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# Projections from inferior temporal cortex to prefrontal cortex via the uncinate fascicle in rhesus monkeys

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**Summary.** In five rhesus monkeys (*Macaca mulatta*) we used anterograde and retrograde tracing techniques to investigate the projection from the inferior temporal cortex (area TE) to the prefrontal cortex as well as the course of the projecting fibers. The results showed that TE projects to both the inferior convexity and orbital surface of prefrontal cortex and that these projections course almost exclusively via the uncinate fascicle. Transection of the uncinate fascicle deprives the prefrontal cortex of virtually all input from TE, but leaves intact inputs from prestriate and parietal visual areas as well as the amygdala. Such transection also leaves intact many projections from TE to targets other than the prefrontal cortex, including the amygdala, ventral putamen, tail of the caudate nucleus, and pulvinar.

**Key words:** Inferior temporal cortex – Prefrontal cortex – Uncinate fascicle – Temporo-frontal connections – Monkeys

## Introduction

Ablation of the inferior temporal cortex in monkeys produces a modality-specific impairment in visual learning and memory (for reviews, see Gross 1973; Dean 1982). The impairment is similar in some ways to visual agnosia in man, and can be understood as a disorder in the identification of visual stimuli (Gaffan et al. 1986; E.A. Gaffan et al. 1986).

In visual associative learning tasks, monkeys associate visual stimuli with other events, which may be non-visual. Since the inferior temporal cortex itself appears to be concerned exclusively with the visual modality, the association of visual stimuli with non-visual events necessarily involves the intraction of inferior temporal cortex with other areas. Thus, visual associative learning can be analyzed by investigating the interaction of inferior temporal cortex with these areas. For example, disconnection of the inferior temporal cortex from the amygdala specifically impairs the association of visual stimuli with the incentive value of primary reinforcers (Spiegler and Mishkin 1981; Gaffan and Harrison 1987; E.A. Gaffan et al. 1988). Presumably, other types of visual associative learning depend on the interaction of the inferior temporal cortex with areas other than the amygdala. One such area is the prefrontal cortex, which interacts with the inferior temporal cortex by a direct cortico-cortical projection (Kuypers et al. 1965). However, since the exact course of the projecting fibers through the white matter has not been fully described, the feasibility of studying temporo-frontal interactions by surgically disconnecting inferior temporal from prefrontal cortex remains to be established.

One possible way to achieve temporo-frontal disconnection would be to sever the uncinate fascicle, which is a hook-shaped fiber bundle that curves around the anterior part of the lateral sulcus. In man, it is thought to interconnect the medial temporal lobe with the orbital frontal lobe, and the inferior and lateral parts of the temporal lobe with the lateral frontal lobe (Clemente 1985, pp 1100-1102). In monkey, several degeneration experiments have shown a substantial projection from the inferior temporal cortex to the frontal lobe; terminal degeneration following inferior temporal lesions has been seen in the inferior parts of the prefrontal cortex, including the inferior bank of the principal sulcus, the cortex inferior to the principal sulcus, the arcuate sulcus, and the orbital

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surface (Kuypers et al. 1965, pp 253–255; Jones and Powell 1970, Fig. 10; Chavis and Pandya 1976, Fig. 4; Jacobson and Trojanowski 1977). Following such a lesion, degenerating fibers were observed in the uncinate fascicle (Kuypers et al. 1965, p 254). Thus, it seems likely that the cortico-cortical projection to the frontal lobe from inferior temporal cortex passes via this fiber bundle.

Little experimental evidence is available on the organization and function of the uncinate fascicle. This is surprising in view of its clinical importance. Damage to it may be an important factor in surgically produced amnesia (Horel 1978); more generally, an understanding of long cortico-cortical pathways such as the uncinate fascicle is essential for the elucidation of disconnection syndromes.

In the present study, we first verified the projection from the inferior temporal cortex to the frontal lobe, and traced the course of the projecting fibers. We then determined the extent of inferior temporal cortex that is disconnected from the frontal lobe by transection of the uncinate fascicle. Finally, we showed that the projection from visual cortex via the uncinate fascicle is largely specific to Bonin and Bailey's (1947) architectonic area TE.

## Materials and methods

Five juvenile rhesus monkeys (*Macaca mulatta*) weighing between 3.5–4.5 kg were used. One of these monkeys (case 1) received injections of tritiated amino acids in cytoarchitectonic area TE (Bonin and Bailey 1947) of the left inferior temporal cortex. A second monkey (case 2) received injections of bisbenzimide and nuclear yellow, two fluorescent dyes, in the left (case 2A) and right (case 2B) prefrontal cortex, respectively. Two additional monkeys (cases 3 and 4) underwent transection of the left uncinate fascicle followed by injections of the dye bisbenzimide into the left prefrontal cortex. The remaining monkey (case 5) received injections of tritiated amino acids in prestriate area V4 of the left hemisphere.

Surgery was performed under aseptic conditions. The monkey was initially tranquilized with ketamine hydrochloride (10 mg/kg I.M.), then anesthetized with pentobarbitol (I.V., supplemented as needed), and treated with atropine sulfate (0.04 mg/kg I.M.) to prevent excess secretion in the respiratory passages. In all cases except case 1, the cortex to be injected was exposed by removal of a bone flap; in case 1, the bone overlying the temporal lobe was removed by rongeurs.

In cases 1 and 5, we injected an equal-parts mixture of tritiated proline (New England Nuclear L-[2,3,4,5-$^3$H], specific activity 100–140 Ci/mmol) and tritiated leucine (New England Nuclear L-[3,4,5-$^3$H(N)], specific activity 100–140 Ci/mmol). The labeled amino acids, which had been evaporated and then reconstituted in 0.9% saline to give a final concentration of 100 μCi/μl, were injected at a rate of 0.02 μl/2 min. In both cases, three injections of 0.3 μl were made approximately 2 mm apart; in case 1 the injections were made on the exposed surface of the second temporal convolution, while in case 5 they were made along the surface of the prelunate gyrus.

In the remaining three cases, multiple injections of fluorescent dyes were made into sites in prefrontal cortex. These sites were selected to cover the full extent of prefrontal cortex that has been reported to receive projections from the inferior temporal cortex. In case 2A, 20 sites in the left prefrontal cortex were injected with a 10% solution of bisbenzimide in 0.9% saline; and in case 2B, 10 sites in the right prefrontal cortex were injected with a 10% solution of nuclear yellow in 0.9% saline. At each site in both hemispheres, a volume of 0.2 μl was injected. In cases 3 and 4, injections of the dye bisbenzimide were made exactly as in case 2A, except that the left uncinate fascicle was transected prior to injection. Exposure of the uncinate fascicle was accomplished by removing approximately 2 cm of cortex on the lower bank of the lateral sulcus. The transection, which was performed with the aid of an operating microscope, was then made by aspiration of the underlying white matter with a 20-gauge metal suction tube.

