

Somatosensory Cortex of Prosimian Galagos: Physiological Recording, Cytoarchitecture, and Corticocortical Connections of Anterior Parietal Cortex and Cortex of the Lateral Sulcus

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ABSTRACT

Compared with our growing understanding of the organization of somatosensory cortex in monkeys, little is known about prosimian primates, a major branch of primate evolution that diverged from anthropoid primates some 60 million years ago. Here we describe extensive results obtained from an African prosimian, *Galago garnetti*. Microelectrodes were used to record from large numbers of cortical sites in order to reveal regions of responsiveness to cutaneous stimuli and patterns of somatotopic organization. Injections of one to several distinguishable tracers were placed at physiologically identified sites in four different cortical areas to label corticocortical connections. Both types of results were related to cortical architecture. Three systematic representations of cutaneous receptors were revealed by the microelectrode recordings, S1 proper or area 3b, S2, and the parietal ventral area (PV), as described in monkeys. Strips of cortex rostral (presumptive area 3a) and caudal (presumptive area 1–2) to area 3b responded poorly to tactile stimuli in anesthetized galagos, but connection patterns with area 3b indicated that parallel somatosensory representations exist in both of these regions. Area 3b also interconnected somatotopically with areas S2 and PV. Areas S2 and PV had connections with areas 3a, 3b, 1–2, each other, other regions of the lateral sulcus, motor cortex (M1), cingulate cortex, frontal cortex, orbital cortex, and inferior parietal cortex. Connection patterns and recordings provided evidence for several additional fields in the lateral sulcus, including a retroinsular area (Ri), a parietal rostral area (PR), and a ventral somatosensory area (VS). Galagos appear to have retained an ancestral primate arrangement of five basic areas (S1 proper, 3a, 1–2, S2, and PV). Some of the additional areas suggested for lateral parietal cortex may be primate specializations. *J. Comp. Neurol.* 457:263–292, 2003. © 2003 Wiley-Liss, Inc.

Indexing terms: primates; neocortex; motor cortex

We are the only species to reflect on the marvelous complexity of our own brains and how they got that way. Early mammals had small brains, with little neocortex (Kaas and Preuss, 2002), whereas modern humans have huge brains that are disproportionately devoted to neocortex. This neocortex is subdivided into a large number of functionally distinct and specialized areas that are interconnected to form large processing hierarchies. How did our brains evolve from the much simpler, small brains of early mammals? This is a difficult question to address directly because brains don't fossilize. We can obtain only impressions of the sizes and shapes of brains from the endocasts of recent skulls compared with those of ancient

ancestors. Thus, any comprehensive understanding of how human brains evolved must come from comparative studies of the brains of mammals that exist today. Extant

Grant sponsor: National Institute of Health; Grant number: NS16446.

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Received August 8, 2002; Accepted 29 October, 2002.

DOI 10.1002/cne.10542

Published online the week of January 27, 2003 in Wiley InterScience (www.interscience.wiley.com).

mammals vary greatly in brain size, complexity, and organization. However, common features in taxonomic groups probably reflect retentions from a common ancestor (Northcutt, 1984).

We were interested in studying the organization of somatosensory cortex in *Galago garnetti* because they are an available member of the prosimian radiation of the primate order. Primates emerged as a distinct line of evolution over 60 million years ago and soon formed the three major prosimian, tarsioid, and anthropoid radiations (Purvis, 1995). The anthropoid radiation led to New World and Old World monkeys, apes, and humans. As a result of years of intensive study, a broad outline of the organization of somatosensory cortex of monkeys has emerged (Kaas, 1983; Kaas and Preuss, 2002). In brief, anterior parietal cortex contains four rostrocaudally arranged strip-like representations of body receptors, area 3b or S1 proper, area 3a, and areas 1 and 2. Lateral parietal cortex in the lateral sulcus contains two well-studied somatosensory representations, the second somatosensory area (S2) and the parietal ventral area, (PV), as well as several other less understood areas. Posterior parietal cortex includes a number of somatosensory, visuomotor, and multimodal areas (Lewis and Van Essen, 2000). Areas in these three regions interconnect and connect to other systems, especially with motor areas of the frontal lobe. Many of these features of parietal cortex organization of monkeys appear to be shared by humans (Kaas, 1990), and thus they appear to be basic features of anthropoid brains. Possibly, these features emerged as specializations of the brains of early anthropoids, or even earlier with the first primates or their ancestors.

In an attempt to address such basic questions, we studied the organization of somatosensory cortex in galagos. Previously, S1 (area 3b) had been identified by microelectrode mapping methods (Carlson and Welt, 1980; Sur et

al., 1980). A systematic representation of the body surface that was characteristic of S1 in other species (or area 3b representation in monkeys) was found to be coextensive with a koniocortical region that was less differentiated than area 3b of monkeys but was clearly primary sensory cortex. There were suggestions of other areas, but only S2 was mapped and identified (Burton and Carlson, 1986; Garraghty et al., 1991).

