Commissural Columns in the Sensory-Motor Cortex of Monkeys [1]

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ABSTRACT Callosally projecting cells and the terminal ramifications of their axons were identified in the monkey sensory-motor cortex by retrograde and anterograde labeling techniques, often by double labeling cells and axons in the same animal.

Bundles of callosal fibers terminate in small column-like zones 0.5-1 mm wide in the motor cortex (area 4) and in the first (SI) and second (SII) somatic sensory areas. Such columns are aligned in register to form elongated strips extending mediolaterally in the long axes of the pre- and postcentral gyri. Significant portions of area 4, SI and SII, in regions corresponding to the representations of the hand and foot, are not callosally connected.

The cells of origin of callosal fibers in SI are largely confined to layer IIIB and form columns and strips corresponding to the above. In connected zones of SI, the callosal connection is reciprocal and precisely point-to-point. This and the laminar distribution of the terminal ramifications of callosal fibers (to layers I-IV) suggest that callosal fibers may arise from and terminate upon exactly homotopic, column-like groups of layer IIIB pyramidal cells.

Commissurally projecting cells and their terminal ramifications are not limited to particular architectonic fields or particular parts of fields in SI. All architectonic fields of SI project heterotopically to the contralateral SII.

More than 20 years of work has been devoted to elucidating the functional capacities of the cerebral hemispheres disconnected by section of the corpus callosum and other forebrain commissures (Sperry, '61, '74; Gazzaniga, '70). Despite the importance of the findings that have emerged from this work, relatively little is known about the functions of the largest commissure, the corpus callosum, in the intact brain. In the visual cortex, it seems clear that callosal fibers serve to ensure the fusion of images across the midline of the visual field (Choudhury et al., '65; Berlucchi et al., '67; Hubel and Wiesel, '67; Berlucchi and Rizzolatti, '68; Berlucchi, '72). In the auditory cortex, callosal fibers seem to provide for a particular type of interaction between inputs from the two ears (Imig and Brugge, '78). But apart from a number of other interesting suggestions (e.g., Kaas et al., '67; Mishkin, '78), these two examples probably remain the only conclusive demonstrations of commissural function in experimental animals.

Though relatively few insights into commissural functions have yet emerged, the corpus callosum nevertheless furnishes a striking example of the precision of connections that can be found in the nervous system. Commissural fibers are distributed only to selected portions of the representations of the visual field, body surface or auditory periphery (Myers, '62; Ebner and Myers, '65; Garey et al., '68; Jones and Powell, '68, '69; Hughes and Wilson, '69; Diamond et al., '69; Pandya and Vignolo, '69; Zeki, '70; Shatz, '78). Curiously,

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in the somatic sensory cortex, at least, the parts devoid of callosal connections seem to vary among species (Yorke and Caviness, '75; Wise and Jones, '76). Within the connected regions, callosal fibers terminate in a pronounced columnar fashion (Jones et al., '75; Shanks et al., '75, '78; Künzle, '76; Goldman and Nauta, '77; Imig and Brugge, '78) that resembles the well-known ocular dominance colunms that are formed by the thalamic input to the striate cortex (Hubel and Wiesel, '77).

The cells of origin of these callosal fibers have now been identified (Jacobson and Trojanowski, '74; Shoumura, '74; Jones et al., '75; Lund et al., '75; Yorke and Caviness, '75; Wise and Jones, '76; Jones and Wise, '77). Though their laminar distribution tends to differ among species and from area to area, these cells are found only in the columnar zones that receive the callosal fibers arising in the other hemisphere (Jones et al., '75; Wise and Jones, '76). In the somatic sensory cortex of rodents, these reciprocally connected zones can be correlated with a particular type of cortical architecture and are largely separate from the zones of major thalamic input (Akers and Killackey, '78; Wise and Jones, '78).

All of the above points indicate a rigid structuring of the callosal system, a structuring that may vary in relation to representational, cytoarchitectonic and species differences and in association with other connections. If the principles governing this rigid structuring could be elucidated, new insights into the functions of the corpus callosum might emerge, but, in addition, the system might serve as a paradigm for studying how connections could be manipulated during growth and development (Wise and Jones, '76, '78).

The present paper deals with the total pattern of callosal cell and fiber distribution in the sensory-motor regions and with some of the finer details of the connectional patterns in the first (SI) and second (SII) somatic sensory areas. Comparable details in the motor cortex (area 4) are provided by the accompanying paper (Jenny, '79). A preliminary account has appeared (Jones et al., '75) and details of thalamic and ipsilateral corticocortical connectivity in the same brains have also been published (Jones et al., '78, '79).

MATERIALS AND METHODS

This investigation was carried out in four rhesus monkeys *(Macaca mulatta),* 43 cynomolgus monkeys *(M. fascicularis)* and 21 squirrel monkeys *(Saimiri sciureus).* Experiments were carried out using the axonal degeneration technique, autoradiography and the horseradish peroxidase technique.

Axonal degeneration was used to "label" the total complement of callosally projecting axons of the sensory-motor regions in three cynomolgus and four squirrel monkeys. Under Nembutal anesthesia and with aseptic precautions, one hemisphere was gently retracted and the corpus callosum divided with a fine, suction-pipette. After a 6-day survival period, the brains were fixed by perfusion with 10% formol-saline. Not less than one month later, frozen sections were cut parasagittally at 30 μm and every third or every fifth stained for degenerating axons by means of the Wiitanen ('69) technique. Alternating series of sections were stained with thionin.

Autoradiography was also used as an anterograde axonal label. Equal parts mixtures of [^{3}H] leucine and [^{3}H] proline were injected at single or multiple sites in the first somatic sensory area and in certain adjacent areas. The labeled amino acids, which had specific activities ranging from 17-45 Ci per mmole, were evaporated and reconstituted in normal saline to give a final concentration of 50 μCi per μl. They were then injected into the cortex in volumes ranging from 0.03-1 μl, either through a 1-μl Hamilton syringe with a microdrive or with air pressure through micropipettes having tip diameters of 20-50 μm. Injections were made in the known representations of the face, hand, trunk and foot, in some instances after first identifying the representation by recording a multi-unit, evoked response to peripheral somesthetic stimuli. Most of the injections were confined to single cytoarchitectonic fields (areas 3a,b, 1, 2, 4, 5). Some injections were single and small; others,

Abbreviations

CS, Central sulcus
CgS, Cingulate sulcus
Ig, Granular insular cortex
IPS, Intraparietal sulcus
LS, Lateral sulcus
PCS, Postcentral sulcus
Ri, Retroinsular cortex
SI, First somatic sensory area
SII, Second somatic sensory area
tr, Transitional cortex
1-7, Numbered areas of cerebral cortex
I-VI, Layers of cerebral cortex

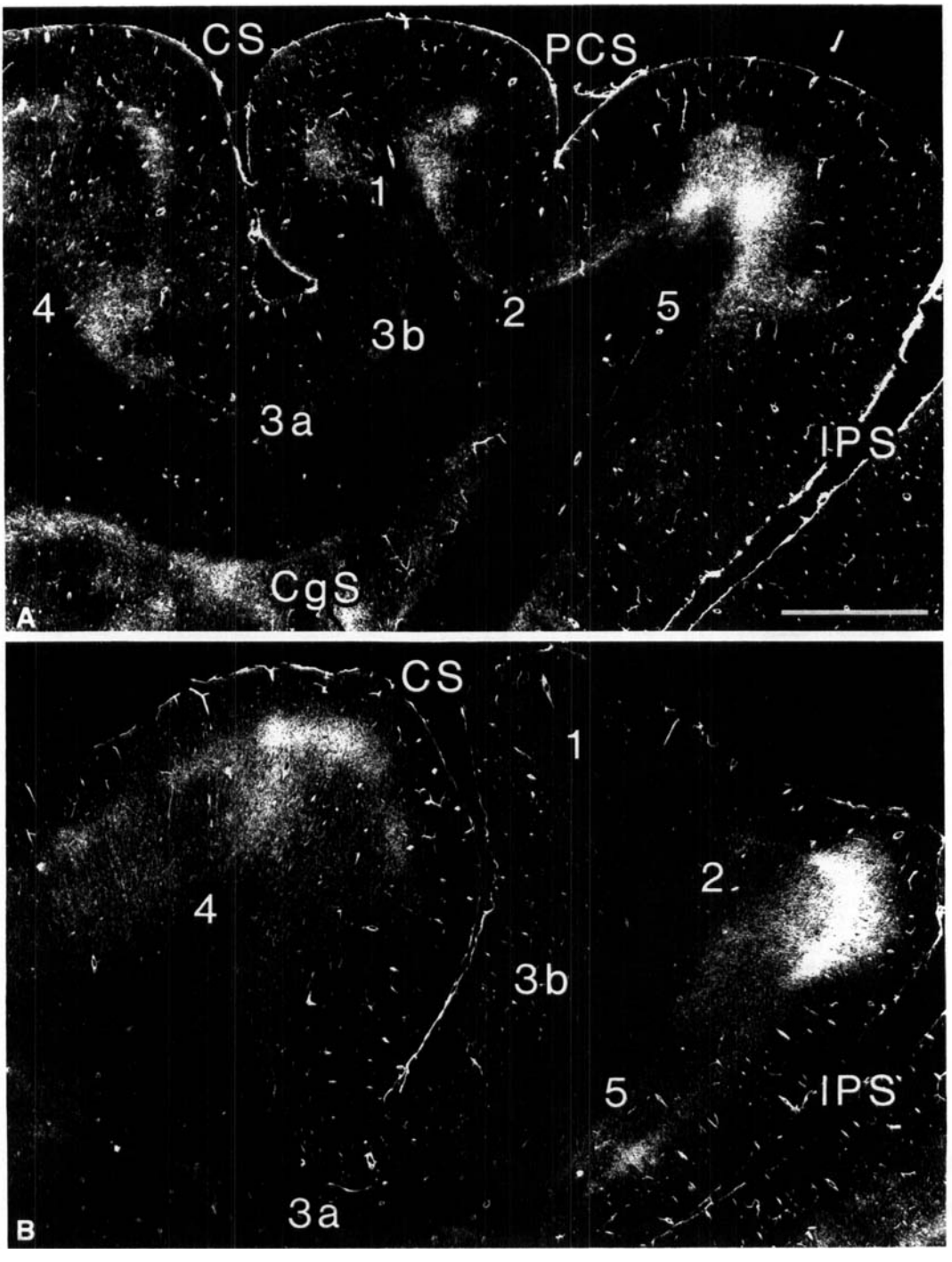

Fig. 1 A,B. Darkfield photomicrographs from sagittal sections of a cynomolgus monkey brain in which the corpus callosum had been cut six days previously. A is through the middle of the postcentral sulcus (PCS), B is 5.5 mm lateral. White areas are columns of degenerating callosal fiber ramifications stained by the Wiitanen method. Architectonic field designations added from examination of an adjacent Nissl-stained section. Degeneration at bottom left in A is in floor of cingulate sulcus. Bar represents 2 mm.