In every case, heart rate, respiration rate, and body temperature were maintained within normal physiological ranges throughout surgery. Following the injections, procedures for all monkeys were the same: the dura was sewn, the bone flap replaced, the wound closed in anatomical layers, and the monkey was given dexamethasone phosphate (0.4 mg/kg I.M.) to minimize brain edema. The monkey was then placed in a warm neonatal incubator until it awoke from the anesthesia.

After either a 7-day (cases 1 and 5) or 2-day (cases 2–4) survival period, the brains were fixed by perfusion with 0.9% saline followed by 4% paraformaldehyde, and then by 5% glycerol in 4% paraformaldehyde. They were then blocked stereotaxically, removed from the skull, photographed, and stored overnight in 10% glycerol in 4% paraformaldehyde at 4° C. After 24 h, the brains were put in 20% glycerol in 4% paraformaldehyde and placed on a shaker at 4° C for 4 days. The brains were then stored at −70° C in 2-methyl butane (95%) until they were cut. Frozen sections were cut in the coronal plane at 50 μm. In cases 1 and 5, every fifth section was processed for autoradiography. These sections were mounted, dipped in Kodak NTB2 emulsion, and exposed at 4° C for 20 weeks. Subsequently, these sections were developed in Kodak D19, fixed, and counterstained with thionin. In cases 2–4, every fifth section was examined for the presence of retrogradely labeled fluorescent cells. These sections were mounted directly from 4.5% saline as the brain was cut, dried at 37° C, and stored without coverslips at 4° C in light-tight boxes. An adjacent series of sections, also spaced 250 μm apart, was stained for thionin in these cases.

For the purpose of analysis, the locations of concentrations of silver grains (cases 1 and 5) and cells labeled with fluorescent dyes (cases 2–4) were charted onto enlarged photographs of the thionin-stained sections. The data were then transferred onto reconstructions of lateral and ventral views of the hemisphere.

## Results

### *Case 1*

Case 1 was prepared to confirm the target areas within prefrontal cortex that receive projections from inferior temporal cortex and to trace the course of the projecting fibers. In this case, the amino-acid injection site was located within cytoarchitectonic area TE, mainly on the lateral surface of the second temporal convolution (Fig. 1). Labeled terminals resulting from this injection were found extensively throughout the inferior