Our experimental approach in exploring somatosensory cortex in galagos involved using microelectrodes to identify S1 (area 3b) and locate sites for the injections of tracers to reveal the other regions of cortex that directly communicate with S1. We also recorded from other regions of parietal cortex in efforts to reveal additional systematic representations of the body, especially the expected regions of S2 and PV, as these areas had been revealed in a number of anthropoid and non-primate taxa (Disbrow et al., 2000). Finding evidence for these two fields, we also injected tracers in identified locations in each of them, as well as in cortex just caudal to S2 (the 7b region of monkeys). Anatomical and physiological results were related to cortical architecture. We conclude from our findings that somatosensory cortex organization in galagos includes basic features that have been retained from non-primate ancestors, while also having complexities that are shared with simians and possibly represent primate specializations.

MATERIALS AND METHODS

General procedures

Patterns of somatotopic organization were revealed in parietal cortex of 11 adult prosimians, *Galago garnetti* (Table 1), by recording from multiple sites with microelectrodes. Animals weighed between 0.8 and 1.2 kg. In nine of

Abbreviations

Body part and receptive field

v	ventral
d	dorsal
D1–D5	digits 1–5
P1–4	interdigital pads
PH	hypothenar pad
PTH	thenar pad
T1	first toe

Sulci and brain anatomy

CC	corpus callosum
CgS	cingulate sulcus
CS	central sulcus
FSa	frontal sulcus, anterior
FSp	frontal sulcus, posterior
ib	inner bank
IPS	intraparietal sulcus
lb	lower bank
LS	lateral sulcus
OB	olfactory bulb
OS	orbital sulcus
RSa	rhinal sulcus, anterior part
RSp	rhinal sulcus, posterior part
STS	superior temporal sulcus
ub	upper bank

Cortical areas and structures

7a–m	medial posterior subdivision of inferior parietal lobe
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7b	anterior subdivision of inferior parietal lobe
7v–m	lateral posterior subdivision of inferior parietal lobe
Amyg	amygdala
BA	accessory basal n. of amygdala
Ce	central n. of the amygdala
CL	claustrum
CMAc	cingulate motor area, caudal
CSMA	cingulate sensorimotor area
ER	entorhinal cortex
FPO	frontopolar opercular area
Ia	agranular insular field
Idg	dysgranular insular field
Ig	granular insular field
L	lateral n. of the amygdala
M1	primary motor area
Pir	pyriform cortex
PMV	ventral premotor area
PR	rostrolateral parietal area
PV	parietal ventral area
Ri	retroinsular area
S1	primary somatosensory area
S2	secondary somatosensory area
VS	ventral somatosensory area
	Tracers
BDA	biotinylated dextran amine
DY	diamino yellow
FB	Fast Blue
FE	Fluoro Emerald
FR	Fluoro Ruby
WGA-HRP	wheat germ agglutinin-horseradish peroxidase

TABLE 1. Summary of Animal Cases Investigated¹

Case No.	Recording sites	Tracer injections	Cutting plane
95-14	3b	3b (WGA-HRP, FB, FR)	Flattened
95-18	3b, S2	3b (WGA-HRP, DY, FB)	Flattened
95-51	3b, S2, PV	3b (WGA-HRP, DY, FR), 1/2 (FB)	Flattened
95-69	3b, S2	3b (WGA-HRP, FR, FB, DY)	Coronal
95-82	S2, PV	S2 (FB, FR, DY)	Flattened
96-32	S2, PV, PR, Ri, VS	S2 (WGA-HRP, DY), PV (FR), 7b (FB)	Flattened
96-72	S2, PV	—	Parasagittal
96-05	S2, PV	—	Coronal
96-88	S2, PV	S2 (FR), PV (FB, DY), 7b (FE)	Flattened
97-08	S2, PV	S2 (DY), PV (WGA-HRP, FB)	Coronal
97-34	3b, S2, PV	3b (DY, FB), S2 (FE), PV (FR, BDA)	Coronal

¹For abbreviations, see text.

these galagos, anatomical tracers were injected into electrophysiologically identified locations in order to label connections between cortical areas. In these animals, microelectrode recordings were briefly used to identify cortical areas of interest and sites for injections. After waiting 4–7 days for the tracers to be transported, additional recordings were made to determine more extensively the somatotopy of parietal cortex, especially anterior parietal cortex (area 3b) and cortex in the lateral sulcus (areas S2 and the parietal ventral area, PV). Anatomical and physiological results were later related to histological distinctions in the processed brain sections. Some of the results have been briefly published elsewhere (Wu et al., 1996).