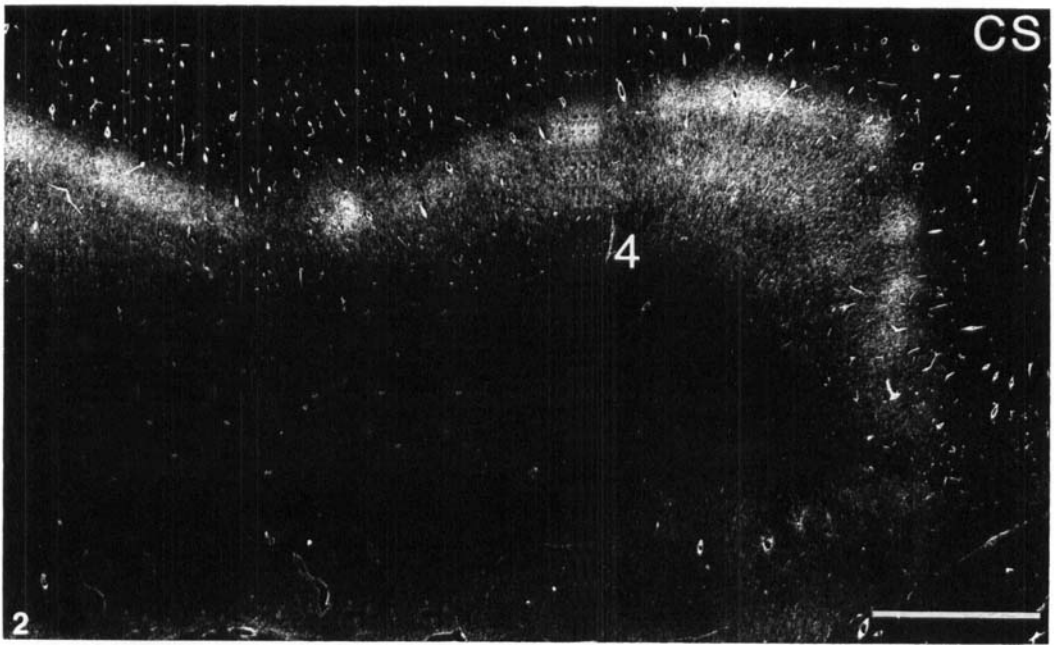

Fig. 2 Sagittal section from motor cortex of same brain illustrated in figure 1 and 3.3 mm lateral to figure 1A, showing multiple columns of callosal degeneration. Bar represents 2 mm.

though individually small, were made in a mediolateral row of up to 14 penetrations so as to involve as much as possible of an individual field without spread to adjacent fields (Jones et al., '78a,b).After survival periods of one, six or seven days, the brains were fixed by perfusion with formol-saline. Thereafter, 20-μm thick paraffin sections were cut parasagittally or horizontally and sections at 100 or 200 μm intervals mounted and dipped in Kodak NTB2 emulsion for autoradiography (Cowan et al., '72). Exposures were for 2, 6 or 12 weeks at 4°C, after which the autoradiographs were developed in Kodak D19, fixed, and stained through the emulsion with thionin.

In two cynomolgus monkeys, five days after cutting the corpus callosum and 12 to 24 hours before killing the animal, tritiated amino acids were injected into the hand area of SI in one hemisphere. Subsequently, alternate frozen sections were stained for axonal degeneration or prepared for autoradiography.

Horseradish peroxidase was used as both a retrograde and as an anterograde marker. Injections of 50% horseradish peroxidase (Type VI, Sigma) in normal saline were made by methods similar to those using tritiated amino acids and described above. After survival periods of 24 or 48 hours the brains were fixed by perfusion with phosphate buffered 0.5-1% paraformaldehyde and 1.5-2.5% glutaraldehyde. Thereafter, frozen sections 50 μm thick were cut parasagittally or horizontally and one-in-two or one-in-five incubated with dilute hydrogen peroxide in one or more of the following substrates: 3,3' diaminobenzidine tetrahydrochloride (La Vail et al., '73), benzidine dihydrochloride (Mesulam, '76), tetramethyl benzidine (Hardy and Heimer, '77) or a freshly made mixture of paraphenylene-diamine and catechol (Hanker et al., '77). All substrates were efficacious for demonstrating retrograde cell labeling though the intensity of labeling was often less with diaminobenzidine than with the others. Tetramethyl benzidine and the Hanker-Yates mixture were also used at long incubations (4-6 hours), with con-

Fig. 3 Surface reconstruction made from Wiitanen-stained sagittal sections of a cynomolgus monkey brain following callosotomy. Short lines represent column-like patches of degeneration as seen in single sections. Rows of stars indicate floors of inferior precentral, central, postcentral and intraparietal sulci. Rows of dotted lines indicate borders of architectonic fields plotted from adjacent Nissl-stained sections. Arrows indicate (from above down): cingulate sulcus, medial border of hemisphere, lateral margin of hemisphere, floor of lateral sulcus. Note strip-like organization of callosal columns and zones devoid of such strips in foot and hand representations.

Figure 3

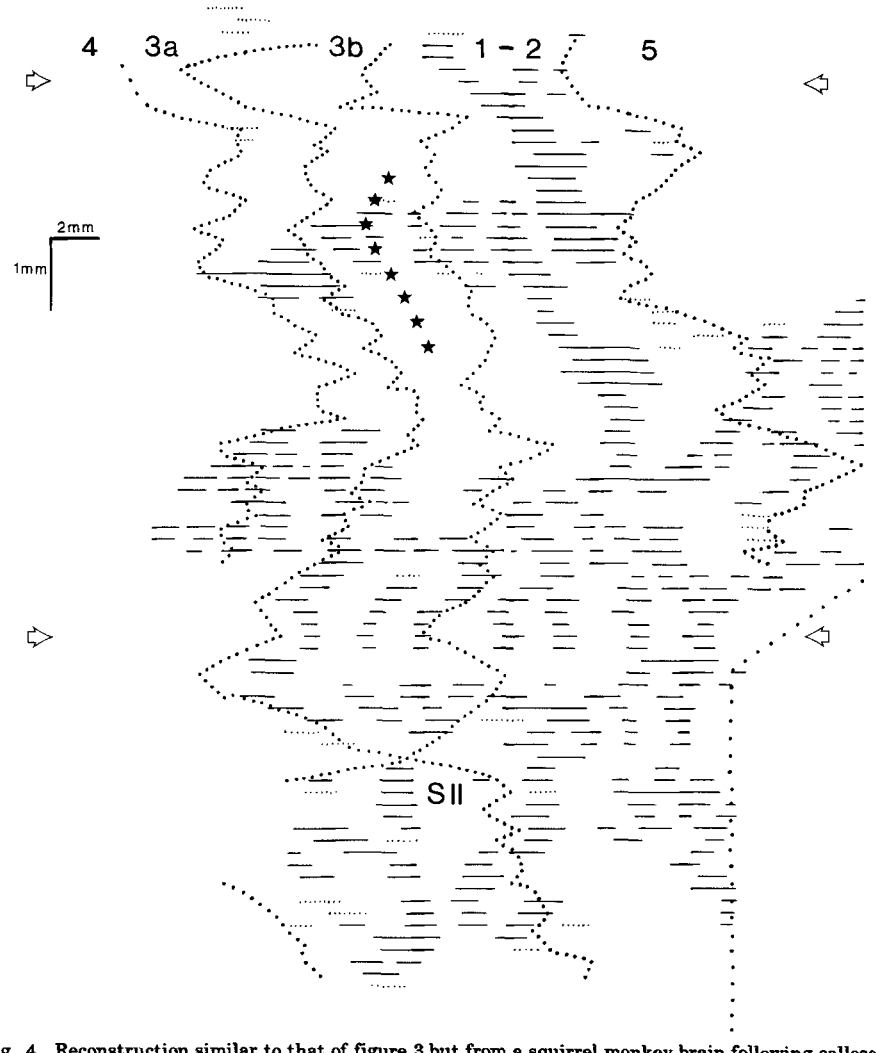

Fig. 4 Reconstruction similar to that of figure 3 but from a squirrel monkey brain following callosotomy. Row of stars indicates floor of central sulcus. Arrows indicate medial and lateral borders of hemisphere.

tinuous renewal of the hydrogen peroxide, to promote intense anterograde axonal labeling. All sections were counterstained with thionin except where anterograde labeling was deliberately promoted. There, the incubated sections were left unstained and an immediately adjacent section, either incubated or not, was stained with thionin.

In two squirrel monkeys, horseradish peroxidase and tritiated amino acids were injected together at the same site and subsequently frozen sections, after incubation in diaminobenzidine, were prepared for autoradiography.

In experiments of all types, the extents of injection sites and the distributions of labeled axons and/or cells were reconstructed on surface maps of the sensory-motor regions, prepared from projection drawings as previously described (Jones et al., '75, '78; Jones and Wise, '77).