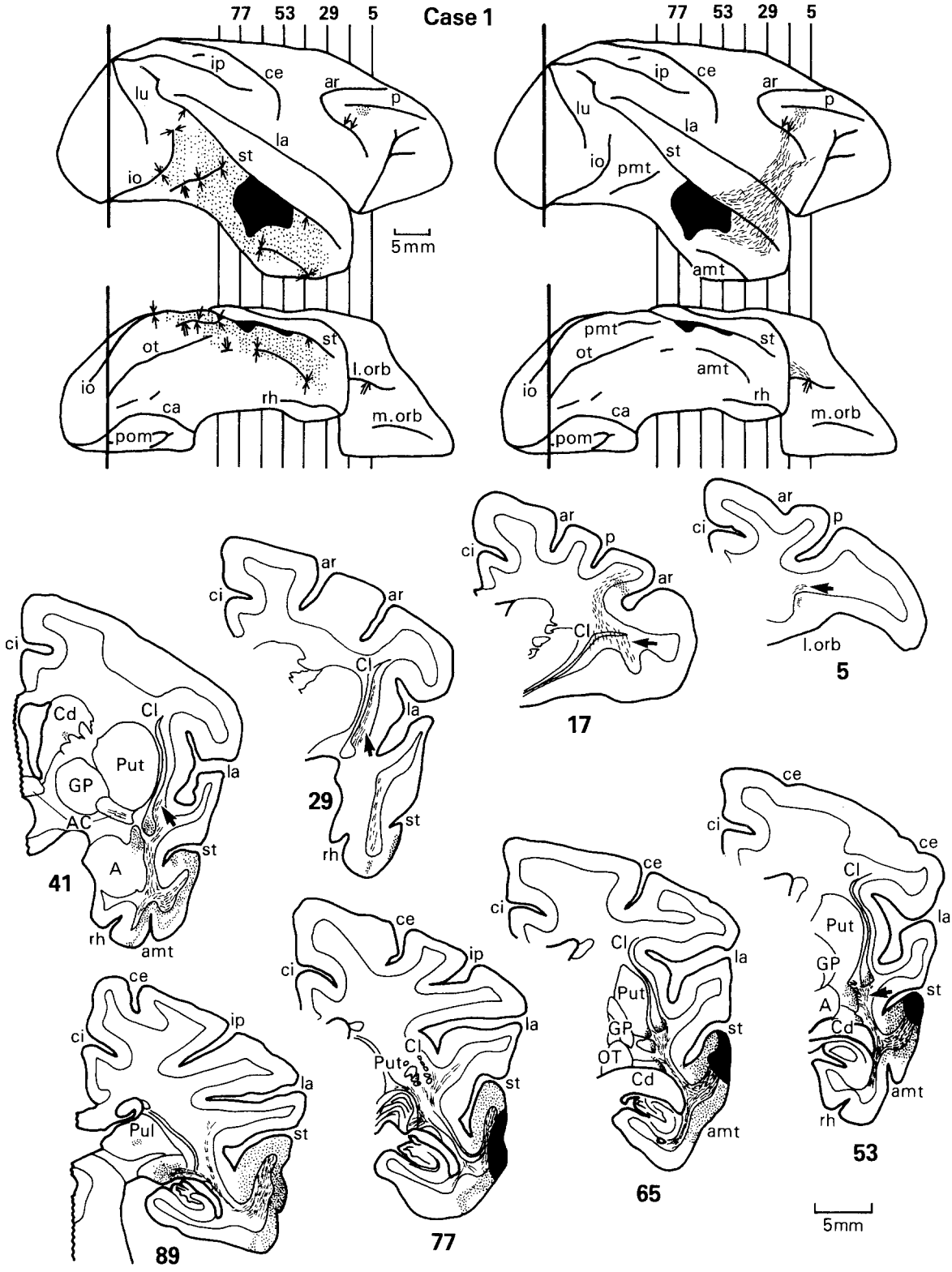


**Fig. 1.** Case 1: Lateral and ventral views of the right hemisphere and selected cross-sections, illustrating tritiated amino-acid injection site (in black) and the distribution of anterogradely labeled terminals (dots) and fibers (dashed lines). On the lateral and ventral views, single-tailed arrows indicate the limits of labeled cortex buried within the bank of a sulcus, while double-tailed arrows indicate a focus of labeled cortex within a sulcus. Numerals indicate the levels from which the cross-sections were taken; the most posterior section analyzed is indicated by a heavy vertical line through the occipital lobe. In the cross-sections, heavy arrows indicate labeled fibers projecting to prefrontal cortex via the uncinate fascicle (see sections 5–53). Abbreviations: A, amygdala; AC, anterior commissure; amt, anterior middle temporal sulcus; ar, arcuate sulcus; ca, calcarine fissure; Cd, caudate nucleus; ce, central sulcus; ci, cingulate sulcus; Cl, claustrum; co, collateral sulcus; GP, globus pallidus; io, inferior occipital sulcus; ip, intraparietal sulcus; l.orb, lateral orbital sulcus; la, lateral sulcus; lu, lunate sulcus; m.orb, medial orbital sulcus; ot, occipitotemporal sulcus; OT, optic tract; p, principal sulcus; pmt, posterior middle temporal sulcus; pom, medial parieto-occipital sulcus; Put, putamen; Pul, pulvinar; rh, rhinal fissure; st, superior temporal sulcus

temporal cortex, extending from the inferior occipital sulcus posteriorly (within the upper quadrant of the central visual field representation of area V4) to almost the temporal pole anteriorly. In addition, patches of labeled terminals were found in three separate sites of prefrontal cortex: within the anterior bank of the inferior limb of the arcuate sulcus, on the inferior convexity just ventral to the principal sulcus, and within the lateral orbital sulcus. Labeled fibers projecting to prefrontal cortex followed a course that ran anteriorly from the injection site for about 5 mm, and then turned dorsally toward the frontal lobe. Further rostrally, these fibers joined the uncinate fascicle, as they ascended lateral to the claustrum in the extreme capsule (see bold arrows in Fig. 1, sections 29–53). One contingent of labeled fibers remained ventral to the claustrum on the orbital surface as it coursed toward its termination in the lateral orbital sulcus, while another coursed dorsally through the claustrum to reach its targets within the arcuate and below the principal sulci (Fig. 1, sections 5 and 17). No fibers arising in area TE appeared to reach prefrontal cortex from a route other than through the uncinate fascicle.

Labeled fibers from inferior temporal cortex could also be traced to their terminations in the claustrum, ventral putamen, tail of the caudate nucleus, amygdala, and pulvinar (Fig. 1, sections 41–89), as well as to the contralateral hemisphere via the anterior commissure (Fig. 1, section 41) and splenium of the corpus callosum (not shown). In none of these cases, except the claustrum, did the projecting fibers course through the uncinate fascicle.

*Case 2A*

Case 2A was prepared to establish the full extent of inferior temporal cortex that projects to prefrontal cortex. Accordingly, in this case we injected the retrograde tracer bisbenzimide into all portions of prefrontal cortex that have been reported to receive inferior temporal inputs. As shown in Fig. 2 (sections 36 and 60), the injection sites covered widespread regions of both the lateral portion of the orbital surface and the inferior convexity, including tissue on the lower bank of the principal sulcus and on the anterior bank of the ventral limb of the arcuate sulcus (Fig. 2, sections 36 and 60). Surrounding these prefrontal injection sites were 'halos' of intense labeling, in which cells in all cortical layers appeared to be labeled. In regions beyond these zones, in the temporal and parietal lobes for example, the labeling was laminar in appearance, such that only the cells in layers 3 and/or 5 were labeled. Within the temporal lobe, the anterior portions of both the superior temporal cortex (cytoarchitectonic area TA) and inferior temporal cortex (area TE) were extensively labeled, as was the temporal pole (area TG). The labeled region included both banks of the lateral and superior temporal sulci, throughout most of their extents. Thus, the prefrontal regions that were injected in this case receive projections from at least the anterior two-thirds of area TE.

Within the parietal lobe, heavy labeling was found in two separate foci of the inferior parietal lobule, one anteriorly in area PF and another posteriorly in area PG. Both foci extended from the surface of the inferior parietal gyrus into the lower bank of the intraparietal sulcus (Fig. 2, sections 148 and 172). Additional labeling in this case was found both in the lateral sulcus, including the insula, and on the medial surface of the hemisphere in cingulate cortical areas 23 and 24.

*Case 2B*

Case 2B was prepared to replicate case 2A, and, as shown in Fig. 3, the nuclear yellow injection sites in case 2B were located in prefrontal areas comparable to those injected with bisbenzimide in case 2A. Temporal lobe regions containing labeled cells in case 2B were virtually identical to those containing labeled cells in case 2A, except that in case 2B the labeling within the inferior temporal cortex was more widespread, extending posteriorly to the level of the inferior occipital sulcus (i.e. extending into area TEO). Thus, in this case, the prefrontal areas that were injected resulted in labeling throughout the entire extent of area TE. Similarly, although parietal lobe regions containing labeled cells in case 2B were the same as those in case 2A, the labeling in case 2B was somewhat heavier, extending continuously from area PF into area PG. As in case 2A, there was additional labeling both in cingulate cortex, which appeared to be confined to area 24, and in the insula.

*Case 3*

The intention in case 3 was to inject the same prefrontal cortical sites as in cases 2A and 2B, but in an animal with the uncinate fascicle transected. As shown in Fig. 4 (section 109), the transection was as intended, including the anterior 2 cm of the fascicle and extending medially from the lateral sulcus through both the extreme capsule and claustrum. Because of the approach through the lower bank of the lateral sulcus, there was some addition-