Surgeries and perfusions

All surgical procedures were approved by the Vanderbilt Animal Care and Use Committee and followed National Institutes of Health guidelines. Before surgery, the animals were premedicated with dexamethasone (2 mg/kg, IM). The initial surgery was carried out under aseptic conditions while the animals were anesthetized with 2% isoflurane. A craniotomy was used to expose parts of anterior parietal cortex near the lateral sulcus. The exposed cortex was kept wet with sterile saline while recordings were briefly made with microelectrodes. After suitable injection sites had been selected, one or more of the following tracers were injected under pressure into the middle layers of cortex (800–1,000 μm below the pial surface) through micropipettes attached to 1- μm syringes: Fluoro Ruby (FR), 10% in distilled water, 0.3–0.5 μl ; Fast Blue (FB) 2% in phosphate-buffered saline (PBS), 0.3–0.5 μl ; Fluoro Emerald (FE), 10% in distilled water, 0.3–0.5 μl ; diamino yellow (DY), 3% in PBS, 0.3–0.5 μl ; biotinylated dextran amine (BDA), 10% in distilled water, 0.3–0.5 μl ; wheat germ agglutinin-horseradish peroxidase (WGA-HRP) 1–2% in saline, 0.03–0.05 μl . After injections, the dura was replaced and covered with absorbable gelatin film, and the opening in the skull was closed with dental acrylic. Animals were given antibiotics (penicillin, 6,000 U/kg) as a precaution and were carefully monitored during recovery from anesthesia and throughout the survival time.

Four to 7 days later, the galagos were anesthetized with ketamine hydrochloride (30 mg/kg, IM) and acepromazine (1–2 mg/kg, IM). Supplementary injections of 20–30% of the original dose were given as needed to maintain surgical levels of anesthesia. The brain surface over somatosensory cortex was re-exposed and covered with silicone fluid to prevent desiccation. Microelectrodes were used to record from additional sites in cortex to identify more fully

cortical areas and somatotopic patterns of representation. Several small electrolytic lesions were then placed with the microelectrodes to mark some recording sites so that results could be later correlated with cortical architecture. The animals were given a lethal dose of sodium pentobarbital (50 mg/kg or more) and perfused transcardially with PBS (pH 7.4), followed by 2% paraformaldehyde in PBS, and then followed by the fixative solution with 10% sucrose. In some cases, the cortex was separated, manually flattened, and stored between glass slides overnight. All tissue was stored in 30% sucrose in PBS overnight before sectioning.

Microelectrode recordings

Microelectrode multiunit recordings were used to identify and characterize the subdivisions of somatosensory cortex in the anterior parietal cortex and vicinity of the lateral sulcus. Upon exposure, an enlarged photograph of the exposed cortex was taken to mark the locations of electrode penetrations and tracer injections. A low-impedance tungsten microelectrode (0.95–1.5 M Ω) was lowered into the middle layers of the cortex using a motor-driven stepping microdrive. In the anterior parietal cortex, electrode penetrations were perpendicular to the cortical surface to reach a depth of 800–1,000 μm , where layer IV granular cells are located. The recordings in parietal cortex confirmed the somatotopy described in an earlier study (Sur et al., 1980) and were used to guide the tracer injections. For the cortical areas buried inside the upper bank of the lateral sulcus, recordings were made by directing the electrode parallel to the cortical layers with an 18–15° angle from vertical, approximately 1–1.5 mm medial to the lateral sulcus. For these penetrations near the lateral sulcus, receptive fields were determined at 100–300- μm intervals through the responsive layers for 4–5 mm in depth, or until responses could no longer be driven by the stimuli.

Receptive fields were defined as the maximal area of the body that evoked a neural response when stimulated at near threshold level (minimal receptive fields). Low-threshold cutaneous receptive fields were those determined by lightly touching the skin with fine probes and gently displacing hairs with camel hair brushes. Recording sites where neurons required more intense stimulation for activation, such as tapping of the skin, were classified as having a higher threshold. Neurons with responses to manipulating muscles or joints and with no obvious cutaneous receptive fields were presumably related to deep receptors. Finally, sites at which neurons did not respond well to cutaneous stimulation were tested for responsiveness to auditory and visual stimulation. The physiological boundary was drawn based on the size of the receptive field, the neuronal responses, and the progression of the changes in the receptive fields. Prior to sacrifice, small electrolytic marker lesions (10 μA for 10 seconds, 500 μm apart at several depths in the same penetration) were placed at physiological boundaries and other sites of interest for later correlation of anatomical and physiological results in histologically processed tissue.

