). More medially, area AGm was easily differentiated from the neighboring areas anterior cingulate (AC) and M1 by its pale band of layer III (Donoghue and Wise, '82). Posterior cingulate cortex (area 29) was subdivided after Vogt and Peters ('81), the lateral border of area 29d was correlated with a sharp drop of myelin and AchE staining (Fig. 1C,D). Anterior and posterior perirhinal areas (areas 13 and area 35) were identified in NiSSL-stained sections by their dense layer II but absence of layer IV (Miller and Vogt, '84a).

Tangential sections. We have constructed a tangential areal map (Fig. 2C) of the flattened cortex, which is based on data obtained from coronal sections, as well as previously published studies on tangential sections. Using myeloarchitecture, as visualized in the photographs of the unmounted sections, cytoarchitecture, and the callosal pattern of connections, we parcelled the flat cortex according to the following criteria. Area V1 and the secondary visual cortex (area 18a and area 18b) were easily identified by the appearance of a dense myelinated zone in area V1 and a slightly lighter zone in area 18a (see Fig. 2A) and by the typical pattern of callosal connections (see Fig. 2B; Olavarria and Van Sluyters, '85; Thomas and Espinoza, '87; Malach, '89). Area A1 appeared as a myelin dense region lateral to area 18a (Fig. 2A; Krieg, '46b). Anterior and medial to area A1 is area 22 (Krieg's area 39, '46b), which borders with secondary somatosensory cortex (S2) and area 18a and consists of a narrow, myelin light strip (Caviness, '75; Olavarria and Van Sluyters, '85).

In the tangential section, primary somatosensory cortex (S1) and area S2 are recognized by their typical myelin dense appearance (Fig. 1A). The border between these two areas was determined according to Nissl stain cytoarchitecture (Welker, '71, '76; Welker and Sinha, '72), and by the lateral callosal band of labeling through which the border passed (Figs. 2B,C; Olavarria et al., '84). The medial border of area S1 was also delineated by bands of dense callosal labeling (Akera and Killackey, '78; Olavarria et al., '84). The borders of the motor areas in the frontal cortex, area M1 and area AGm, were estimated by transforming measured distances from coronal sections, relying on previous parcelation schemes (Donoghue and Wise, '82; Zilles, '85).

As in the coronal sections, the lateral border of the cingulate cortex in tangential sections is defined by a dense myelinization (Fig. 2A,C). We did not attempt to delineate further the subdivisions of area 29 because of the distortion caused by the high curvature of the tissue at this position. The location of the adjacent postsubicular cortex (area 48/49) was estimated according to its position as seen in cortical reconstruction diagrams (Zilles et al., '80; Zilles, '85).

Perirhinal and entorhinal cortices, situated lateral to postsubicular cortex, were positioned according to reconstruction schemes from coronal sections and by using the rhinal fissure as a marker (Miller and Vogt, '84a; Zilles, '85). The anterolateral tip of the tangential section consists of the ventral orbital area (Zilles, '85), designated also area 11 (Caviness, '75; Miller and Vogt, '84a). A myelin dense region that appeared consistently in the location of this area served to mark its border (see Fig. 2A,C).

Determination of the laminar position of a tangential section was based on its relative distance from layer IV, which was conspicuously marked by the “barrels” of the somatosensory cortex (Welker, '76) and high myelination within area 17 (Olavarria and Van Sluyters, '85). These typical patterns could be easily visualized in the sections prior to mounting (Fig. 2).
RESULTS

Classification of injection sites

The rats used in this study were divided into three groups, according to the sensory modalities represented in the areas injected: auditory-visual (Aud-Vis), somatosensory-visual (Som-Vis), and somatosensory-auditory (Som-Aud; see Table 1). Figure 3 depicts the injection sites for each group, as well as the injection sites of cases with only a single injection (Fig. 3C).

We have based the conclusions of this study on the analysis of cases in which each tracer deposit was restricted to a single unimodal region (both primary and secondary sensory areas), verified by analysis of the pattern of thia-
Figure 2
TABLE 1. Location of Injection Sites in Experimental Cases  

<table>
<thead>
<tr>
<th>Plane of Section</th>
<th>Aud-Vis</th>
<th>Som-Vis</th>
<th>Som-Aud</th>
<th>Aud</th>
<th>Som</th>
<th>Vis</th>
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<tr>
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<td>2-2</td>
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<td>4-4</td>
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<td>2-2</td>
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1Additional cases with injections in areas estimated to be connected with the sensory cortices.

Sensory intermodality relationships in rat cortex

The pattern of callosal connections, as viewed in a darkfield photograph taken from an HRP-stained section adjacent to the section shown in A, shows that the pattern of labeling appeared to vary mostly along the tangential plane, we emphasized in this study the analysis of the flattened cortex preparation. Comparison of the different sections from a tangentially sectioned brain (Fig. 5) showed that the pattern of labeling throughout the sections was fairly consistent, although its intensity might have varied. Thus both posterior medial area AGm and area 29 labeling appeared to be more extensive in deeper layers than superficial ones (cf. Fig. 5 section #5 and #13).