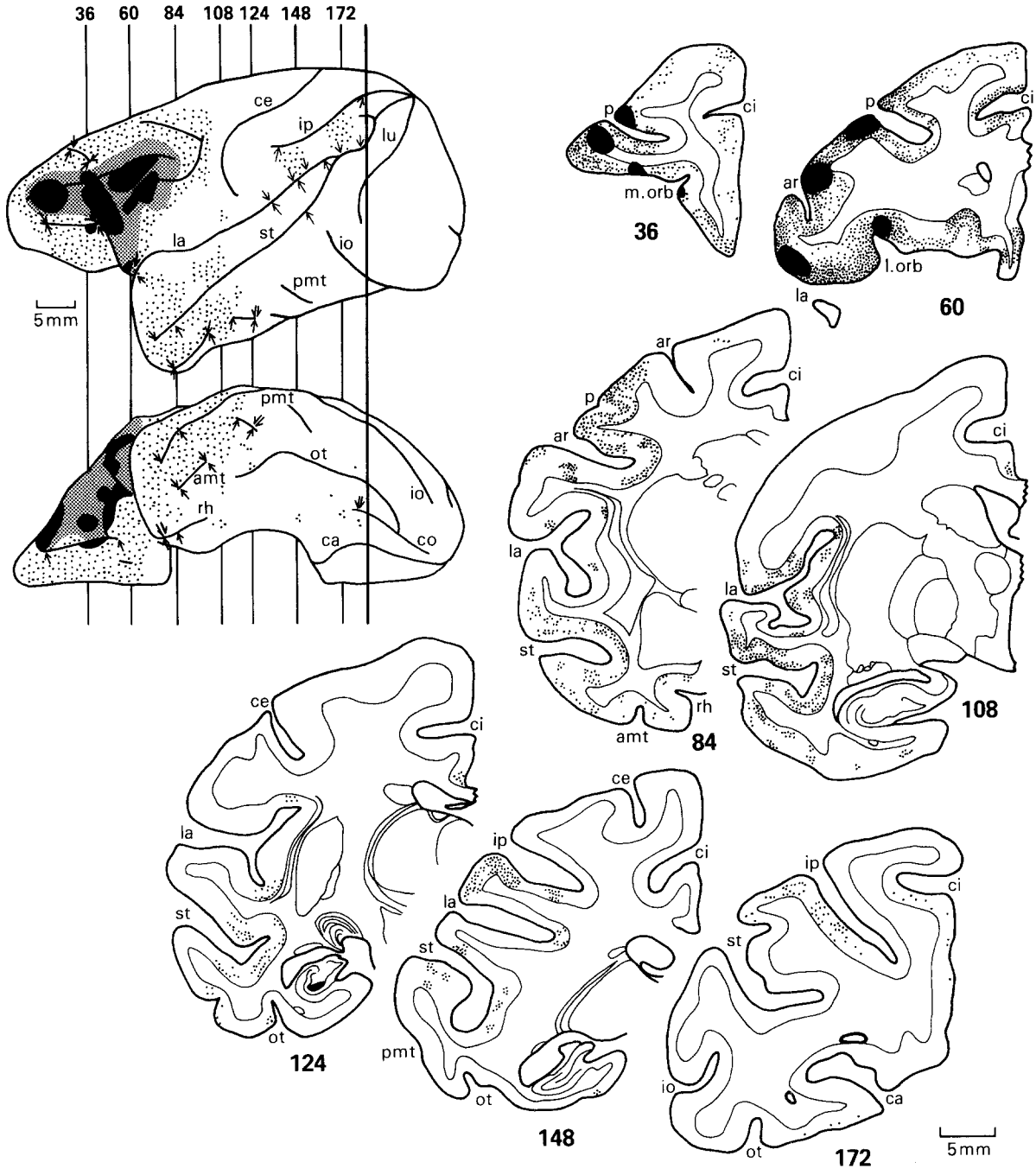


**Fig. 2.** Case 2A: Lateral and ventral views of the left hemisphere and selected cross-sections, illustrating sites injected with the fluorescent dye bisbenzimide (in black) and the distribution of retrogradely labeled cell bodies (dots). Gray area in prefrontal cortex represents 'halo' of injection sites, in which virtually all cells were labeled. See Fig. 1 for all other conventions and abbreviations

al damage to the cortex on the surface of the superior temporal gyrus. The sites injected with bisbenzimide in case 3 closely resembled the injection sites in cases 2A and 2B, except that in case 3 the region injected on the orbital surface extended somewhat more medially. Comparison of the distribution of labeled cells in case 3 with cases 2A and 2B showed a striking difference in the temporal lobe. Unlike cases 2A and 2B, in which there was heavy labeling in the anterior parts of both the superior temporal cortex (area TA) and inferior temporal cortex (area TE), in case 3 these regions