Histology and anatomical analysis

In eight animals, cortex was separated from the brainstem and manually flattened between glass slides. Flattened brain sections were cut at 40–50 μm thickness. Sets

of flattened cortical sections were treated with tetramethylbenzidine (TMB) to reveal WGA-HRP (Gibson et al., 1984), stained for myelin (Gallayas, 1979), mounted unstained for fluorescence microscopy, and stained for cytochrome oxidase (CO; Wong-Riley, 1979). In three other cases, the brains were sectioned coronally or parasagittally at 40 μm . Sets of sections were processed for myelinated fibers, CO, and Nissl substance to reveal the architectonic boundaries. Additional sets of sections were treated with TMB, Avidin-biotin-peroxidase (ABC-kit, Vectastain, Vector, Burlingame, CA) to reveal BDA (Dolleman-Van der Weel et al., 1994) or mounted unstained for fluorescence microscopy. The distance between sections in each set was 160–250 μm .

The locations of cells labeled with fluorescent dyes were charted with a Leitz microscope with an X-Y encoder. Labeled neurons were visualized with 360-nm (for FB, DY), 480–500-nm (for FE), and 530–560-nm (for FR) wavelength excitation filters. Sections processed for HRP were examined under darkfield illumination, and the locations of injection sites and transported label were charted. Enlarged drawings of brain sections were used to plot labeled neurons and axon terminals from every section reacted with TMB or mounted for fluorescent microscopy. In addition, lesions placed at physiological boundaries, blood vessels, and tissue artifacts were also used in these reconstructions. For the flattened cortex, five sections were superimposed across a series of brain sections to reconstruct the distribution of labeling that covers the entire thickness of the cortex. For the coronal and parasagittal sections, the labeling was drawn based on each section. Adjacent sections stained for myelin were drawn at the same magnification, and architectonic boundaries, blood vessels, lesions, and tissue artifacts were marked on these sections. By matching these landmarks, architectonic boundaries were added to sections with tracers. The final reconstruction of each label was represented as the relative density. Recording sites were related to these surface-view reconstructions by using marker lesions and were determined by measuring the distance from marker lesions and other landmarks. The sizes and locations of areas based on recording data were later compared with the configuration reconstructed from flattened sections. In the cases in which the brain was sectioned coronally or parasagittally, drawings of sections included electrode track damage, lesions, and architectonic boundaries. The sections were geometrically rotated, aligned, and “flattened” using procedures described by Van Essen and Maunsell (1980). Distances between electrode tracks along the length of the lateral sulcus were corrected to reflect the cosine of the angle between the thickness of the coronal sections and the angle formed between the horizontal stereotaxic plane and the electrode tracks (Burton and Carlson, 1986).

Figure preparation

Photographic images of brain sections were acquired by using a Leaf MicroLumina digital scanning camera mounted on a Nikon E800 microscope. Brain sections were scanned and the digital images were adjusted for brightness and contrast with Adobe Photoshop 4.0 software, but they were not altered in any other way. The composition of images with text and scale bars was done with Canvas 5.0 software.

RESULTS

The experiments were designed to reveal the organization of somatosensory cortex in prosimian galagos. Microelectrode recordings were used to identify and delimit functionally distinct fields in anterior parietal and lateral parietal cortex, and patterns of connections were determined to indicate how somatosensory fields interact and connect to motor and limbic areas. Results are presented in three sections. First, the somatotopic organizations and neuronal response properties of somatosensory areas are described. Second, we relate the architectonic features of the somatosensory representations. Finally, we describe the areal patterns of cortical connections resulting from injections of tracers into physiologically identified locations in somatosensory areas. Proposed subdivisions of somatosensory cortex are shown in Figure 1.

Microelectrode recordings

Anterior parietal cortex

S1 proper or area 3b. One systematic representation of the contralateral body surface has features that have identified it as the homolog of primary somatosensory cortex in non-primate mammals (S1 proper; Kaas, 1983) and the area 3b representation of monkeys and other primates. The overall somatotopic features of area 3b of the greater galagos (*Galago garnetti*) used in this study correspond to those described previously for galagos (Sur et al., 1980; Carlson and Welt, 1980). Area 3b is located between the posterior frontal sulcus (FSp) and the intraparietal sulcus (IPS) (Fig. 1). Neurons were highly responsive to light touch on the skin and the displacement of hairs. Neurons did not habituate to repetitive stimulation within the receptive field, and receptive fields were smaller than for other areas. The receptive fields were smallest on the glabrous digits and lips and were largest for the trunk.

Recordings revealed a medial to lateral representation of body parts progressing from hindlimb and tail, trunk, forelimb, to face (Figs. 2, 3, 10). The most medial extent of area 3b, representing the tail and leg, occupied the dorsal cortex of the medial wall of the cerebral hemisphere bordering the caudal portion of the cingulate motor area (CMA_c) and part of the cingulate sensorimotor area (CSMA), described previously (Wu et al., 2000). In cortex of the dorsolateral surface, the large forelimb representation occupied about one-third of the total area. More laterally, part of the radial portion of the arm was represented, followed by the neck, lower face, and chin. The upper lip and lower lip were represented most laterally near the lip of the lateral sulcus. The representation of the oral cavity was not explored, but results from New World monkeys (Jain et al., 2001) suggest that the tongue and teeth are represented in cortex immediately rostral to that devoted to the lips.