RESULTS

Total distribution and columnar organization of callosal fibers

The total distribution of callosal fibers is best demonstrated by experiments in which the corpus callosum was cut and the degenerating fibers were stained by the Wiitanen

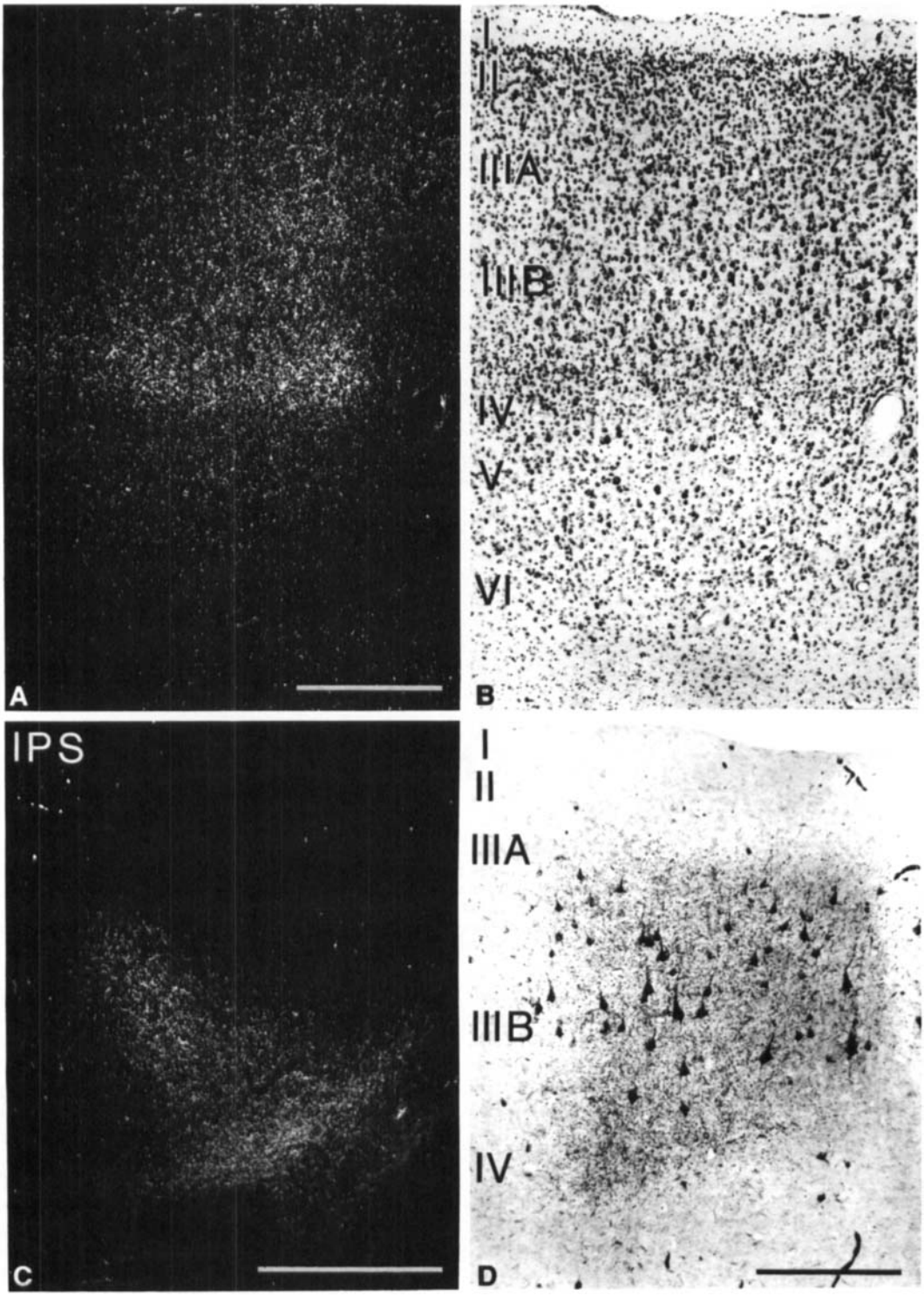

Fig. 5 A,B. Darkfield and brightfield photomicrographs from same part of area 1 of a squirrel monkey brain, showing restriction of axoplasmically transported "terminal" labeling to granular and supragranular layers following injection of [^{3}H] amino acids at a homotopic point in the contralateral hemisphere. C. Similar column of autoradiographic labeling from area 2 in floor of intraparietal sulcus, following a homotopic injection. D. Exact correspondence of retrograde and anterograde labeling in area 1 following injection of horseradish peroxidase at a homotopic site. Uncounterstained, tetramethylbenzidine substrate, cynomolgus monkey. In A-C, bar represents 500 μm; in D, 250 μm.

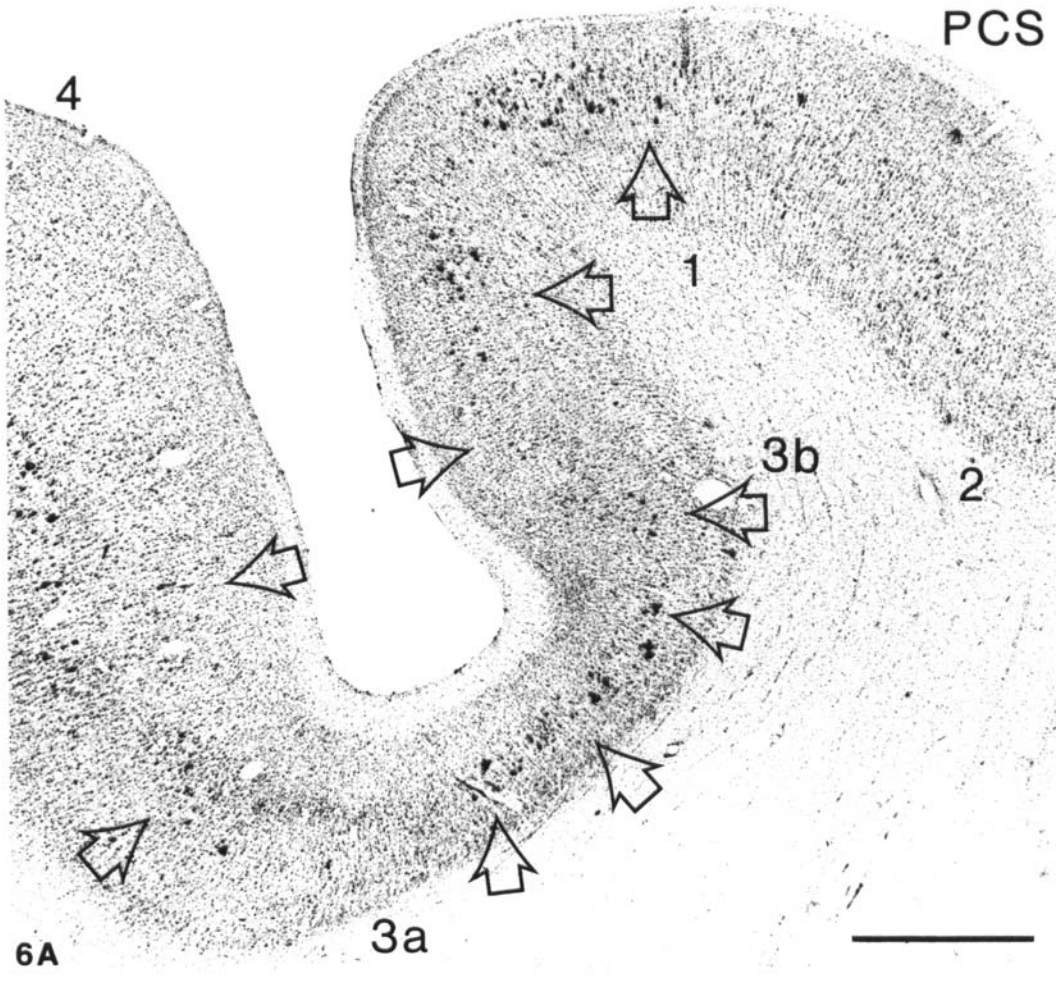

Fig. 6A Sagittal section through the lateral end of the postcentral sulcus (PCS) indicating retrogradely labeled cells in areas 4, 3, 1 and 2 following a large injection of horseradish peroxidase contralaterally, centered in SI trunk representation. Labeled cells (arrows) are found in most parts of areas 3 and 1. All are in layer III. Cynomolgus monkey, tetramethylbenzidine, thionin counterstain. Photomicrograph slightly underexposed to enhance labeled cells. Betz cells in area 4 are not labeled but are intensely stained with thionin.

technique (figs. 1-4, 11). In a series of sagittal sections, especially when examined under darkfield conditions (figs. 1, 2, 11), two features are obvious. First, large parts of the postcentral and certain parts of the precentral gyrus and superior parietal lobule, are completely free of the characteristic dust-like patches that indicate degenerating terminal ramifications (figs. 1, 2). Second, where such "terminal" degeneration is present, it tends to form multiple, clumped patches (figs. 1, 2). These are particularly well seen across the antero-posterior extent of the precentral gyrus (fig. 2), in the banks of the intraparietal sulcus and (in tangential array) in the face and tail representations of SI (fig. 1). Where multiple patches are seen in a single section, they are consistently 0.5-1 mm wide and separated from their neighbors by gaps of varying degrees of completeness, measuring 0.25-0.5 mm. The widest patches appear in area 2 close to the lip of the intraparietal sulcus (fig. 1), the narrowest in parts of area 3 in the floor of the central sulcus (fig. 10). The most regularly-sized and spaced are in area 4 (fig. 2). Each patch consists of large numbers of mainly vertical degenerating axons traversing layers VI and V of the cortex and ending in a

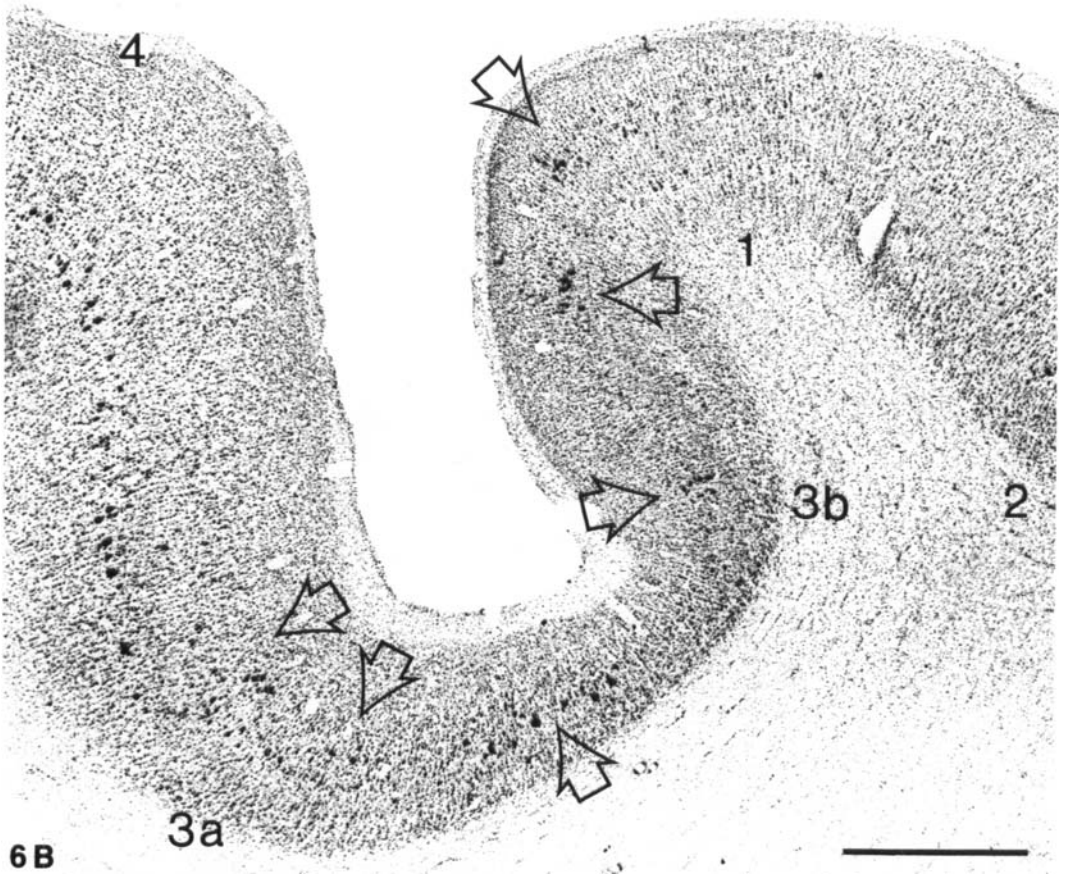

Fig. 6B Section 2 mm lateral to that shown in figure 6A showing reduction in number of labeled cells. In A and B, bar represents 1 mm.