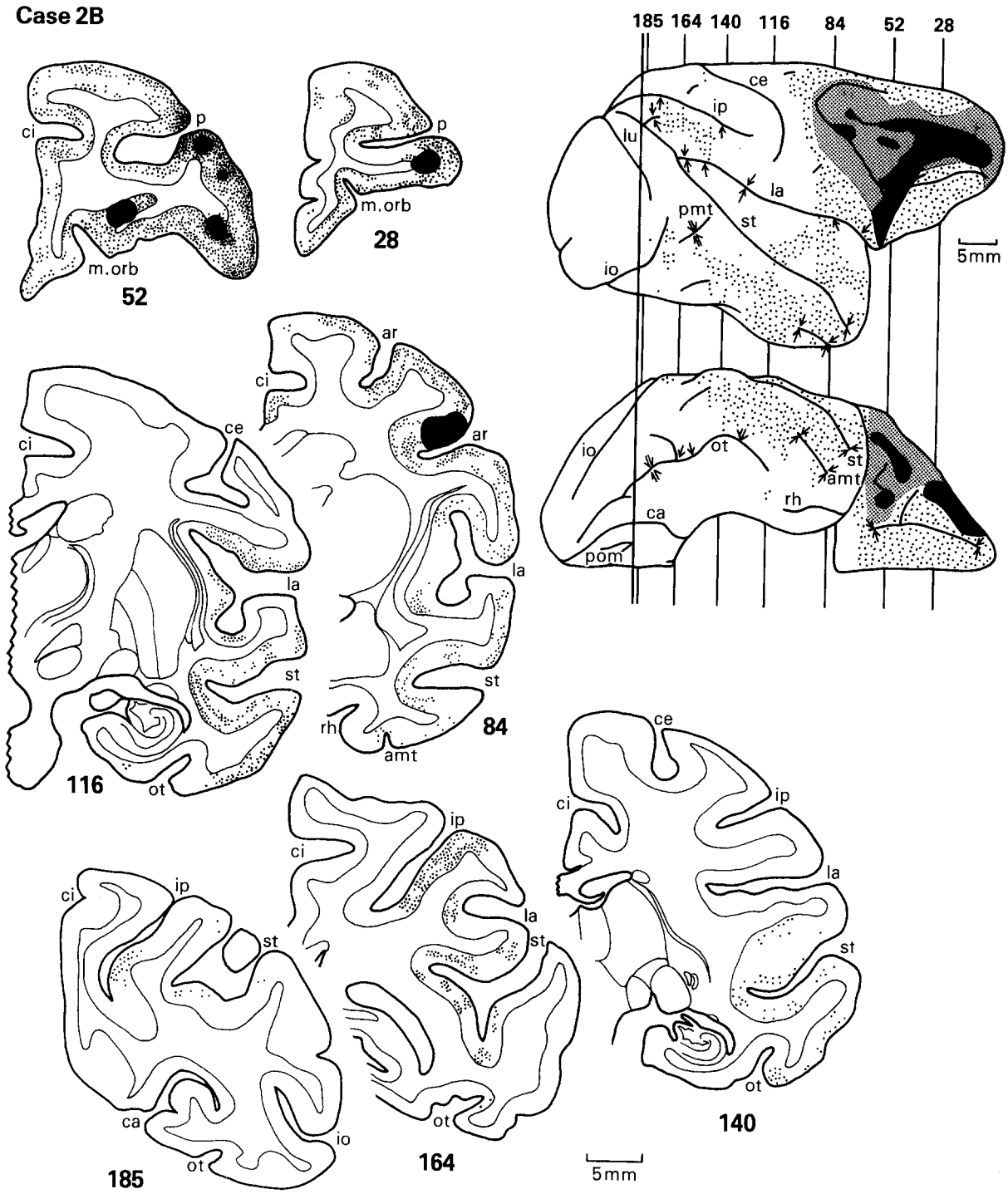


**Fig. 3.** Case 2B: Lateral and ventral views of the right hemisphere and selected cross-sections, illustrating sites injected with the fluorescent dye nuclear yellow (in black) and the distribution of retrogradely labeled cell bodies (dots). See Figs. 1 and 2 for all other conventions and abbreviations

were largely unlabeled, except for cortex on the upper and lower banks of the superior temporal sulcus, which was moderately labeled. In all other regions of cortex, the distribution of labeled cells in case 3 was virtually identical to that found in cases 2A and 2B. Thus, areas PF and PG (including both the inferior parietal gyrus and the lower bank of the intraparietal sulcus) in the parietal lobe were heavily labeled, as were the insula and cingulate areas 23 and 24. The results from case 3 therefore demonstrate that superior and inferior temporal cortex, exclusive of the superior temporal

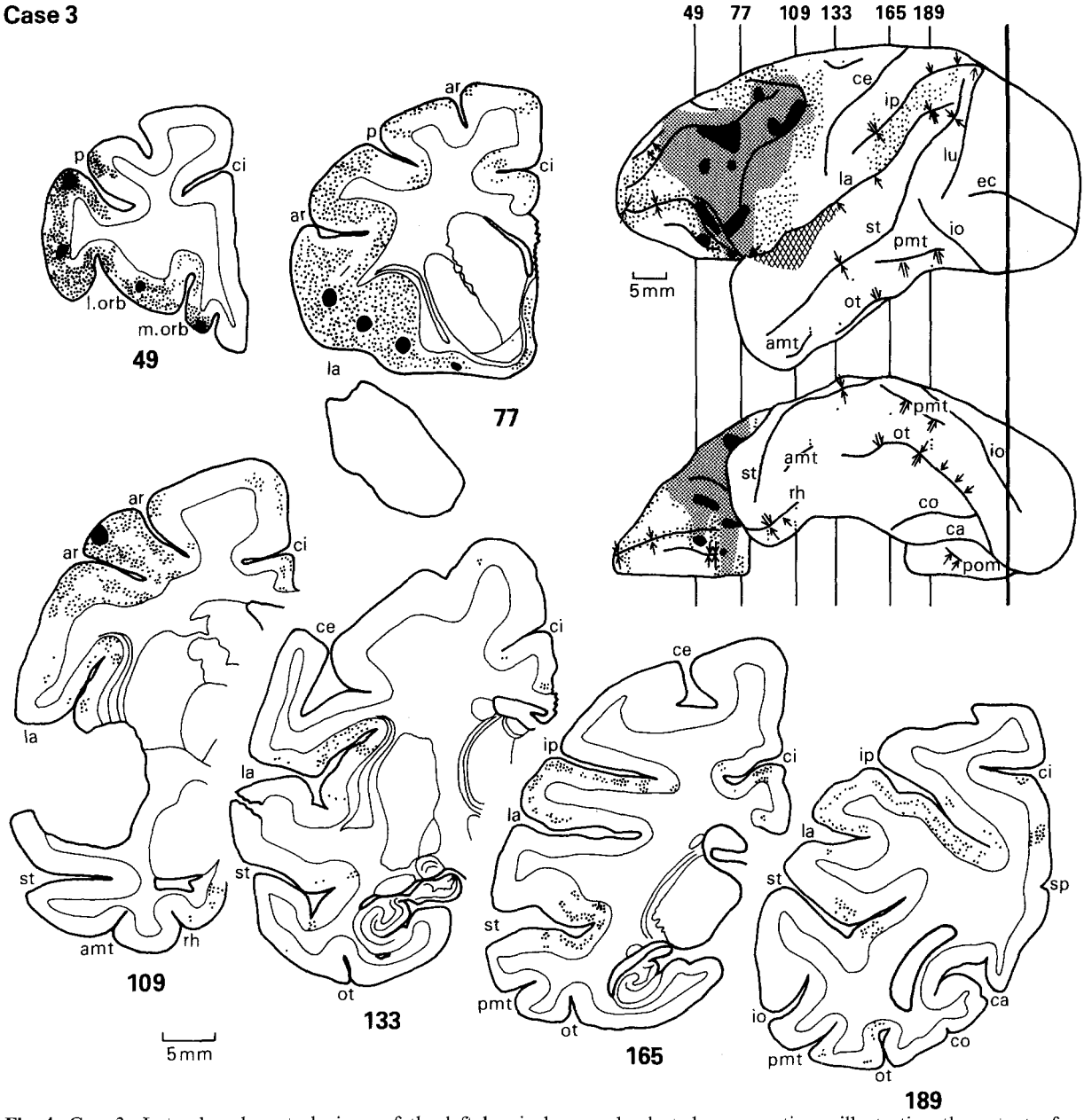


**Fig. 4.** Case 3: Lateral and ventral views of the left hemisphere and selected cross-sections, illustrating the extent of uncinate fascicle transection (cross-hatch on lateral view), sites injected with bisbenzimide (in black), and the distribution of retrogradely labeled cell bodies (dots). See Figs. 1 and 2 for all other conventions and abbreviations

sulcus, project to prefrontal cortex via the uncinate fascicle, but that parietal, insular, and cingulate cortex do not. The results from case 3 also provide strong evidence that the projection from the amygdala to prefrontal cortex is not via the uncinate fascicle. Despite complete transection of the uncinate fascicle, case 3 showed amygdalar labeling in the lateral, lateral basal, medial basal, and accessory basal nuclei that was virtually identical in location and density to the amygdalar labeling seen in cases 2A and 2B, in which the uncinate fascicle was intact. Figure 5 illustrates labeling in the amygdala for cases 2A and 3.