The recordings also revealed details of the organization of area 3b. Within the hand representation, the glabrous digits were rostral, the glabrous pads more caudal, and the hairy surface of the hand most caudal (Figs. 2, 3, 4A). The distal digit was rostral to the proximal phalange, and the representations of the digits from 1 to 5 were in a lateromedial sequence. The ulnar side of the arm joined the hand representation to those of the shoulder and trunk in more medial cortex, as the radial side of the arm joined the hand representation laterally to the neck and

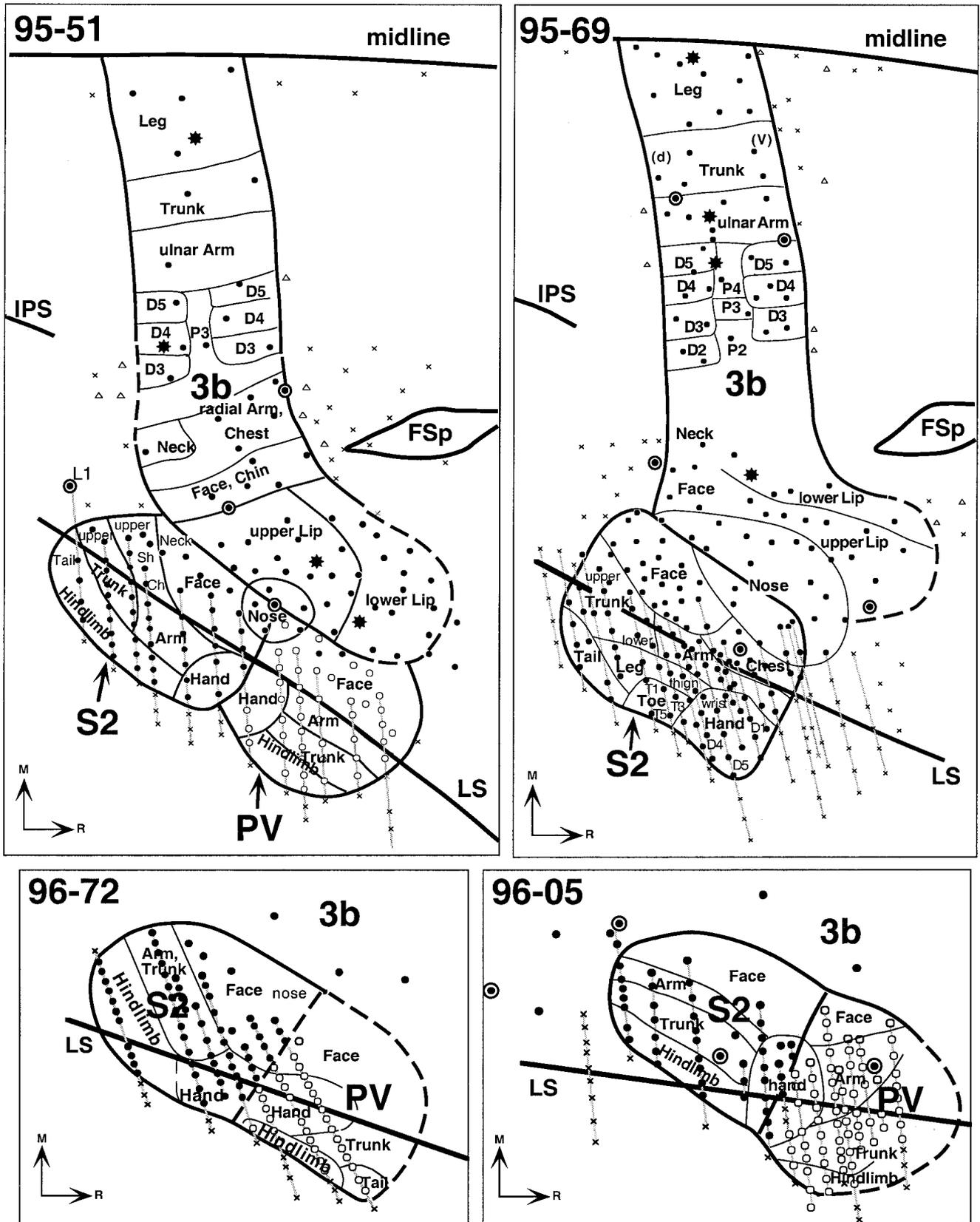


Fig. 3. Somatotopic organizations of areas 3b, S2, and PV in different cases. Upper left corner of each box indicates the case number. Solid lines mark the boundaries derived from the electrophysiological mapping data; dashed lines show the boundaries derived from the myeloarchitecture. Stars mark the sites where tracers were placed after the recording session. The locations of the electrolytic lesions (marked by a dot in a circle) were used to help align the cytoarchitectonic and electrophysiological maps. The open black and gray circles