dense mass of dust-like "terminal" particles in layers II-IV (figs. 1, 2). Where patches appear in the floor of a sulcus such as the central or intraparietal, degenerating axons may be obliquely oriented with respect to the parasagittal plane and, thus, the axons and the terminal patch to which they give rise can appear in different sections. This is shown in figure 1A where degenerating axons appear in the floor of the postcentral sulcus but there is no corresponding terminal degeneration in the overlying layers.

Surface reconstructions of the type illustrated in figures 3 and 4 when compared with figure 13D, show the relationship of the acallosal zones to the traditional representation maps in SI and area 4 as determined by evoked potentials and surface stimulation (Woolsey, '58). They also indicate that the column-like terminal patches of callosal degeneration are aligned in register so as to form strips oriented more or less mediolaterally across the pre- and postcentral gyri.

In the macaque monkeys, patches of cortex completely devoid of callosal degeneration occupy two parts of the postcentral gyrus. One, extending approximately from the level of the anterior end of the intraparietal sulcus to the lateral end of the postcentral sulcus, is interpreted as the greater part of the representation of the hand, as demonstrated in classical evoked potential maps. The second, extending approximately from the level of the medial end of the postcentral sulcus to a little beyond the medial margin of the hemisphere, is interpreted as the representation of the foot. Posterior to the SI cortex, similar degeneration-free patches are also present in area 5.

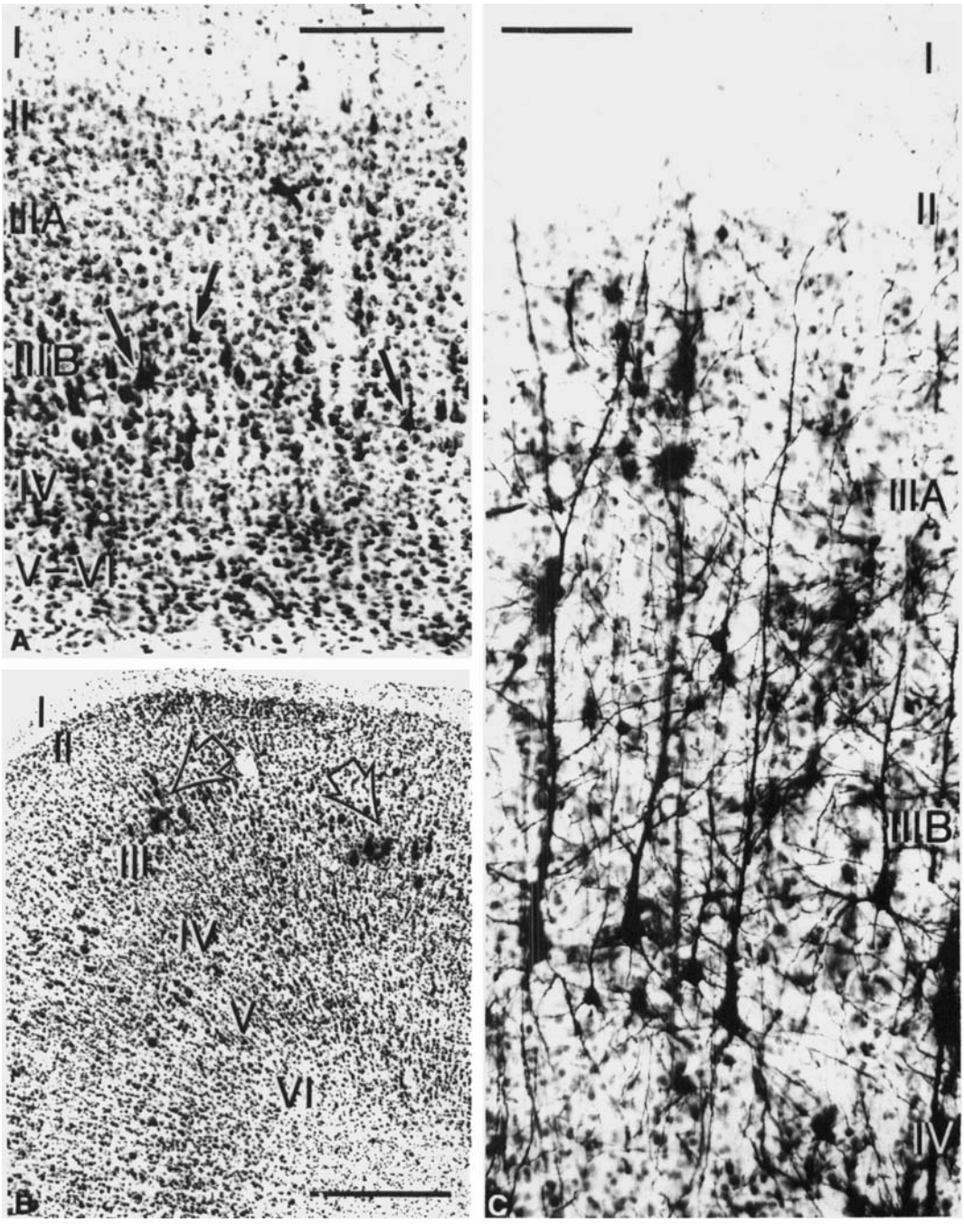

Fig. 7A. Retrogradely labeled cells (arrows) in floor of intraparietal sulcus, homotopic to an injection of horseradish peroxidase. Many unlabeled cells of layer IIIB are of approximately same size. Cynomolgus monkey, benzidine, thionin counterstain. Bar represents 250 μm. B. Two columns (arrows) of retrogradely labeled cells in area 1 following a single injection of horseradish peroxidase at a homotopic site. Cynomolgus monkey, tetramethylbenzidine, thionin counterstain, bar represents 500 μm. C. Golgi-Cox preparation, counterstained with thionin to show dendritic ramifications of large layer IIIB pyramids, many of which have callosally projecting axons. Area 1, cynomolgus monkey. Bar represents 100 μm.

These are to a large extent directly continuous with the bare patches in SI, though that in relation to the hand representation is displaced medially and is split into two zones by a strip of callosal degeneration.

Anteriorly, the degeneration-free patches extend through area 3a in the floor of the central sulcus [5] into the motor cortex (area 4). In area 4, the bare patches are relatively less extensive than in SI. That in relation to the foot representation does not extend out of the anterior bank of the central sulcus. That in relation to the hand representation, though largely in the central sulcus, reaches the summit of the precentral gyrus.

In squirrel monkeys, the pattern of callosal degeneration follows a pattern similar to that in the macaques (fig. 4).

The strips formed by the alignment in register of the degenerating bundles of callosal fibers are of variable length and their numbers vary from one part of the representation to another. The longest and most complete strips are found in area 4. There, they are aligned essentially in the long axis of the precentral gyrus, though strips that are on the surface of the gyrus in the middle part of its medio-lateral extent tend to incline posterolaterally and descend into the anterior bank of the central sulcus laterally. In macaques, up to nine strips appear but they tend to separate from and reunite with one another at intervals so that the number is variable. At the edges of the unconnected zones of area 4, the more posterior strips generally end blindly so that the total number of strips is reduced in adjacent zones.

In SI the longest strip is found running almost uninterruptedly along the posterior border of SI, though it becomes much reduced and in some places absent, at the posterior border of the unconnected hand representation (fig. 3). Elsewhere in SI, shorter strips appear, with a general orientation in the long axis of the post-central gyrus (fig. 3). These strips bear no consistent relationship to the architectonic fields of SI as we identify them (Jones et al., '78a). In connected zones, they occupy parts of area 3b, 1 and 2. A single strip in area 3b tends to remain within that area but in areas 1 and 2, a single strip can extend from one field into the other. The strips are not concentrated at the borders of the fields.

The unconnected zones in SI, similarly, incorporate parts of areas 3b, 1 and 2.

The callosal columns also form strips in areas 6 and 5 and in SII. In these areas their orientation is a little less regular than in area 4 or SI, but there is a tendency for them to follow the same mediolateral orientation as those in the other areas (figs. 3, 4, 9). Unconnected zones in all three areas and in the part of area 6 previously identified (Jones and Powell, '68; Jones et al., '78a) as the supplementary motor area of Woolsey ('58), are thought to correspond to hand and foot representations.

Finer organization of the columns

The extent of the terminal ramifications within the columns of callosal fibers is clearly visible in material stained for axonal and terminal degeneration and in material in which callosal axons are anterogradely labeled with horseradish peroxidase (figs. 1, 2, 5D). But finer details of the distribution within a column are provided by the autoradiographic material (figs. 5A-C). Depending on their size, single injections of isotopically labeled amino acids made in appropriate parts of the cortex (see below) lead to transported label in one or more columns in the contralateral cortex. Generally speaking, any injection of 1 mm^2 or less in extent labels only one commissural column. Larger injections label more. At short survivals (12-14 hours), labeling of terminal ramifications tends to exceed that of the parent axons. This shows that the terminal ramifications are very sharply confined to the granular and supragranular layers, at least in SI, SII and the parietal cortex (figs. 5A-D). There is virtually no labeling in the infragranular layers. Each labeled column at these survivals consists of a dense band, co-extensive with layer IV and forming the widest part of any column. The column narrows in layer III and many of the grains are aligned vertically; this part of the column splays out again in the upper part of layer III and extends into layer II and the deeper part of layer I. There, it may become as wide again as in layer IV, but, in comparison with layer IV, the grain density is markedly diminished. In some of the wider columns, particularly in SI at the lip of the intraparietal sulcus, two vertical components may ascend from a common, wide layer IV component (fig. 1).