A closer examination of the arrangement of labeled cells in the peripheral ring areas revealed two types of connectivity patterns. In the first type neurons projecting to the auditory areas appeared to be intermingled with neurons projecting to visual areas. Areas manifesting such a neural arrangement included area 11 at the frontal pole, area 13, and area 35. The second type was a modality-specific pattern in which neurons projecting to two sensory modalities occupied separate but neighboring territories. In this type of pattern, a minor level of intermingling of neurons projecting to different targets was often evident. Areas of this segregated type included posterior medial area AGm, posterior medial area M1, medial area 18b, and area 29.

In order to verify the reciprocity of connections to sensory cortices, four additional cases received tracer injections in areas identified as projection targets of sensory cortices. In the following sections we present our results while considering each group of cases separately.

Auditory-visual cases

We analyzed both coronally and tangentially sectioned brains of the Aud-Vis experimental cases. A representative coronally sectioned case is depicted in Figure 4. However, the overall pattern of labeling is more clearly seen in the tangentially sectioned cases, as shown in figures 5 and 6. Both auditory and visual cortices appear to be extensively connected with a series of areas arranged in a ringlike manner around the sensory cortex. The auditory cortex is connected to area 11, posterior medial area M1, anterior and medial area 18b, posterior area 13, area 35, and areas 48/49. Injections in visual cortex resulted in labeling within area 11, posterior medial area AGm, posterior areas S1 and S2, area 22, posterior area 13, area 35, and areas 48/49. In area 29 a band of labeled cells was present, following visual cortex injections, near the lateral border. In coronal sections this band was localized to the lateral subdivision, area 29d. A few labeled cells were also found in the anterior cingulate cortex; however, this labeling was difficult to detect in tangential sections because of the flattening procedure.

Additional labeling could be discerned in more central portions of the cortex, in areas located roughly between the different sensory modalities. Cells labeled by the auditory injection were present at an area located between the somatosensory and visual representations (e.g., Fig. 6B,C), and cells connected to the visual cortex could be seen in area 22 bordering on area S2 (which may be considered as an auditory-somatosensory transition zone).

In almost every injection involving the visual cortex, a few labeled cells were found in the auditory cortex and vice versa (see Figs. 5,6). The belt of secondary sensory areas surrounding the primary areas usually contained a larger number of cells sending projections to the other sensory modality. Area 36, which has been ascribed both visual and auditory functions (Cipolloni and Peters, '79; Vaughan, '83; Miller and Vogt, '84), was accordingly labeled by both injections (see Fig. 6).

We did not conduct a thorough laminar analysis of the labeling pattern; however, our impression was that in most of the outer ring areas, labeled cells were located in layers II–III and V. No clear laminar, modality-specific segregation was observed in areas that appeared to project to both sensory modalities (Fig. 4). Since the pattern of labeling appeared to vary mostly along the tangential plane, we emphasized in this study the analysis of the flattened cortex preparation. Comparison of the different sections from a tangentially sectioned brain (Fig. 5) showed that the pattern of labeling throughout the sections was fairly consistent, although its intensity might have varied. Thus both posterior medial area AGm and area 29 labeling appeared to be more extensive in deeper layers than superficial ones (cf. Fig. 5 section #5 and #13).

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Area 11. This area was often difficult to preserve in the flattening process, but in both coronally sectioned material and in successfully flattened hemispheres a labeled cluster of cells was present (Figs. 4–6). Within this cluster, neurons projecting to the visual areas were clearly intermingled with neurons projecting to the auditory cortex. This pattern is shown in detail in Figure 7.

Areas 13 and 35. In the lateral zone encompassing areas 13 and 35, neurons projecting to the auditory and visual cortex were intermingled (Figs. 5,6). However, within area 35, as can be seen in Figure 6 and in the more detailed Figure 8, the intermingling was more pronounced in the posterior part, whereas the anterior part was mostly dominated by neurons projecting to the auditory cortex.

Areas 48 and 49. The postsubicular and parasubiculum cortices are situated at the most posterior aspect of flattened cortex. The neurons labeled by the different tracer injections were found to be partly intermingled and partly

Small bars mark the same blood vessels as shown in A. C. The areal subdivisions in the tangential section, based on the patterns shown in A and B. The thick lines delineate borders of areas that were defined mainly by myeloarchitectonic criteria. Thin lines demarcate borders of areas determined using the callosal pattern (marked by shaded areas) and other criteria (see methods). Dashed lines indicate location of borders whose position was less certain. Scale bar = 1 mm.
A schematic representation of all the injection sites in the experimental cases. A. Auditory-visual cases (prefix AV). The location of FG injections is marked by circles, injections of DY are marked by triangles. Full symbols represent the cases shown in this manuscript. B. Somatosensory-visual cases (prefix SV). Symbols are the same as in A. C. Somatosensory-auditory cases (prefix SA), represented by circles and triangles as in A. This figure also includes cases with single injections in sensory areas (squares), as well as cases with injections in the medial aspect of the cortex (stars, prefix Add).