*Case 4*

Although case 4 was prepared to replicate case 3, histological examination revealed that transection of the uncinate fascicle in case 4 was not complete; for approximately 2.5 mm of the 2-cm transection, there was sparing of fibers located medially within the extreme capsule, as indicated by the bold ar-

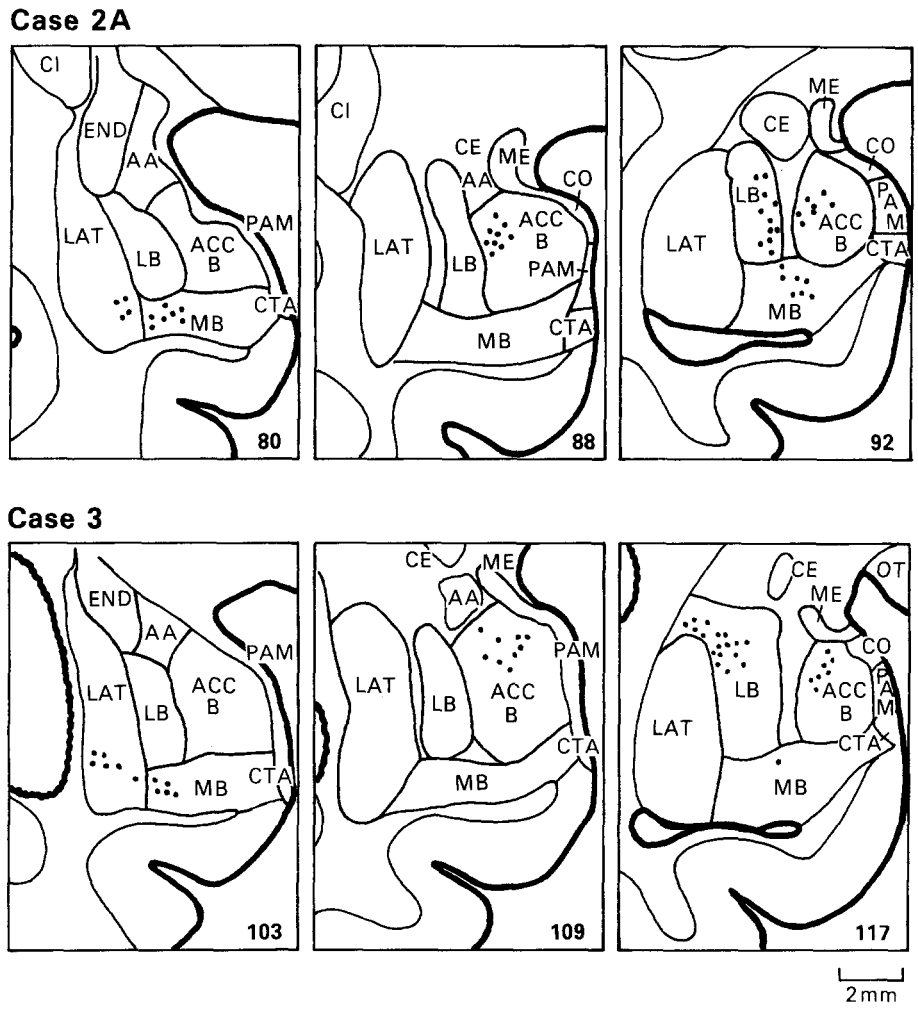


**Fig. 5.** Distribution of retrogradely labeled cells in the amygdala following injections of bisbenzimide into prefrontal cortex of case 2A (upper row), in which the uncinate fascicle was intact, and case 3 (lower row), in which the uncinate fascicle was transected. In case 3, the jagged line at the left of the panels indicates the border of the transection. For both cases, numeral at the lower right of each panel indicates the rostrocaudal level from which the cross-section was taken. Classification of the amygdaloid nuclei is based on the architectural descriptions of the primate amygdala by Crosby and Humphrey (1941). Abbreviations: AA, anterior amygdaloid area; ACC B, accessory basal nucleus; CE, central nucleus; Cl, claustrum; CO, corticoamygdaloid transition area; CTA, cortical transition area; END, endopiriform nucleus; LAT, lateral nucleus; LB, lateral basal nucleus; MB, medial basal nucleus; ME, medial nucleus; OT, optic tract; PAM, periamygdaloid cortex

rows in Fig. 6 (also see bold arrow in section 97). Nonetheless, the distribution of labeled cells in case 4 confirmed the results found in case 3. In case 4, as in case 3, both the superior temporal cortex (area TA) and inferior temporal cortex (area TE) showed only a few scattered labeled cells, while the cortex on the upper and lower banks of the superior temporal sulcus was moderately labeled. In addition, as in case 3, inferior parietal cortex (areas PF and PG) and cingulate cortex (areas 23 and 24) were labeled in case 4, although the labeling in case 4 did not appear to extend as far posteriorly in either region as the labeling in case 3. Finally, the labeling in both the insula and amygdala in case 4 was virtually identical to that found in case 3.

*Case 5*

Although it is known that visual cortical areas posterior to TE, such as prestriate areas V4 and MT, project to prefrontal cortex (Barbas and Mesulam 1981; Ungerleider and Desimone 1986), we saw only a few labeled cells in these areas in our cases with prefrontal injections (e.g. case 2B, Fig. 3, section 185, within area MT in the superior temporal sulcus). This was presumably because these prestriate areas project to the frontal eye field, which is located deep within the arcuate sulcus (Bruce and Goldberg 1985) and was largely excluded from the injection sites. To determine whether prestriate areas project to prefrontal cortex via the uncinate fascicle, we injected a large expanse of area V4 in case 5. In this case, the amino-acid injection site was located on the prelunate gyrus, within the lower quadrant of the central visual field representation of area V4 (Fig. 7). Posterior to the injection site, labeled terminals were located in areas V2 and V3, and, anterior to the injection site, they were located both in area TEO of posterior inferior temporal cortex and in area TE of anterior inferior temporal cortex. As expected, an additional patch of labeled terminals was found within prefrontal cortex on the anterior bank of the inferior limb