At longer survival periods (6-7 days), the autoradiographically labeled columns have a similar shape but the density of grains is high-

[5] For our definition of area 3a, see Jones et al. ('78a,b).

er. Though labeled axons are now clearly visible in layers V and VI, they do not obscure the basic shape and position of the column of "terminal" labeling in layers I-IV.

Columns of autoradiographic labeling at all survival periods in areas 4 and 6 are not so clearly confined to the more superficial layers of the cortex. Though the "terminal" labeling is clearly concentrated in layers I-III with its greatest density in the deeper part of layer III, a certain amount of diffuse label, resembling labeling of terminal ramifications, is also seen among the labeled axons in the deeper layers.

Reciprocity of commissural columns in SI

Injections of horseradish peroxidase, of varying sizes and made into SI, demonstrate by retrograde transport the cells of origin of the callosal projection to this area. As previously described (Jones et al., '75; Jones and Wise, '77), they are almost exclusively the larger pyramidal cells that are concentrated in the deeper half to two-thirds of layer III (layer IIIB, figs. 5D, 6, 7, 10) in areas 3, 1 and 2. By using substrates more sensitive than diaminobenzidine, we have been able in very rare sections to demonstrate a small number of callosally projecting cells in layer VI of SI. The number is always extremely small in comparison with the number labeled in layer III and very small in comparison with the rather high proportion of commissurally projecting cells observed in layer VI of the motor cortex following injections of the contralateral area 4 (P. L. Strick, personal communication and our own unpublished observations).

Even our largest injections of horseradish peroxidase in macaques involved only a relatively small proportion of the body representation in SI. The largest affected the trunk and hand or the trunk and foot representations (figs. 6, 8, 9). Following such injections, the distribution of retrogradely labeled cells in the appropriate parts of the contralateral cortex follows a pattern very similar to that shown for the distribution of callosal fibers in the axonal degeneration experiments. In single sagittal sections, the retrogradely labeled cells form column-like clusters 0.25-0.75 mm wide, clearly in positions comparable to those in which anterogradely labeled axonal columns are seen. The sizes of the cell columns at different sites also vary in much the same manner as the axonal columns. Among the labeled cells that form the column, there are usually many other layer IIIB cells of comparable size that are unlabeled (fig. 7).

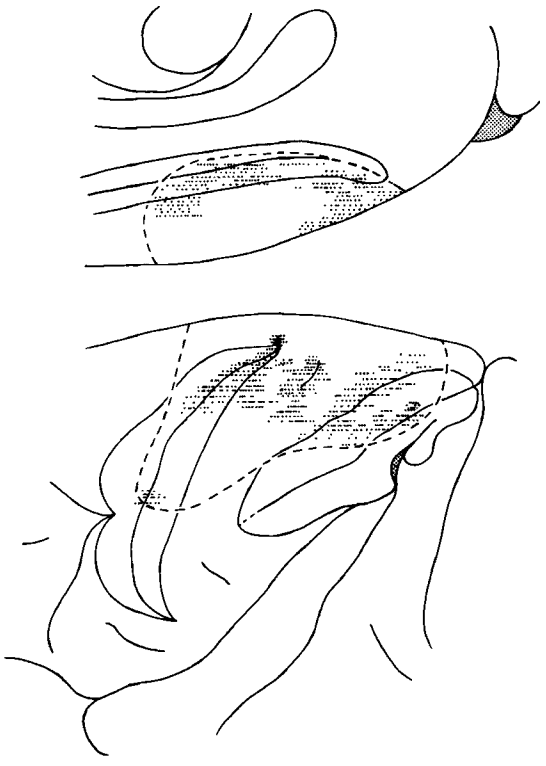

Fig. 8 Surface view, taken in part from a photograph of a cynomolgus monkey brain, but with cingulate (CgS), central (CS) and intraparietal (IPS) sulci drawn as though opened out. Interrupted line indicates total extent of a large injection of horseradish peroxidase in one hemisphere and dots indicate positions of retrogradely labeled cells in contralateral hemisphere. Note absence of retrograde labeling from hand and foot representations of SI.

When surface maps are reconstructed from sagittal sections (figs. 8, 9) the retrogradely labeled cell columns in SI also form parts of strips. These are more or less mediolaterally aligned and though in no experiment have we retrogradely labeled cellular strips across the full mediolateral extent of the postcentral gyrus, the strips are in positions virtually identical to the axonal strips. Patches devoid of labeled cell strips appear in similar positions in the hand and foot representations (figs. 8, 9). The longest columns of retrogradely labeled cells were seen in squirrel monkeys for, in the smaller brain, our injections labeled a greater proportion of SI.

The exact reciprocity of columns of callosally projecting cells and columns of callosal axons is clearly seen in preparations in which anterograde and retrograde labeling had been combined (figs. 5D, 10). Where horseradish

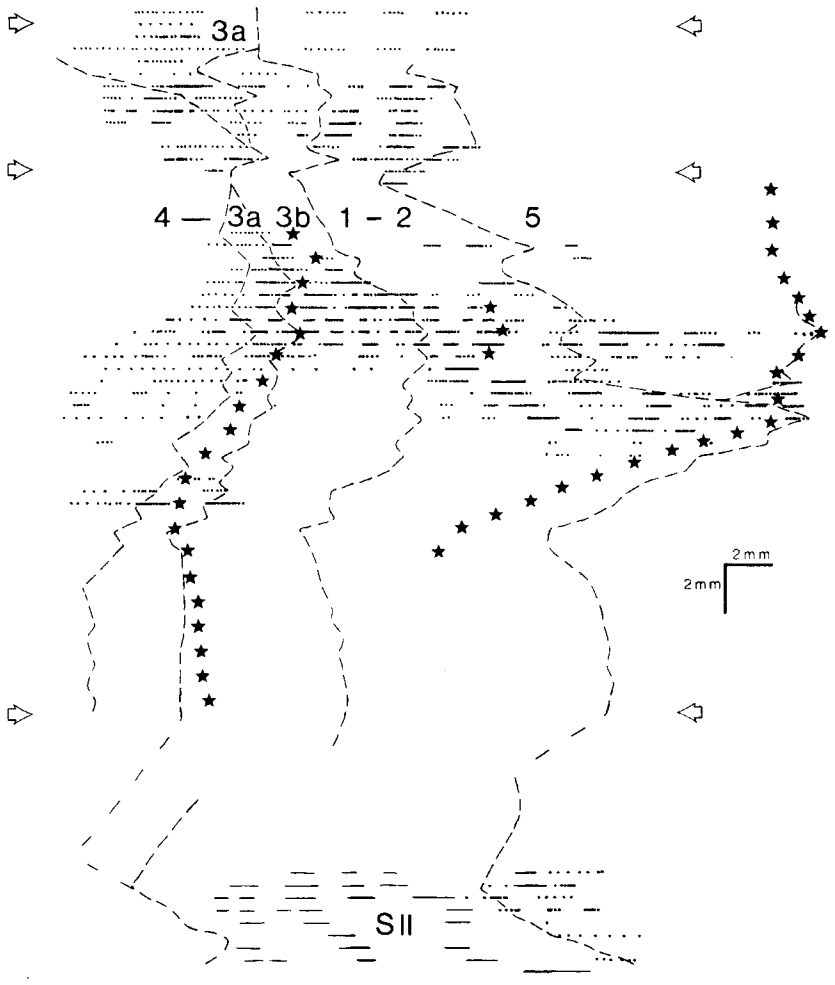

Fig. 9 Surface reconstruction made in same way as that illustrated in figure 3 but from a cynomolgus monkey that received a large injection of horseradish peroxidase centered in trunk representation. Dots represent retrogradely labeled cells which form strips, similar to strips of callosal axon ramifications. Lines in SII indicate anterograde labeling of heterotopic projection from SI.

peroxidase had been used as the double marker, the correspondence of anterograde axonal and retrograde cellular labeling is unerringly precise (figs. 5D, 10). In all parts of SI where an anterogradely labeled column is present, it also contains retrogradely labeled cells, and vice versa. Within these, the width of the anterogradely labeled column corresponds exactly to the width of the retrogradely labeled column. There are no columns labeled by only one mode in SI. However, in SII, which receives a heterotopic projection from the contralateral SI, only anterogradely labeled columns are visible (fig. 11).

The number of double-labeled columns is fewer in SI when horseradish peroxidase and autoradiographic labeling are combined, for the injections are smaller, but in every labeled column there is, again, exact correspondence of the two labels.

Point-to-point nature of the SI callosal projection

The point-to-point nature of the SI callosal projection is demonstrated by experiments in which small injections of [^{3}H] amino acids or of horseradish peroxidase were made in various parts of the area. The majority of the injections were placed in individual architectonic fields, as indicated in the MATERIALS AND