Fig. 3.

segregated into separate territories. This is shown in detail in Figure 9. As can be seen, in the anterior part of this region the neurons projecting to the two different sensory areas were confined within separate territories. However, more posteriorly there was a clear overlap zone containing intermingled populations of cells.

Area 29. Figure 10 shows the labeling of auditory and visually projecting cells in area 29 and the adjacent area 18b. As can be seen, the two populations of neurons were segregated in neighboring territories, with the auditory projecting neurons localized at the medial border of area 18b. Note, however, that even within this segregated pattern of labeling, the separation was not absolute.

Posterior medial AGm. Strong labeling was present in this area following tracer deposits in the visual cortex. This group of labeled neurons seemed to be basically unimodal in nature as only scant connections were maintained here with auditory cortex. This can be seen clearly in Figure 11, which shows the typical elongated cluster of cells filled by retrograde transport from the visual areas, together with the corresponding computer mapping, which points out the few auditory connected cells found in this territory. Inspection of all Aud-Vis cases (see Figs. 5, 6) suggested some tendency for clustering of the auditory projecting cells in a bandlike arrangement, but their density was too low to reveal a clear-cut segregation.

An obvious question is whether the "segregated" pattern was spuriously produced by the particular positioning of the tracer injections within the respective sensory maps. To investigate such a possibility, the location of the injection sites within the two sensory representations was varied in the different cases. In all cases, the segregation or intermingling of the labeled neurons in the peripheral areas remained consistent (Fig. 6).

Finally, a result that was constant across all cases was the striking paucity of double-labeled cells, even in areas where neurons labeled by the two kinds of tracers were thoroughly intermingled.

In summary, the results from the Aud-Vis experimental group revealed that the auditory and visual cortices were connected with several common areas, most of them located within a peripheral cortical ring. Two patterns of labeling could be observed within these areas. In the medially located areas, neurons projecting to different sensory modalities were segregated into separate territories, and in the anterior and lateral part of the cortex, these neurons were found to be intermingled.

Somatosensory-visual cases

The pattern of connections revealed by injections into the somatosensory cortex closely resembled the pattern previously described by Akers and Killackey (’78). The pattern of connections as revealed in a coronally sectioned brain is illustrated in Figure 12. Tangential cortical sections from representative cases are shown in Figures 13 and 14. In case SV-4 (Fig. 13) a minor spread of tracer deposit from the visual cortex into area S2 occurred, as was evident by the thalamic labeling; however, the resulting cortical pattern of label was in agreement with that seen in all the other cases.

As can be seen, somatosensory cortex received projections principally from two directions: from areas in the frontal cortex, namely, area M1 (Donoghue and Parham, ’83), anterolateral area AGm, and area 11, and from areas directly lateral to area S2, namely, area 13 and a zone located at the border of area 13 with area S2. In addition, a few projections originated posteriorly to the injection site, within area 22, from an intermediate area between auditory and somatosensory cortices.

The connections of the visual cortex, as already seen in the Aud-Vis results, were mainly to areas located within the peripheral ring, namely (going clockwise), posterior medial area AGm, area 11, area 13, area 35, areas 48/49, and area
Fig. 4. Distribution of labeled cells in a case injected in auditory and visual cortices (AV-3), sectioned in the coronal plane. In the center, a schematic, dorsolateral view of the cortex shows the location of auditory and visual injection sites and the corresponding levels for each of the coronal sections. Injection sites (section #164) are filled for the auditory site and contain diagonal lines for the visual site. The diffusion zone is delineated by the empty contour around the injection sites. Large dots represent cells labeled by the auditory injection and small dots represent labeling from visual injections. Here, and in the following figures unless otherwise stated, each dot corresponds to 2–4 labeled cells. Small arrows near the boundaries of the section mark the borders of the cortical areas. Thin line within the sections marks the border between layers IV and V. Scale bar = 1 mm.
Figure 5
In coronal sections labeling appeared also in the anterior cingulate cortex. A few direct connections between the visual cortex and the somatosensory cortex were found in our cases; these were mostly restricted to the posterior lateral parts of area S1 (vibrissae and eyebrow fields; Welker, '76; Olavarria et al., '84), posterior area S2, and the anterior parts of secondary visual cortex.

The laminar pattern of labeled cells shows, as before, labeling mainly in layers II-III and V (Fig. 12). However, the somatosensory projections from area 13 seemed to be restricted to the deeper layers (see Fig. 12, section #127).

The pattern of labeling in the Som-Vis cases showed a tendency for neurons projecting to the somatosensory cortex to be segregated from the neurons projecting to the visual cortex. This trend was evident in all our Som-Vis cases independent of the exact site of tracer injection in either sensory cortices (Figs. 12, 13, 14). It is notable that cells labeled by injections in the somatosensory cortex were basically absent from posterior cortical areas such as area 29 and areas 48/49, which contained many visual projecting neurons. There were usually no double-labeled neurons in this group of cases. Below is an area by area description of the labeling patterns.