represent the recording sites where neurons were responsive to cutaneous stimuli and rapidly habituating. Note that neurons in areas 3b and S2 had sustained responses to cutaneous stimuli, whereas neurons in PV were rapidly habituating to cutaneous stimuli. Areas 3b, S2, and PV share a common border along the 3b face representation. Areas S2 and PV exhibit somatotopic organizations that are mirror images of each other. Conventions as in Figure 2. Scale bars = 1 mm.

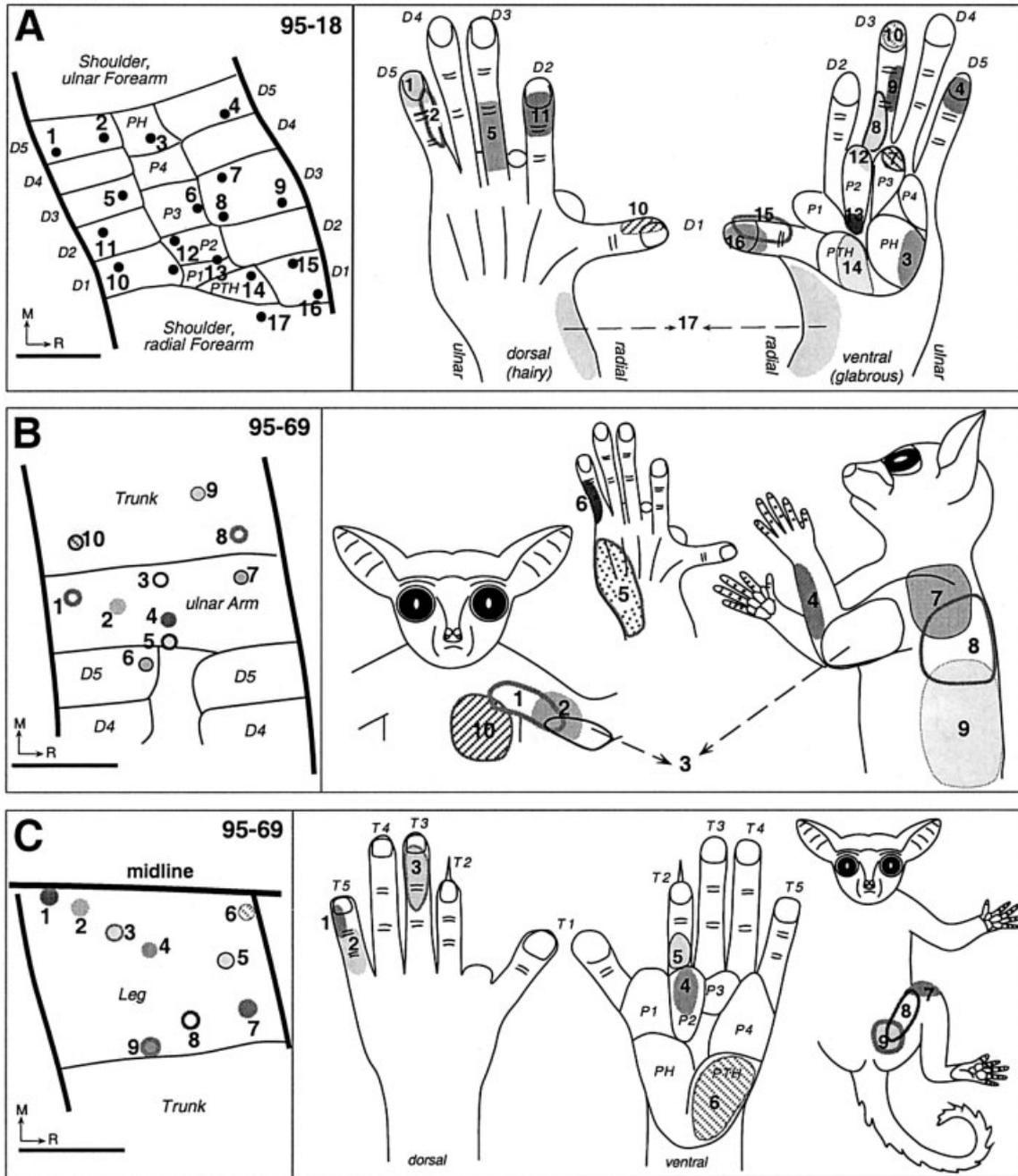


Fig. 4. Receptive fields of 3b neurons. Receptive fields are marked with matching numbers for the corresponding recording sites in different major body representations of hand (A), arm and trunk (B), and hindlimb (C). The left panels illustrate simplified maps showing the progression of recording sites (as numbered) in mediolateral and

rostrocaudal sequences. The right panels show the receptive fields on the body drawings numbered to match the numbers of the recording sites. Note that 3b neurons have small and well-ordered receptive field sizes. Conventions as in Figure 2. Scale bars = 1 mm.