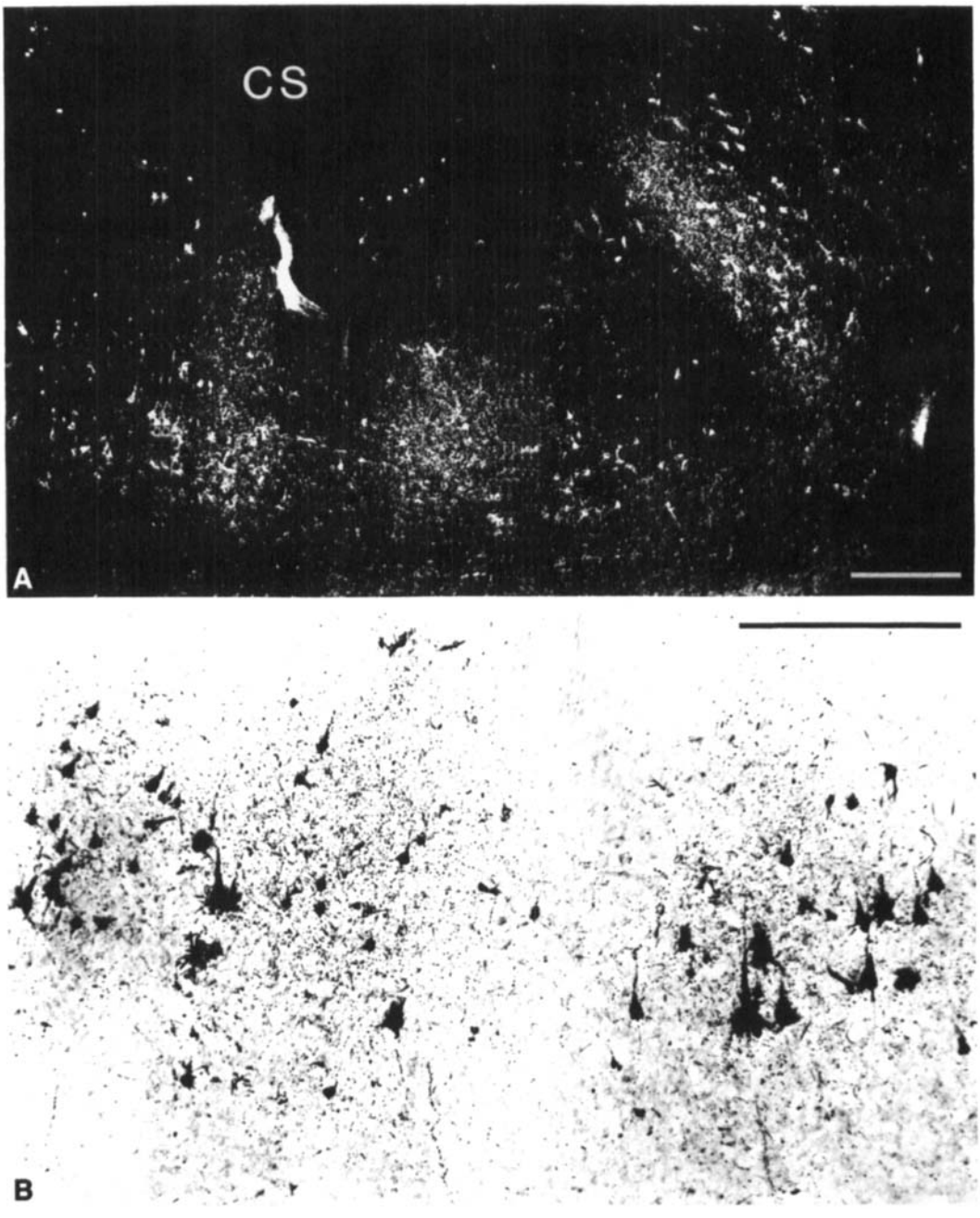

Fig. 10 Darkfield (A) and brightfield (B) photomicrographs respectively from floor of central sulcus and from area 1 in trunk representation of a cynomolgus monkey that received a large injection of horseradish peroxidase in contralateral postcentral gyrus. Note multiple columns and exact correspondence of anterograde and retrograde labeling. Tetramethylbenzidine, uncounterstained. Bar represents 250 μm.

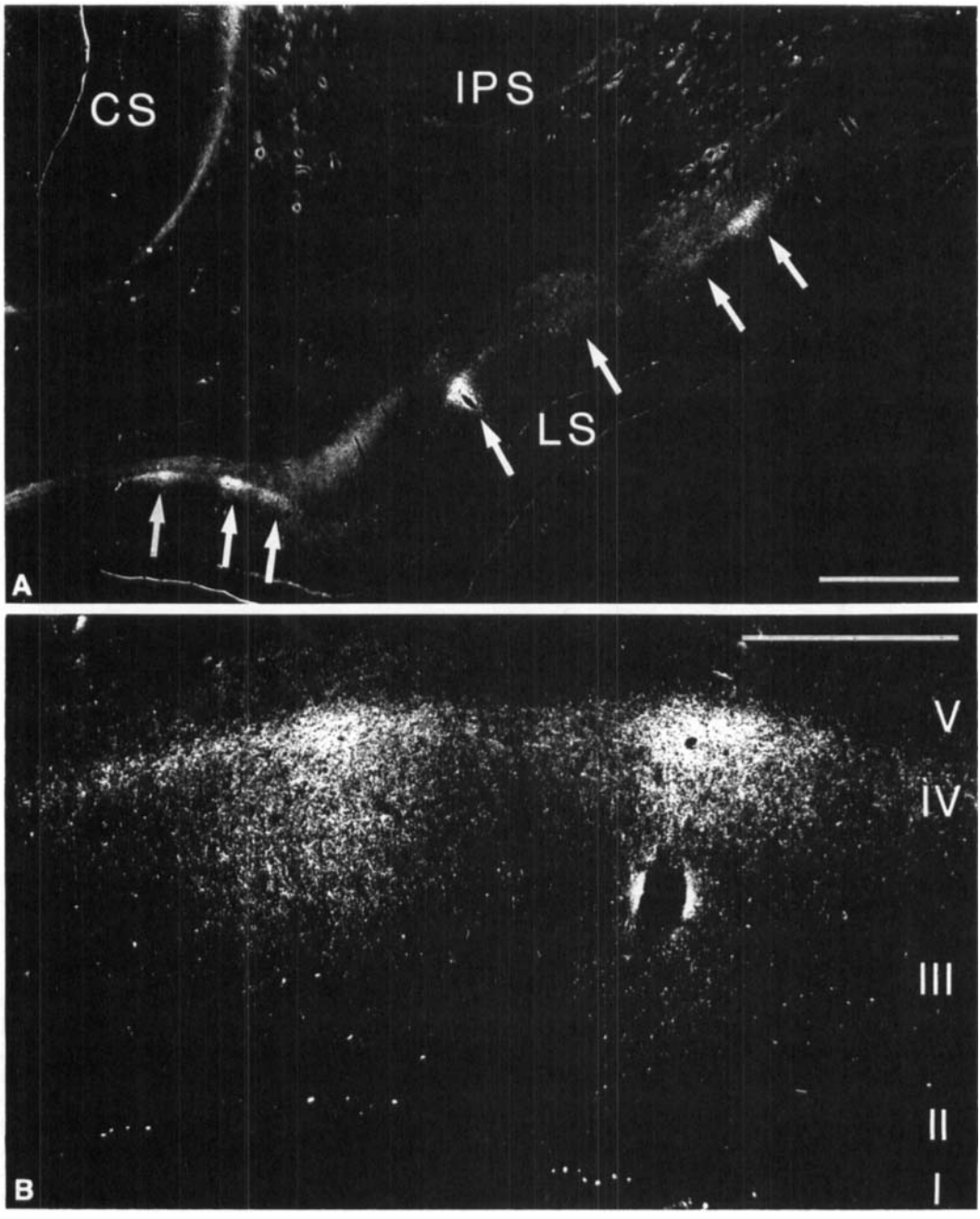

Fig. 11 Low (A) and higher (B) magnification darkfield photomicrographs from different parts of SII area in the same animal illustrated in figure 10, showing anterogradely labeled callosal columns in granular and supragranular layers. There is no retrograde labeling. Tetramethylbenzidine, sagittal sections, LS lateral sulcus. Bars represent 2 mm in A, 500 μm in B.

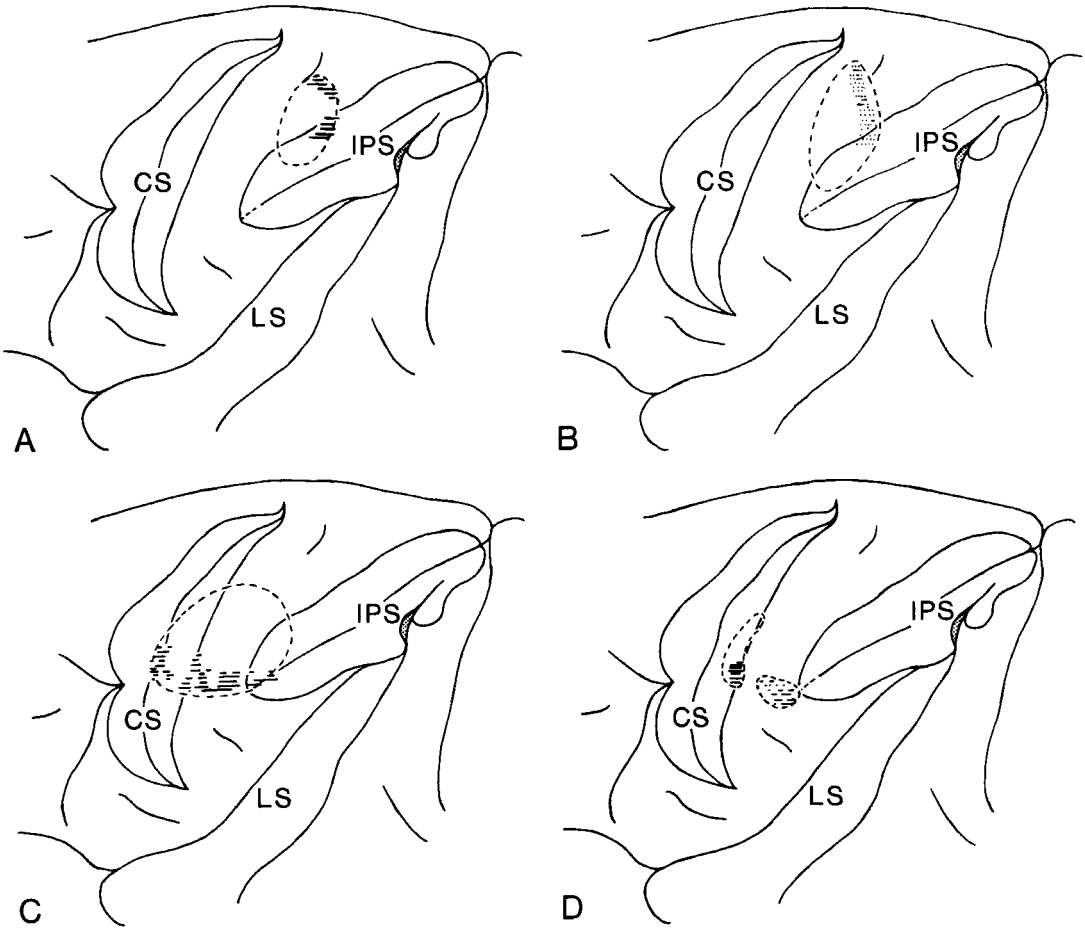

Fig. 12 A-D. Representative experiments illustrating the topography of the SI callosal projection. In figures 12 and 13 an interrupted line indicates the extent of an injection of horseradish peroxidase or [^{3}H] amino acids in one hemisphere and rows of dots or short lines respectively indicate the extent of retrograde or anterograde labeling in the contralateral hemisphere.