**Area AGm.** The visual projecting zone in the posterior medial area AGm appeared distinct from its neighboring region in area M1, which projects to the somatosensory cortex. Only at the border between these regions could a small overlap zone be discerned in which neurons projecting to the somatosensory and visual cortices were intermingled (Figs. 12–14). It is not clear whether this overlap may be caused by developmental “noise” or may reflect a genuine mechanism for cross-modal convergence. At the anterolateral aspect of AGm, only neurons projecting to the somatosensory cortex were found.

**Area 11.** The projections to the somatosensory and visual cortices appeared to originate from separate zones within area 11. The neurons projecting to the somatosensory areas were located in a distinct band, posterior to the visual projecting zone (see Fig. 13B–C).

**Area 13.** This area was found to contain two separate groups of labeled cells: At the border between area 13 and area S2, a large cluster of cells was labeled mainly by injections in the somatosensory cortex, and more laterally, along the rhinal fissure, an elongated strip of labeled neurons contained both visual and somatosensory projecting cells that were intermingled (Figs. 13, and 14). This was the only area in the Som-Vis cases where a complete overlap of the zones projecting to the two sensory modalities was revealed.

In summary, the results described above present a picture of clear segregation of the areas connected to the visual cortex and the areas connected to the somatosensory cortex in the cerebral cortex of the rat, with the exception of narrow borderline zones and a lateral strip in area 13.

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**Somatosensory-auditory cases**

In this group of experiments, only flat cortical preparations were studied. Figure 15 shows four sections taken from case SA-2 to illustrate the tangential distribution of the connections throughout the depth of the cortex; Figure 16 shows representative sections from three other Som-Aud cases. These cases illustrate the typical connections of somatosensory and auditory cortices as shown previously. Thus the auditory cortex was connected with the peripherally located areas (going clockwise) medial area 18b, posteromedial M1, area 11, posterior area 13, area 35, and areas 48/49. The somatosensory cortex was connected with area M1, antero-lateral area AGm, few cells in area 11, and area 13.

The overall impression is that areas projecting to the somatosensory and auditory cortices are segregated from each other (Figs. 15, 16). Thus the labeled neurons projecting to the somatosensory cortex in anterior area AGm and in area 11 were clearly segregated from the patch of neurons in area 11 projecting to the auditory cortex. Similarly, the neurons projecting to the auditory and somatosensory cortices in area M1 were also segregated from each other. In fact, the entire medial part of the cortex, namely, medial area 18b, posterior area M1, and posterior medial area AGm, was labeled exclusively by transport from the auditory cortex. Again, lateral area 13 stands out in being the only area containing a clear intermingled pattern of labeling by the two tracers. Note that in all the Som-Aud cases studied, no double-labeled cells were present.

To summarize, in the Som-Aud cases, similar to the Som-Vis cases, the pattern of labeled neurons points to separation between the regions projecting to the somatosensory and auditory areas, with the exception of lateral area 13.

**Additional cases**

To verify the reciprocal nature of some of the connections studied here, we conducted an additional four experiments. In these cases, tracers were injected at sites along the medial cortex estimated to be target areas of the projections from the sensory areas. Two representative cases are depicted in Figure 17, which includes injections placed at area 29 and medial area 18b and injections placed at the frontal cortex, posterior medial area AGm, and area M1. Case Add-11 (Fig. 17A) was injected in medial area 18b and in area 29. The pattern of labeling demonstrates that the afferents to these areas originated mostly from secondary sensory areas. Thus following the injection in medial area 18b, most of the labeled cells in the auditory areas were found in the secondary areas 36 and 22. Similarly, the injection in area 29 produced only a few labeled neurons in the primary visual cortex, whereas many labeled neurons...
Fig. 6. Distribution of labeled cells in representative sections taken from four auditory-visual cases. Symbols are the same as in Figures 4 and 5. The sections in all cases were taken from middle layers IV and V. Arrows point to fields of labeling which are of particular interest (see text). A. Case AV-10. Area outlined by rectangle is shown in detail in Figure 9. B. Case AV-14. C. Case AV-11. D. Case AV-4. Scale bars = 1 mm each. Note that the general pattern shown in Figure 5 remains consistent across different cases and following displacements of the injection sites.
Fig. 7. Labeled cells in area 11 following an injection in auditory and visual cortices. Details from section #13 case AV-8 (Fig. 5C). Inset shows the cortical location of this enlargement (filled rectangle) in relation to the primary sensory areas. A. Detailed distribution of cells in area 11, corresponding to rectangle #4 in Figure 5C. The outlined rectangle in this figure delineates the area shown in B, C, and D. Symbols are the same as in Figure 4, except that here each dot represents 1-2 cells. Scale bar = 250 μm. B. Drawing of the cells in rectangle of A, according to the microphotographs shown in C and D. FG cells are depicted by the dot textured cells, the contour of DY cells is drawn with a thick line. The blood vessels that appear in C and D are delineated by the dashed line. Scale bar = 20 μm for B–D. C. High power microphotograph of cells in the outlined rectangle of A, taken under UV illumination. Note the two types of labeled cells: FG cells (full arrows), corresponding to the dotted cells in B, were more grainy in appearance and labeled processes could be seen emerging out of the cells. Under UV illumination these cells had golden-yellow fluorescence. DY cells (unfilled arrows) corresponding to unfilled cells in B, were more smooth and ellipsoid in shape without any processes. Under UV illumination these cells had green fluorescence. D. Same picture as in C, under blue-violet illumination. The FG labeled cells could hardly be seen under this light, whereas the DY labeled cells were very conspicuous. Note the intermingled arrangement of the cells projecting to the visual and auditory cortices.

were found in secondary areas 18a and anterior 18b. Interestingly, an intense projection to area 29 originated from anterior area 18b, at a region corresponding to Krieg’s (‘46a) area 7.