area 3b and just rostral to the face representation in S2. More distant to the area 3b border and into the upper bank of the lateral sulcus, the hand and forelimb representations are followed by the hindlimb representation. The trunk and tail are represented more rostrally. Neurons in PV were responsive to taps and light touch on the body surface, as well as the brushing of body hairs. The

responses were generally less vigorous than those for neurons in area 3b, or in S2, and the neurons tended to respond less well when stimuli were rapidly repeated. The receptive fields were usually larger than those in S2 (Fig. 6). Neurons with receptive fields on the hand, for example, often had receptive fields that also extended into the forearm (receptive fields 3, 4, 9, 10, and 11, in Fig. 6).

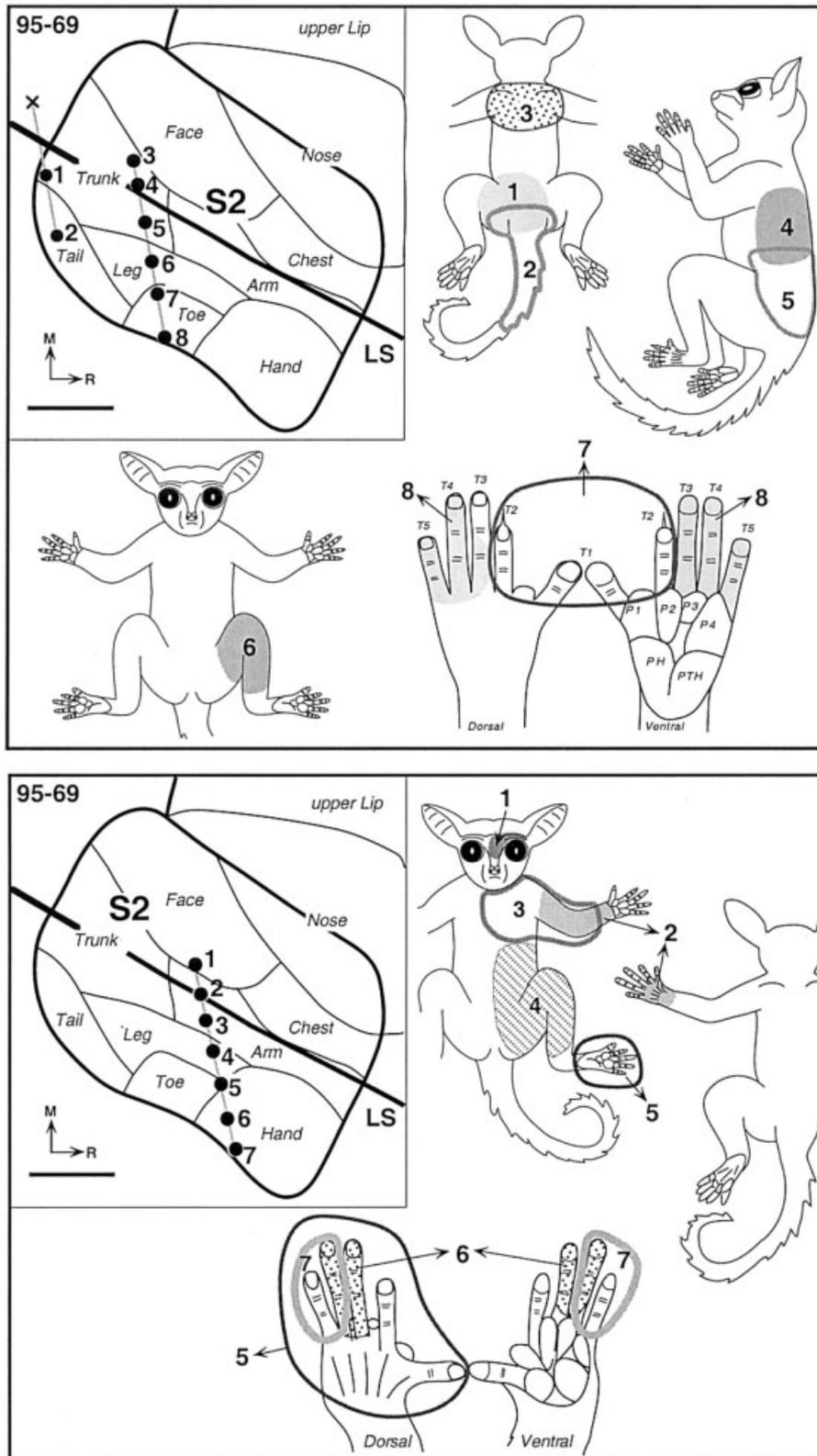


Fig. 5. Receptive fields of S2 neurons. The recording sites are numbered and shown in the upper left corner; the receptive fields corresponding to the recording sites at different distances along the electrode penetrations are indicated. Receptive fields in S2 are generally larger than those for 3b (compare with Fig. 4). Conventions as in Figure 2. Scale bars = 1 mm.