METHODS, and occupy hindlimb, trunk, forelimb and face representations (figs. 12, 13). In each case the position of the injection in relation to the body representation could be controlled by the distribution of anterograde or retrograde labeling in the thalamic ventrobasal complex (Jones et al., '79). It is found that only injections situated in zones labeled anterogradely or retrogradely in the experiments described above, lead to labeling in the contralateral cortex (figs. 12, 13). Figure 13B shows the positions and sizes of injections in face, proximal forelimb, trunk and proximal hindlimb representations and the extent of the ensuing axonal or cellular labeling contralaterally. The columns of labeled cells or fibers in corresponding parts of the opposite SI are exactly homotopic to the injection site and of comparable extent (figs. 12, 13). For example, an injection of isotope in the trunk region measuring 2.8 mm by 0.9 mm in extent led to contralateral labeling in columns extending over a total area of 2.6 mm by 0.8 mm. Injections in zones in the hand or foot representations and not containing transported label in the earlier experiments do not lead to any contralateral labeling, either anterograde or retrograde (fig. 13C). Any injection extending from a callosally-connected into a non-connected zone (fig. 12) results in a pattern of contralateral labeling interrupted by a non-labeled region comparable in size to the involve-

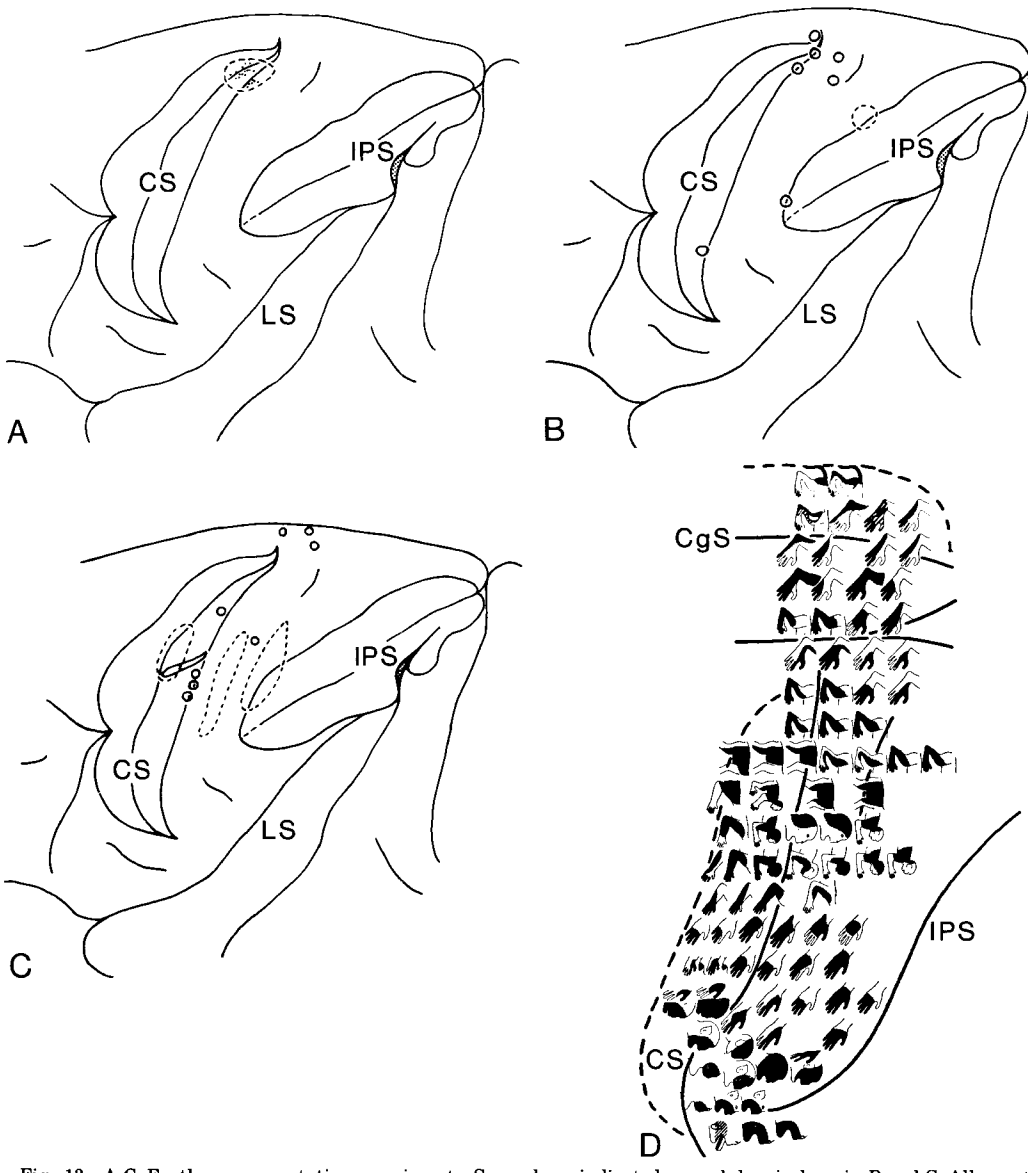

Fig. 13 A-C. Further representative experiments. Several are indicated on each hemisphere in B and C. All punctate injections illustrated in B led to contralateral labeling at a homotopic site and in the contralateral SII. Punctate injections illustrated in C did not result in contralateral labeling. D. Evoked potential map reproduced with permission from Woolsey ('58) indicating broad pattern of body representation in parts of rhesus monkey SI lying above the tip of the intraparietal sulcus. Depths of central and cingulate sulci are indicated by interrupted lines. Compare with figures 3, 4, 8, 9, 12, 13 of present paper.

ment by the injection of the unconnected hand or foot representation. Injections of isotope that cause labeling of the contralateral SI are also associated with one or more labeled columns in the contralateral SII (figs. 3, 4, 9, 11). Where there is no labeling of the contralateral SI, there is, similarly, no labeling of the contralateral SII (fig. 13C).

The labeling of callosally projecting cells or callosal axonal ramifications in SI shows no predilection for particular architectonic fields. Transcallosal labeling is situated in the

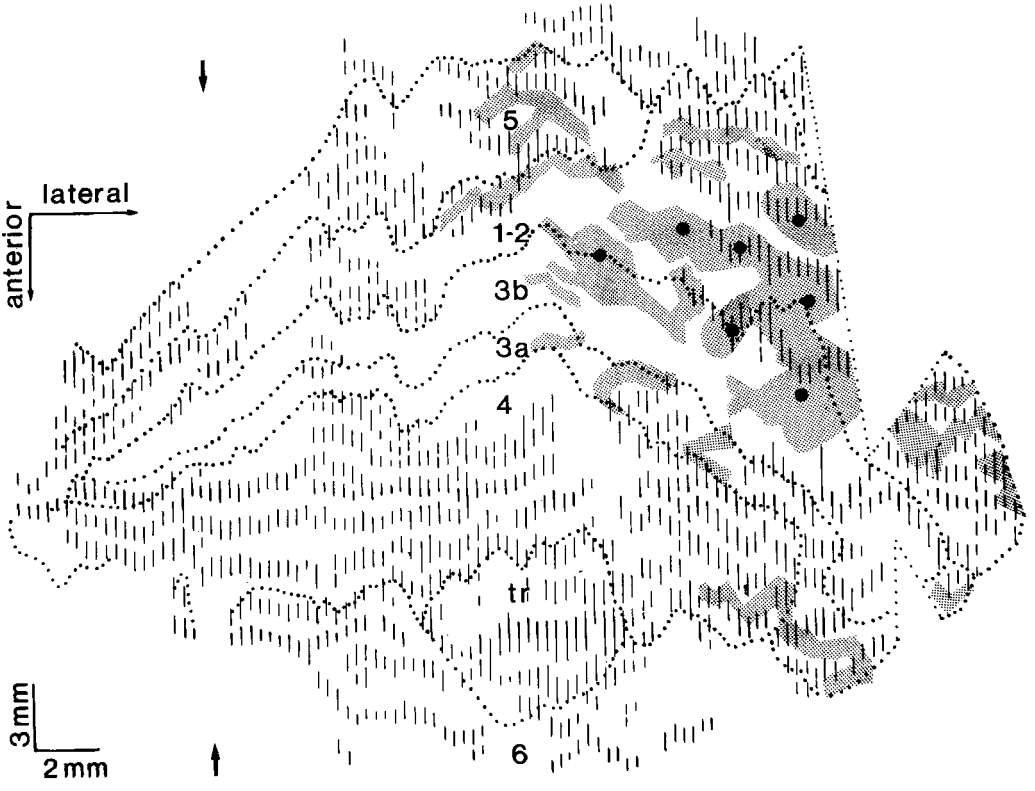

Fig. 14 Surface reconstruction from a cynomolgus monkey showing strips of degenerating callosal fibers caused by callosotomy six days previously and distribution of ipsilateral cortico-cortical fibers (stipple) demonstrated by multiple injections (dots) of [^{3}H] amino acids 24 hours before killing the animal.

same field or fields injected contralaterally. Appropriate parts of areas 3, 1 and 2 all project callosally to their counterparts and receive from their counterparts. Injection of one field does not cause labeling of a completely different field contralaterally (figs. 12, 13) except in the case of the heterotopic projection to SII. Appropriate parts of areas 3, 1 and 2 all project to SII. Callosally unconnected parts of SI do not project to SII and, thus, a central part of SII, presumed to contain the representations of the fore- and hindpaws and their digits, is always free of callosal labeling (figs. 1, 2, 9, 14, 15).

Relationship of callosal to ipsilateral labeling

One of the two experiments in which callosal fibers were labeled by degeneration methods and ipsilateral corticocortical fibers by autoradiography (Jones et al., '78) is illustrated in figures 14, 15. The injection of isotope is multiple and takes in a good deal of the hand representation(s) in areas 3, 1 and 2. The ensuing labeling of ipsilateral fibers, as seen in autoradiographs from sections alternate to those stained for degeneration, is plotted onto the same map as the callosal degeneration, using blood vessels, section contours and similar features as landmarks. It is clear that there is a considerable overlap between callosal and ipsilateral labeled columns, but in certain parts of areas 4 and 5 and in SII, there is a clear alternation.