In addition, many areas within the peripheral ring contained labeled cells following these injections. Thus both of the injections produced labeling in posterior medial area AGm, area 11, area 35, and areas 48/49.

Figure 17B shows the pattern of labeled cells following injections in area M1 and posterior medial area AGm. Here again, projections to the medial aspect of the cortex originated mostly from secondary sensory areas. Thus the injection in area AGm labeled cells in lateral area 18b and in auditory area 22, with a few labeled cells in area A1. A cluster of labeled cells was also observed in area S1. It is not clear whether these labeled cells are due to true connections of posterior medial area AGm with posterior S1 (e.g., Reep, ‘84; Sesack et al., ‘89), or to spread of label from the injection site into area M1. Labeled cells were present also in the peripheral ring areas: medial area 18b, area 29, and a few cells in area 13.

The injection in area M1 (Fig. 17b) labeled several locations mostly in the anterior half of the hemisphere: area S1 and area S2, area 11 and area 13.
To summarize, this set of experiments demonstrates that most sensory projections to the peripheral areas 29, medial area 18b, and posterior medial area AGm originate from secondary auditory and visual cortices and indeed appear to reciprocate the feedback projections from these areas to the sensory areas. In addition, these medially located areas appear to be connected between themselves, as well as with other areas located within the peripheral ring.

Double-labeled neurons

The vast majority of labeled neurons contained a single tracer. However, in several cases we did identify with certainty the presence of a few double-labeled neurons. The majority of these doubly labeled neurons were in cases belonging to the Aud-Vis cases (Figs. 5, 6, 10A, 11). They were found primarily in the ring of peripheral areas including area 35, areas 49/49, area 29, and posterior medial area AGm, with equal frequency in areas exhibiting "segregated" or "intermingled" patterns of labeling.

DISCUSSION

Methodological considerations

Before discussing the results, it is important to note several methodological points. A major concern in this study was the determination of the effective uptake zone of the tracers injected. In studies of the rat cortex, this issue is particularly acute because of the smallness of the cortical mantle. Indeed, some of our injections fell close to the border between two different sensory areas and the effective zone of transport may have included both sensory modality representations. We have tried to reduce this problem by varying the location of the injection sites within each sensory area and by using the thalamic labeling as an additional indicator in the definition of the effective uptake zone. Furthermore, our approach was to address only global issues regarding the connectivity of entire sensory modality representations, ignoring more detailed analysis, e.g., the connections between primary and secondary cortices or between different parts of the sensory maps.

Another point to be considered is the possibility of "false negatives" of double-labeled neurons; in other words, when the labeling intensity of one tracer is far stronger than the other, the weak tracer might fail to be detected. Since FG and DY label separate cell compartments and have distinguishable excitation and emission spectra (Keizer et al., '83; Schmued and Fallon, '86), the frequency of such misses is likely to be low.

The main emphasis of the present study was on the tangential distribution of connections rather than detailed laminar analysis. This was facilitated by the method of cortical flattening. However, in this approach, angular parts of the cortex undergo a certain distortion, which may lead to misinterpretation of the location of the labeled cells. Therefore results from tangentially sectioned cortices were complemented with data from coronal sectioned cases.

Finally, it should be emphasized that since the fluorescent tracers employed were transported only retrogradely, most of our data concerns the organization of feedback pathways to sensory cortex rather than the forward projection pattern. However, on the basis of our own data (e.g., see Fig. 17) and numerous other neuroanatomical studies, it can be safely assumed that the vast majority of cortical pathways are reciprocal in nature. Still, the possibility remains that on a finer scale, differences might exist between the patterns of forward and feedback connections.

Connections of sensory cortices in the rat, comparison to previous single tracer studies

Our results confirm and extend the data presented by previous studies that employed the use of a single tracer. Figure 18 brings together in a schematic form the major results of the present study. As can be seen, the overall layout of the sensory connections is from a centrally located sensory surface onto a peripherally located ring of areas. Most of these areas fall into the category of association areas (e.g., Pandya and Seltzer, '82; Miller and Vogt, '84a). This layout appears to fit within the general scheme of sequential flow of sensory information in the cortex suggested by studies in primates (Pandya and Seltzer, '82; Pandya and Yeterian, '85): from primary sensory areas, in successive steps to association, and then limbic cortices. In the following section we discuss the projections to the sensory cortices from each of the association areas.

Area 29. In agreement with Vogt and Miller ('83) and Torrealba et al. ('84), our results show strong connections between the cingulate cortex (area 29d) and the visual cortex.