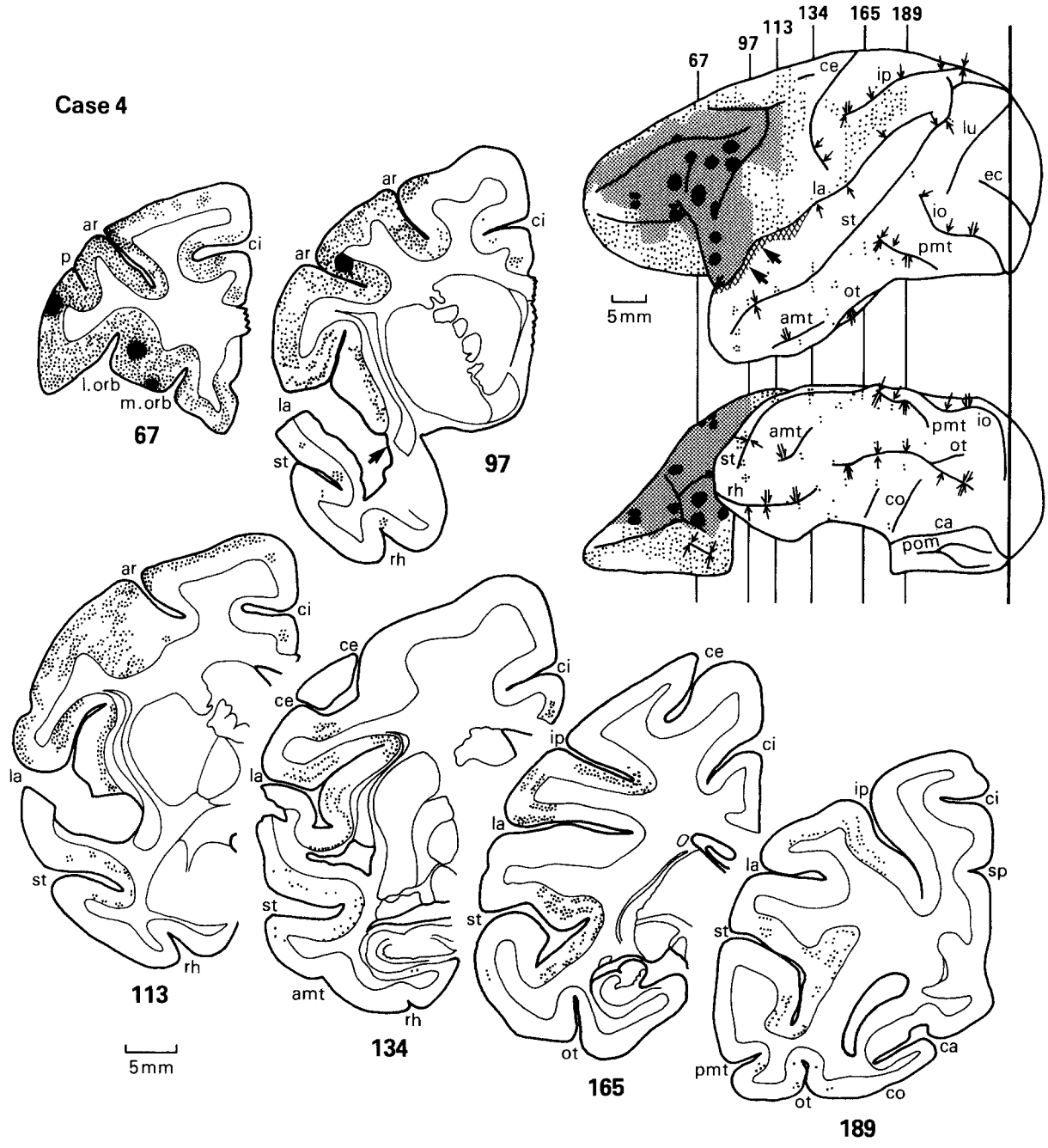


**Fig. 6.** Case 4: Lateral and ventral views of the left hemisphere and selected cross-sections, illustrating the extent of uncinate fascicle transection (cross-hatch on lateral view), sites injected with bisbenzimide (in black), and the distribution of retrogradely labeled cell bodies (dots). The heavy arrows on the lateral view indicate the 2.5-mm region in which fibers of the uncinate fascicle were incompletely transected (also see arrow in section 97). See Figs. 1 and 2 for all other conventions and abbreviations

of the arcuate sulcus. Labeled fibers projecting to prefrontal cortex followed a path from the injection site that coursed rostrally beneath the superior temporal sulcus for approximately 5 mm (Fig. 7, sections 58 and 74), then turned dorsally to course through the claustrum (Fig. 7, sections 94 and 114), and continued forward to their targets on the anterior bank of the arcuate sulcus. Thus, the projection to prefrontal cortex from area V4 is not via the uncinate fascicle.

Labeled fibers in case 5 could also be traced to their terminations in the claustrum and genu of the caudate nucleus (Fig. 7, sections 114 and 74, respectively), ventral putamen, pulvinar, and superior colliculus (data not shown), as well as to the contralateral hemisphere in the splenium of the