DISCUSSION

In this study we have been concerned primarily with the finer details of callosal fiber organization in the somatic sensory cortex. However, data have also been presented relevant to the motor cortex and, when taken together with the results of the accompanying study (Jenny, '79), these data permit us to

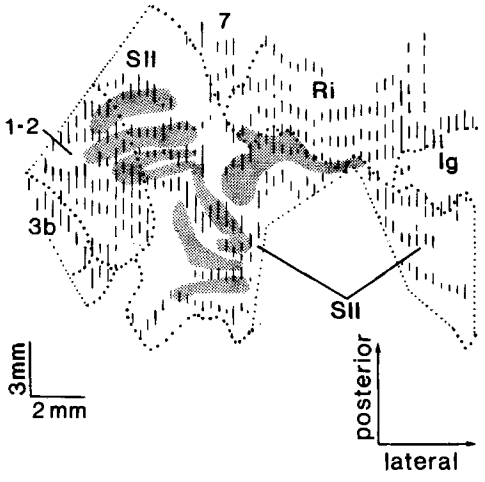

Fig. 15 Reconstruction of the SII area of animal illustrated in figure 14 showing distribution of callosal fibers (lines) and of corticocortical fibers from ipsilateral SI.

make certain generalizations about callosal connectivity in the sensory-motor regions as a whole.

The callosal projection is finely structured so that, in connected parts of the motor and sensory representations, only homotopic points are connected. In SI, the connection is not only point-to-point, but it is reciprocal in the sense that a column-like zone receiving callosal fibers also contains the only cells that project back to the homotopic column in which those fibers arise. Heterotopic projections do occur insofar as callosally connected parts of SI project also to the contralateral SII; and callosally connected parts of area 4 project also to the supplementary motor area. However, neither of these heterotopic projections is reciprocal.

We have not been able to show that any parts of SI project preferentially to the contralateral SII. In our material, projections to the contralateral SII after injections of SI are demonstrated only when a homotopic SI projection is also demonstrated. In this, our work conflicts with the briefly reported work in the cat of Caminiti et al. ('78).

Current ideas on the organization of sensory cortex tend to stress thalamic input as an underlying basis of columnar properties (Mountcastle, '57; Powell and Mountcastle, '59; Hubel and Wiesel, '68, '74, '77; Merzenich and Brugge, '74). In the SI cortex, individual columns are traditionally believed to represent a different place and a specific submodality. The point-to-point nature of the callosal connection in SI implies that the column-like groupings of callosal terminal ramifications could be terminating in relation only to particular column-like groupings of cells whose columnar organization and response properties were specified by thalamic inputs. In the SI cortex, therefore, in callosally connected zones, callosal fibers could be seen as connecting together sensory columns with exactly the same submodality properties and with symmetrical place properties in the original sense of Mountcastle ('57).

The main reservation about this view stems from the fact that the strips formed by the callosal columns are aligned mediolaterally across the postcentral gyrus. Although anatomical studies (Jones et al., '79) have now confirmed the implications of early single unit studies that clusters of thalamic cells project to punctate (or "columnar") zones in SI, it is unknown whether the columns of thalamic terminations form strips having the same orientation as the strips of callosal columns. Powell and Mountcastle ('59) found that microelectrode penetrations traversing area 3b of SI mediolaterally usually encountered single units with abrupt shifts of receptive field position, as though crossing from one sensory column to another. Penetrations traversing area 3b anteroposteriorly, on the other hand, did not encounter abrupt shifts, as though remaining within a sensory column. This would imply that sensory columns based upon thalamic input in area 3b are aligned in anteroposterior strips. If this sequence is carried from area 3b into areas 1 and 2, such columns would be aligned, not in parallel with the callosal columns, but at right angles to them. The small anteroposterior strips of callosal fiber labeling described by Jenny ('79) in the motor cortex are formed by bundles of fibers that, when aligned in register with similar adjacent bundles, would make up the mediolaterally oriented larger strips of our material.

In the only cortical area, the visual, in which columns based upon thalamic input have been clearly demonstrated to be aligned in strips (Hubel and Wiesel, '74, '77), callosal fibers connect only a small part of the representation and their distribution has been incompletely documented. However, the major-

ity of the ocular dominance strips meet the representation of the vertical meridian at right angles and the little data that are available on callosal fibers indicate that these form a strip along the representation of the vertical meridian (Cragg, '69; Zeki, '70, '78; Karol and Pandya, '71). In a considerable portion of the visual field representation, therefore, the callosally connected strip crosses the ends of the thalamic strips more or less at right angles. Obviously, it would be of great interest to know if a comparable organization were present in SI. Whatever the resolution of this issue, it is clear that because thalamic fibers are distributed through all parts of SI (Jones, '75; Jones and Burton, '76) and callosal fibers in an interrupted fashion, some parts of SI are dominated by thalamic input while others receive thalamic and callosal inputs. The effect of this upon neuronal response properties in the SI area has not yet been ascertained.

In SI of rats (Akers and Killackey, '78; Wise and Jones, '76, '78), there is a clear dissociation of the terminal zones of callosal fibers and of thalamic fibers arising in the ventrobasal complex. Moreover, each fiber system ends in a clearly distinguishable cytoarchitectonic region. In monkeys, there is no dissociation of thalamic and callosally connected zones, and the reciprocally connected strips of callosal cells and fibers do not bear any consistent relationship to the architectonic fields of SI. Strips and, conversely, unconnected zones are found in parts of areas 3b, 1 and 2. In our material, the strips do not seem to be concentrated solely at the borders of architectonic fields as proposed by Shanks et al. ('75, '78). A single strip, especially in areas 1 and 2, can move across an individual field and from field to field.

In not being related in any obvious way to particular parts of architectonic fields, the callosal fiber distribution cannot be used to shed light on the question of multiple representations of the body surface in areas 3b, 1 and 2 (Merzenich et al., '78; Jones et al., '79). For example there is evidence that axial parts of the body are represented in posterior parts of areas 3b and in posterior parts of area 2 (Jones et al., '78, '79). If callosal fibers followed the representation of axial parts only, as often proposed (Ebner and Myers, '65; Jones and Powell, '69; Pandya and Vignolo, '69), then they should distribute to posterior parts of both areas. Instead, callosal fibers, though in the form of strips interrupted by gaps, spread across all parts of the three fields in some regions and are absent from all parts of the three fields in others. The map of callosal fiber distribution does not rule out multiple representations in the fields of SI, but it still permits interpretation in terms of a single body map based upon evoked potentials (Woolsey, '58; fig. 13D).

Apart from a very small number in layer VI, the callosally projecting cells of SI are clearly identifiable as belonging to the group of large pyramidal cells of layer IIIB (Jones et al., '75; Jones and Wise, '77; present study). This cell type can often be seen to be concentrated in particular parts of areas 3, 1 and 2 in Nissl-stained preparations of normal material (Jones et al., '78). These regions of concentration of layer IIIB cells have been correlated with zones of callosal connectivity in SI as well as in other cortical areas (Shoumura, '74; Glickstein and Whitteridge, '76; Jones and Wise, '77). In Golgi preparations (fig. 7C; S.H.C. Hendry and E. G. Jones, unpublished), layer IIIB pyramidal cells in SI have basal dendrites that descend into layer aiv where they branch extensively. Their apical dendritic system fans out as a series of branches forming a wide tuft in layer I. This type of dendritic organization matches rather precisely the position and shape of the columns formed by the terminal ramifications of callosal fibers (fig. 6). The present experiments show that within such a column lies a close-packed group of layer IIIB cells projecting to the other side. Therefore, the terminal ramifications, as manifested by the shape of their column, appear to be conforming to the combined, total dendritic field of a callosally projecting group of cells. Given this and the precise reciprocity of the callosal system, it is difficult to avoid the suggestion that callosal fibers originate from and terminate upon the same class of pyramidal cell. This suggestion is supported by electron microscopic evidence in other species (Jones and Powell, '70). It is as yet unknown whether the same cells have collateral axons to the contralateral SII or whether separate cells in the same column project only to SI or to SII.

The relationship of the callosal columns or strips to similar columns and strips formed by ipsilateral cortico-cortical fibers and their cells of origin (Jones et al., '78) is also not yet completely clear. In our experiments that combined axonal degeneration and autoradiography (figs. 14, 15), some callosal strips in

SI and SII clearly alternated with corticocortical strips, but in many regions there was substantial overlap. Similarly, where callosally projecting cells were retrogradely labeled in layer IIIB, many relatively large unlabeled cells lay among them (fig. 7). Cells in this layer do not project to subcortical sites (Jones and Wise, '77). Conceivably, the unlabeled layer IIIB cells form a separate population projecting only to the contralateral SII, but their size is also within the range of ipsilateral, corticocortically projecting cells (Jones and Wise, '77). Therefore, it is more likely that the unlabeled cells are also indicative of a substantial overlap of zones of ipsilateral and contralateral corticocortical influence. We do not know whether within these zones some layer IIIB cells have both ipsilaterally and contralaterally projecting axon branches, though our previous results (Jones and Wise, '77) have not favored this.

Because we do not yet know to what extent there is a dissociation of callosally and ipsilaterally connected corticocortical zones, we cannot say whether the strips of callosal cell and fiber columns are set up by competition with ipsilateral cell and fiber systems during development. Nevertheless, the callosal system shows such a remarkable degree of fine organization that it is interesting to consider what other developmental influences could promote this. Our results in other species (Wise and Jones, '76, '78; Wise et al., '77, '79) indicate that callosally projecting cells and their fiber ramifications in the opposite cortex are initially diffusely distributed and only acquire their characteristic columnar patterns during the first few days of postnatal life. In the rat this is also true of certain other cortical efferent systems whose cells of origin in the adult of that species are also unevenly distributed (Wise et al., '78, '79). Obviously the increasing size of the cortex may play some role in forcing an initially limited number of callosal cells and axons into restricted zones. In concert with this, the development of the pre- and postcentral gyri in the primate might have the effect of promoting the formation of mediolaterally aligned strips. But is unlikely that mechanical factors are the sole determinants of callosal column formation and, by comparison with other developing neural systems (Cowan, '73; Landmesser and Pilar, '74), one might expect that a substantial number of callosal cells would die during this period. Whether death of callosally projecting cells occurs in preferential zones of the sensory-motor cortex, whether this death is entirely pre-programmed or based upon failure of the growing axon to colonize synaptic sites because of competition with other axon systems in particular zones of the opposite cortex, are questions that remain to be answered. As pointed out above, competition for synaptic space with ipsilateral corticocortical fibers is unlikely and our results in rats (Wise and Jones, '78) would tend to rule out a competition between thalamocortical and callosal fibers. The work of Shatz ('78) on the visual cortex of the Siamese cat indicates that patterns of callosal connectivity are set up during development on the basis of representational cues. The precise, point-to-point nature of the callosal connectional pattern in the monkey sensory-motor cortex implies a close association with the representational map of body topography. However, until it is determined exactly what parts of the body are represented in the callosally connected zones, it is difficult to predict what cues might promote the characteristic dissociation of these callosally connected zones in the development of the sensory-motor cortex.

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