Area 18b (medial). Area 18b contained a longitudinal band of neurons projecting to the auditory cortex along the medial border with area 29d. Miller and Vogt ('84a) described similar connections of this area with the auditory cortex. Our results extend their finding to include the entire auditory representation.

Area AGm. The extensive connections of the posterior medial part of area AGm with the visual cortex have been noted by a number of investigators (Vogt and Miller, '83; Miller and Vogt, '84a; Reep et al., '84; Torrealba et al., '84). These connections support the suggestion that this area may be the rat homologue of the primate frontal eye fields (Leonard, '69; Hall and Lindholm, '74; Crowe and Path-
Fig. 9. Distribution of labeled cells in areas 48/49 after injections in visual and auditory cortices. A. Photomicrograph taken from section #13 of case AV-10 (corresponding to the square in Fig. 6A), taken under UV illumination, which shows the FG labeled cells, as well as the DY labeled cells (faint labeling at the bottom half). Arrows point to major blood vessels; scale bar = 100 μm. B. Same area as in A, and at the same scale. Blue-violet illumination shows the DY labeled cells which appear brighter than in A. C. Schematic diagram showing distribution of labeled cells in the same area shown in A and B. Symbols are the same as in Figure 7. Arrows point to the blood vessels shown in A and B. Scale bar = 100 μm. Note that the cells projecting to auditory and visual areas are intermingled in the posterior portion of the area shown here.

Connections with the auditory and somatosensory cortices have been mentioned by Reep et al. (’84; see also Sesack et al., ’89). However, in our study only weak connections were demonstrated with the auditory cortex, whereas somatosensory cortex injections failed to label this part of area AGm. It should be noted, however, that most of our injections were probably not within the projection field of the posterior medial area AGm, namely, the posterior parts of the somatosensory cortex (see Reep et al., ’84). In contrast, our results show in several cases some labeling in the anterolateral part of AGm, following injections in somatosensory areas (Figs. 12-16).

Area 11. This area was found to contain neurons projecting to the visual cortex as well as neurons projecting to the auditory cortex. Although the connections with the visual fields have been previously documented (Vogt and Miller, ’83; Miller and Vogt, ’84a), we have been unable to find any previous reference to the connection of area 11 with auditory cortex in the rat. In addition, our study indicates that somatosensory cortex is connected with area 11. It should be stressed, however, that the neurons projecting to the somatosensory cortex never appeared to intermingle with neurons projecting to the visual or auditory cortices (Figs. 14, 18).

Areas 13 and 35. Within the borders of area 13, two groups of labeled cells were noticeable. The large cluster of neurons mainly connected with the somatosensory cortex, which consistently appeared on the myeloarchitectonically defined border between area S2 and area 13 (Fig. 18), may correspond in location to area 14 of Krieg (’46a) and Caviness (’75). In a similar location, other researchers have described terminations of fibers from the primary and secondary somatosensory cortex (Akers and Killackey, ’78; Guldin and Markowitsch, ’83), and from area 18a (Miller
Fig. 10. Detailed maps of labeled cells’ distribution in area 29 following an injection in auditory and visual cortices (case AV-8, Fig. 5C). A. Anterior area 29 (rectangle 2). B. Posterior area 29 (rectangle 1). Symbols are the same as in Figure 7. Scale bars = 200 µm. As can be seen in these diagrams, the two types of labeled cells are essentially segregated, though some small scale mixing is present, especially in medial area 18b.

Areas 48 and 49. The connections of the postsubicular and parasubiculum regions (areas 48/49) with the visual system were previously reported by Vogt and Miller ('83). This study describes for the first time a neuronal path from this region to the auditory cortex, thus suggesting an additional indirect link between the auditory system and the hippocampal formation. The neurons projecting to these two sensory areas were intermingled in some parts of areas 48/49 but segregated in others. It was difficult to determine in our material whether the visually connected, anteriorly located band in this area was part of the postsubiculum or the posterior pole of area 18a (see also Olavarria and Montero, '84; Malach, '89).

Centrally located areas. In addition to the peripheral association areas, labeled neurons were also found in more centrally located regions, which due to their position between the sensory cortices may be considered as transition zones.

At the anterior part of area 18b, we found cells that project to the auditory cortex (Figs. 6, 10A). This site appears to correspond to area 7 according to the parcellation of the rat's cortex (Krieg, '46a). This region has been ascribed an associative role (Miller and Vogt, '84a; Torralba et al., '84); however, it has previously been associated with visuosomatic responses rather than with visuoauditory or somatoauditory responses (Wagor et al., '80; Pinto-Hamuy et al., '87). It should be noted that in some cases this strip of auditory projecting cells appeared to extend anteriorly into the area previously defined as part of the primary motor and somatosensory cortices (Donoghue and Wise, '82; Neafsey et al., '86).