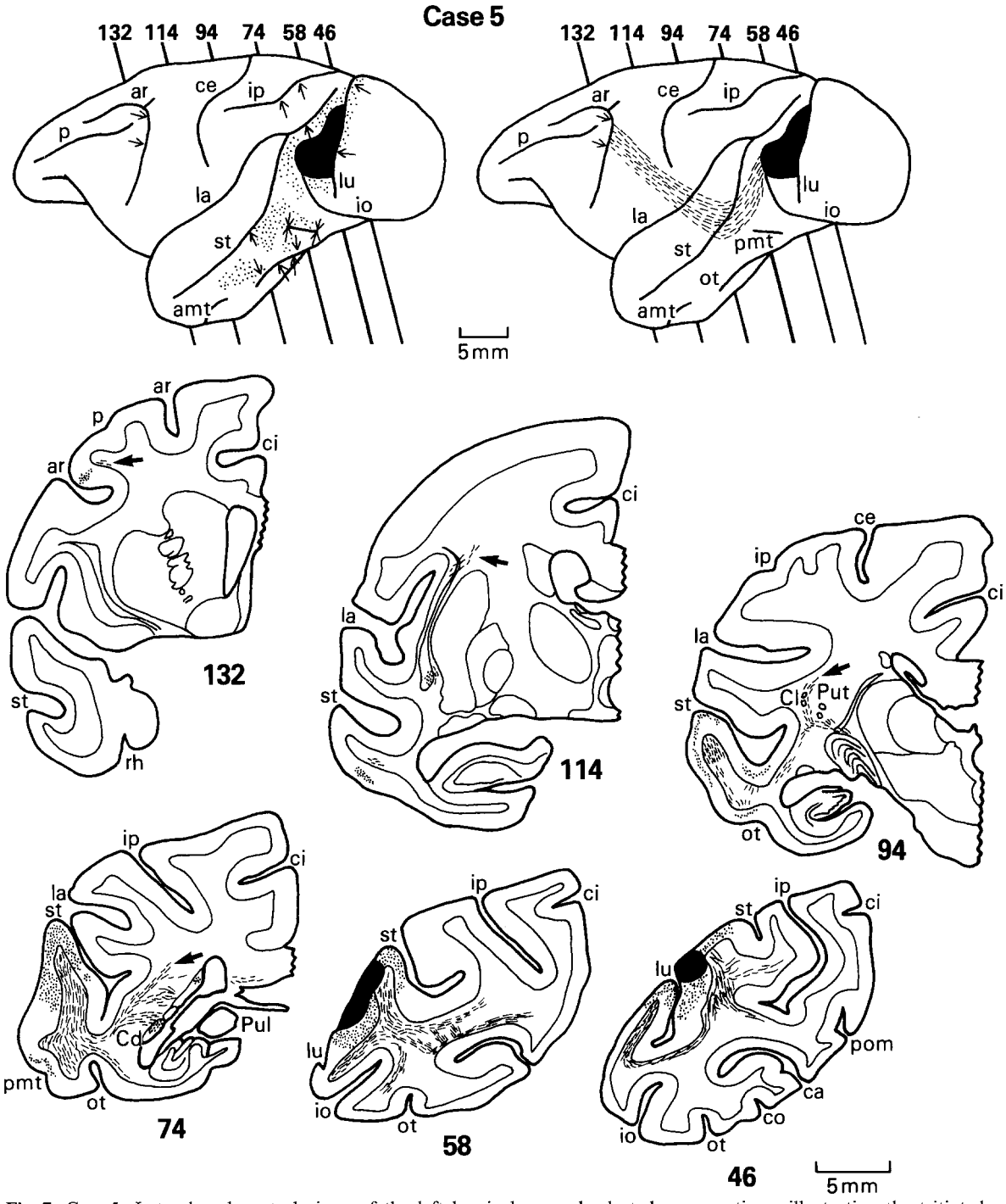


**Fig. 7.** Case 5: Lateral and ventral views of the left hemisphere and selected cross-sections, illustrating the tritiated amino-acid injection site (in black) and the distribution of anterogradely labeled terminals (dots) and fibers (dashed lines). In the cross-sections, heavy arrows indicate labeled fibers projecting to prefrontal cortex (see sections 74–132). See Fig. 1 for all other conventions and abbreviations

corpus callosum (Fig. 7, section 74). In none of these cases did the projecting fibers course through the uncinate fascicle.

## Discussion

The present study was undertaken to examine the projection from inferior temporal cortex to the frontal lobe, and, in particular, to delineate the course of the projecting fibers. Autoradiographic results from case 1 demonstrated that inferior temporal cortex, or architectonic area TE, projects to both the inferior convexity of prefrontal cortex as well as to the lateral portion of the orbital surface, which is in good agreement with the results of earlier degeneration studies (Kuypers et al.

1965; Jones and Powell 1970; Chavis and Pandya 1976; Jacobson and Trojanowski 1977). In addition, all fibers projecting to prefrontal cortex in case 1 were found to course through the uncinate fascicle.

Cases 2–4 were prepared to determine the extent to which interactions between the inferior temporal cortex and prefrontal cortex depend on the uncinate fascicle. Retrograde labeling after fluorescent dye injections of prefrontal cortex in these cases demonstrated that the inferior convexity and lateral orbital surface receive direct projections not only from inferior temporal cortex, but also from the anterior portion of superior temporal cortex, the inferior parietal cortex, the cingulate cortex, and the insula, confirming prior reports (Jones and Powell 1970; Chavis and Pandya 1976; Jacobson and Trojanowski 1977; Pandya et al. 1981; Petrides and Pandya 1984, 1988), but only those fibers arising from the inferior temporal and anterior superior temporal cortex pass through the uncinate fascicle. Recently, Petrides and Pandya (1988) similarly found that fibers projecting from the anterior portion of the superior temporal gyrus to prefrontal cortex travel as part of the uncinate fascicle. Taken together, the results thus indicate that transection of the uncinate fascicle disconnects virtually all of the inferior temporal cortex and the anterior portion of the superior temporal cortex from their prefrontal targets.

Transection of the uncinate fascicle does not, however, disconnect cortex within the superior temporal sulcus from its prefrontal targets. In cases 3 and 4, in which the uncinate fascicle was transected, the distribution and density of labeling in the banks of the superior temporal sulcus was comparable to that found in cases 2A and 2B, in which the uncinate fascicle was intact, indicating that this portion of the temporal lobe projects to prefrontal cortex via a route other than the uncinate fascicle. While the upper bank of the superior temporal sulcus is polysensory (Bruce et al. 1981), the lower bank is exclusively visual and therefore considered to be part of area TE (Desimone and Gross 1979). Apparently, the projecting fibers arising from this portion of area TE remain separate from those arising from the remainder of the area. Whether these separately projecting pathways have functional relevance remains to be seen. However, we have recently found that the superior temporal sulcal portion of area TE is connected with occipito-parietal cortical areas, while the remainder of area TE is not (Boussaoud et al. 1987), which is suggestive of functional segregation within TE.

Although the inferior temporal cortices of cases 3 and 4 were largely devoid of labeled cells as a result of uncinate fascicle transection, in both cases the absence of labeling was not absolute. A few scattered cells were found along the entire extent of area TE, but seemed to be most prevalent in the anterior portion of the area. Because transection of the uncinate fascicle was complete in case 3, the axons arising from these labeled cells must have traveled outside the uncinate fascicle. Although the route of these axons to prefrontal cortex is unknown at present, it is possible that they coursed through the amygdala and then, like amygdalar cells projecting to prefrontal cortex, traveled via the external capsule (Amaral and Price 1984), in contradistinction to the route for temporal cortical projecting fibers, which is through the extreme capsule. In this connection, it is important to note that we found amygdalar labeling unaffected by uncinate fascicle transection, which is further evidence that the uncinate fascicle does not carry amygdalo-frontal projections. Interestingly, despite the fact that there was some sparing of the uncinate fascicle in case 4, the absence of labeling within the inferior temporal cortex in this case was just as profound as in case 3, in which the transection was complete. It would therefore appear that the locus and extent of sparing in case 4 was insufficient to preserve a temporo-frontal connection.

While transection of the uncinate fascicle may effectively interrupt temporo-frontal interactions, the results from cases 3–5 indicate that such transection does not interrupt the flow of information to the frontal lobe from a number of visual processing areas outside TE, including those within inferior parietal and prestriate cortex. In addition, such transection also leaves intact many other outflow pathways from the inferior temporal cortex. Thus, pathways projecting from area TE to the amygdala, tail of the caudate nucleus, ventral putamen, and pulvinar should be largely unaffected by uncinate fascicle transection.

From these findings, one might expect that, in the visual domain, the functional effects of uncinate fascicle transection would be quite selective. Recent behavioral experiments have found that the involvement of the frontal lobe in visual learning is particularly important for conditional rule-learning, in which visual information must be combined with other sources of information (Gaffan and Harrison 1988, 1989). Thus, one functional role of the uncinate fascicle may be to facilitate the use of visual information in conditional rule-learning, a hypothesis we are currently testing.

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