Another transitional zone may be present between the somatosensory and auditory cortices. Area 22 is situated within this region (Caviness, '75; Olavarria and Van Sluyters, '85) and its anterolateral aspect probably corresponds in part to areas 39 and 40 of Miller and Vogt ('84a). We have shown that anterior area 22 is connected with visual and somatosensory modalities (Fig. 18); yet it seems that its primary role is as a secondary auditory area in view of its connections with area A1 and its physiological properties (Krieg, '46b; Sally and Kelly, '88).
Connections between the sensory cortices

Our results (Figs. 6, 14, 16), as well as those of previous studies, indicate that in the rat, unlike cats and primates, direct connections also exist between the sensory cortices themselves (Miller and Vogt, '84a; Olavarria and Montero, '84; Torrealba et al., '84). The region in area S1, which is connected to the visual cortex, appears to correspond to the somatotopic eye and head representation (Welker '76). Miller and Vogt ('84a) suggested that this area may have some role in the coordination of eye movements and the visual stimuli observed.

Patterns of interrelationship between modality specific pathways

The novel aspect of our study was the use of a double-label, tract-tracing paradigm, which enabled us to approach directly the question of the relation between different modality specific pathways in the association areas. If one assumes that adjacent neurons have a higher probability for mutual interaction, then an intermingled arrangement of neurons, projecting to different sensory modality representations, may indicate a higher level of "cross talk" between different modalities. Our study suggests that areas of this type may include frontal area 11, perirhinal areas 13 and 35, and postsubicular areas 48/49 (Fig. 18). Alternatively, association areas of the "segregated" type, which include mostly one type of modality specific cells, can be presumed to be involved more with unimodal sensory processing. Areas with such a segregated arrangement of projections include posterior medial area AGm and cingulate area 29d (Fig. 18).

In trying to group the areas containing segregated populations of unimodal projecting neurons versus those containing intermingled neurons, it becomes evident that the former areas are more prevalent on the medial aspect of the hemisphere, whereas the latter are found at the anterior and lateral aspects. The significance of this organization is not clear at present, but it is interesting to note that a similar subdivision of areas was proposed on evolutionary and embryological grounds (Sanides, '69; Pandya and Yeterian, '85).

Even within the so-called unimodal territories, there are often a few neurons projecting to other sensory modalities (for example, see area AGm in Figs. 6, 11), which leaves open the possibility that some intermodality analysis occurs. Particularly interesting is the issue of the border zones between adjacent unimodal areas connected to different sensory modalities (e.g., see Figs. 6, 14, 16) where an intermingled pattern of labeling is more prevalent. Does such organization present a functional principle by which cross-modality integration is implemented, or is it merely the result of developmental errors? A more detailed analysis of the response properties of neurons at such transition zones will be necessary to answer this question.

It should be remembered that even within the intermingled group of cells, some micro-scale segregation might still be present. In this respect it is important to note the striking absence of double-labeled neurons in our results, namely, neurons projecting simultaneously to two different sensory modalities. It could be assumed that an area that integrates polysensory information would have a greater likelihood to send bifurcating axons as feedback to different...
sensory areas. Yet our findings suggest that at the feedback level, modality specificity is conserved. Alternatively, the possibility still remains that such bifurcating axons do exist and we have consistently failed to inject their two target fields simultaneously.

It is interesting to note that the auditory and visual areas display a stronger resemblance to each other, in terms of their pattern of connections to the association areas, than to the somatosensory cortex. As can be seen in Figure 18, area 11, area 35, and areas 48/49 project to both auditory
Fig. 13. Tangential distribution of labeled cells in a series of tangential sections taken from a case injected in somatosensory and visual cortices (SV-4). Arrows point to labeled fields of particular interest. Symbols as in Figure 12. A. Section #9, layers III-IV. B. Section #13, layers IV-V. C. Section #15, layer V. D. Section #19, layers V-VI. Scale bars = 1 mm each. It is noteworthy that apart from lateral area 13, the cell clusters labeled by the somatosensory and visual cortex injections were segregated.
Fig. 14. Distribution of labeled cells in tangential sections of four different cases injected in somatosensory and visual cortices. Sections were taken from layers IV-V. Symbols are as in Figure 13. **A.** Case SV-3. **B.** Case SV-2. **C.** Case SV-1. **D.** Case SV-5. Scale bars = 1 mm. Note that the overall segregation of cells projecting to the somatosensory cortex from cells projecting to the visual cortex is consistent in all these cases in spite of the variability in the location of injection sites.
Fig. 15. Distribution of labeled cells following injections in somatosensory and auditory cortices. These schematic diagrams show four tangential sections, taken from the flattened cortex of case SA-2. Large dots represent label from somatosensory injection site, small dots represent label from auditory injection site. A. Section #5, estimated at layers II-III. B. Section #9, layers II-III. C. Section #13, layer IV. D. Section #17, layer V. Symbols are as in figure 13. Scale bar = 1 mm. Note the segregation of cells labeled by somatosensory cortex injection from cells labeled by auditory cortex injections.
Fig. 16. Pattern of labeling in three additional cases injected in somatosensory and auditory cortices. Sections drawn are from layers IV-V. A. Case SA-1. B. Case SA-3. C. Case SA-4. Symbols are as in Figure 13. Scale bars = 1 mm. Note that apart from lateral area 13, the connections to auditory and somatosensory cortices remained segregated in different cases having different combinations of injection sites.

and visual areas, and the projection zones from the medial cortex (area 29d, medial area 18b, posterior medial area AGm, and posterior area M1) to these two regions are adjacent. Projections to somatosensory cortex do not overlap any of these regions.

An interesting feature suggested by documented work of other investigators, as well as by our data, is that the association areas described in this study are strongly interconnected (Meibach and Siegal, '77; Deacon et al., '83; Vogt and Miller, '83; Miller and Vogt, '84a; Reep et al., '84).
Thus these areas may constitute a functionally related family of association areas (Berson and Graybiel, '83; Olson and Jeffers, '87) or a distributed network (Goldman-Rakic, '88).

Finally, the possibility that the cross-modality integration may occur at the subcortical level should also be considered in view of the wealth of cortical connections, afferent and efferent, to subcortical structures. The cortical association areas have been shown to be connected to the limbic system (Meibach and Siegal, '77; Kosel et al., '82), the thalamus (Domesick, '69; Leonard, '69, Guldin and Markowitsch, '83), and to subcortical motor structures (Domesick, '69). However, it was beyond the scope of this study to investigate thoroughly this possibility.

**Comparison to association areas in cats and primates**

It is obviously difficult to draw homologies between such diverse species as the rat, cat, and monkey, but specifically for that reason, any parallels that can be drawn carry added significance in suggesting common mammalian principles of organization.

Regarding the segregation of sensory pathways related to area AGm, a suggestive parallel could be found in studies of connections between the frontal cortex and the posterior parietal cortex in monkeys (Cavada and Goldman-Rakic, '89). Thus somatosensory linked area 7b and visually linked area 7a were found to be connected with different subdivisions of the frontal cortex. A comparable phenomenon might also exist in cat area 6 where a clear segregation of somatosensory and visual connections was observed (Olson and Jeffers, '87; Olson and Lawler, '87). Finally, a study of the connections of prefrontal cortex of the cat suggests that its various sectors maintain specific connectivity patterns with different sensory cortices (Cavada and Reinoso-Suarez, '85).

Our results suggest that orbitofrontal and perirhinal areas should contain overlapping connections of different modalities. Such overlapping connections were indeed described (Jones and Powell, '70; Pandya and Seltzer, '82; Pandya and Yeterian, '85) among the peripheral areas in the frontal and parahippocampal cortices in primates. Interestingly, physiological studies in primates reveal auditory-visual and visual-gustatory interactions in the orbitofrontal cortex, which is a likely homologue of the rat area 11 (Benevento et al., '77; Thorpe et al., '83). A rough rostrocaudal topography of parahippocampal connections with the sensory areas, similar to the ones described here for the perirhinal areas 13 and 35, was described by Room and Groenewegen ('86) and Witter and Groenewegen ('86), but because these studies were based on injections of single tracers, it is difficult to assess the level of connectional intermingling in these cases.

It is unclear whether the more centrally located transition zones in the rat cortex, e.g., area 7 of Miller and Vogt (see also Krieg, '46a), could be considered analogues to the...
Fig. 18. Summary diagram of the pattern of connections of the sensory cortices with the association areas as revealed by this study. Three different rasters represent clusters of labeled cells, which project to the three sensory cortices as shown left to the scheme. In regions where only few cells were labeled, empty triangles, squares, or circles are drawn, corresponding to visual (Vis), auditory (Aud), or somatosen-sory (Som) injection sites, respectively. Note the ringlike arrangement of the areas containing the clusters of labeled cells. This diagram illustrates the areas in which neurons projecting to different sensory modalities are intermingled, and the areas where these neurons are segregated according to their target sensory area. Note that the tendency for intermingling is more prevalent on the anterior and lateral sides of the hemisphere.

highly developed association areas described in the monkey cortex, such as the subdivisions of area 7 (Pandya and Seltzer, '82; Mesulam, '83; Goldman-Rakic, '88; Andersen, '89; Cavada and Goldman-Rakic '89), or areas in the superior temporal sulcus (Jones and Powell, '70; Benevento et al., '77; Bruce et al., '81; Pandya and Seltzer, '82). It is interesting to note that physiological studies suggest that some of these transition areas might serve a polysensory function (Benevento et al., '77; Bruce et al., '81; Duhamel et al., '89).

Conclusions

The main goal of this study was to explore directly the connectivity patterns that might subserve cross-modality integration in the cerebral cortex of the rat. We have found such patterns in several cortical areas, mainly on the outer realm of the hemisphere. The level of connectional cross-modality overlap varies markedly between these areas, whereas on the single cell level, feedback projections remain modality-specific. The physiological significance of the circuitry revealed in the present study remains to be determined.

ACKNOWLEDGMENTS

We thank Drs. C.R. Olson, J. Olavarria, M. Segal, and R. Eilam for helpful comments on the manuscript; M. Harel for technical assistance; G. Sirton, Division of Laboratory Computers, for computer programing, and the Graphics Department for assisting with the figures. This work was supported by grants from the U.S.-Israel B.S.F grant 88-00275 and Israeli Academy of Sciences, B.S.R grant 527/89 to R. M.

LITERATURE CITED