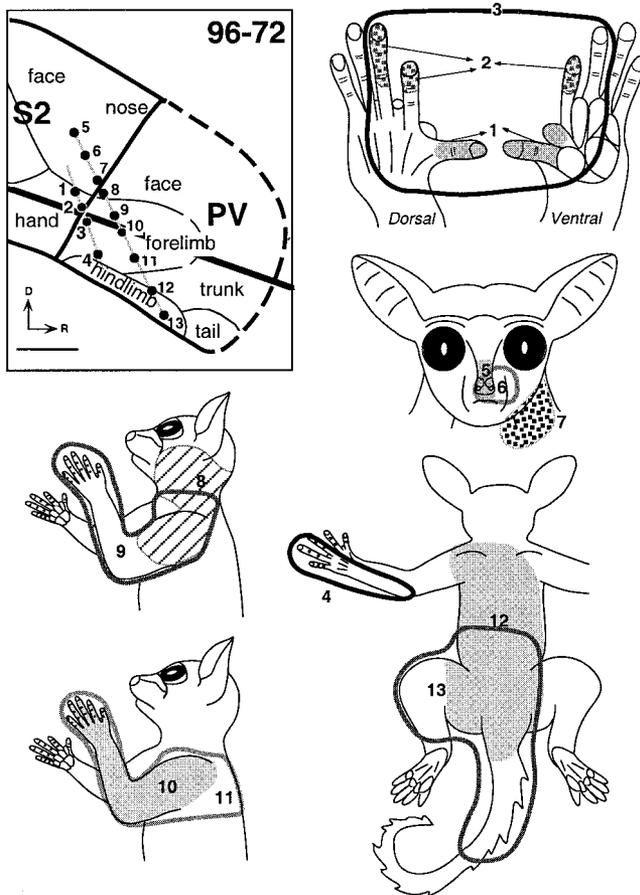


Fig. 6. Receptive fields of PV neurons. Note the progression of receptive fields from the face (sites 5–7) and forelimb (sites 1,2) of S2 to the face and neck (site 8), forelimb (sites 9–11, 3–4), and trunk and hindlimb (sites 12–13) of PV. The receptive fields for the same body representation in PV were generally larger than in S2. Conventions as in Figure 2. Scale bars = 1 mm.

Additional areas in cortex of the lateral sulcus. In monkeys, there is evidence for the existence of several somatosensory areas along the borders of PV and S2 (Krubitzer and Kaas, 1990; Krubitzer et al., 1995; Qi et al., 2002; Coq et al., 1998). Just rostral to PV, a parietal rostral area (PR) is known largely as a region with S2 and PV connections. Deep to S2 in the fundus of the lateral sulcus, a ventral somatosensory area (VS) forms another representation of the body (Cusick et al., 1989). More recently, microelectrode recordings have revealed that the body surface is also represented deep to PV in a pattern that seems to mirror that in VS (Coq et al., 1998). The two deep representations have been referred to as VSc (caudal VS) and VSr (rostral VS). Cortex caudal to S2 near the fundus of the lateral sulcus, the retroinsular area (Ri), has also been described as responsive to cutaneous stimuli (Robinson and Burton, 1980a,b; Friedman et al., 1986; Krubitzer et al., 1995).

Our recordings produced limited evidence for somatosensory representations in addition to S2 and PV in the cortex of the lateral sulcus. This cortex was sometimes unresponsive to somatosensory stimuli (e.g., Fig. 8), pos-

sibly because of the depth of anesthesia or the electrode being too deep or too superficial. In other instances, recordings were obtained from neurons in some of this tissue. For example, recordings were obtained from cortex along the deep (ventral) border of PV in case 92-32 (Fig. 9C-2). By position, this cortex corresponds to PR of macaques (Krubitzer and Kaas, 1990), and this term is used here. The region is a dysgranular portion of insular cortex. The superficial part of PR was responsive to the forelimb and arm and the deeper part of the lower trunk. Neurons responsive to touch on the face were not found. The neurons responded to light touch on the body and to movement of hairs, but the responses rapidly habituated with repeated stimulation. The receptive fields were larger than those for neurons in PV, and the responses were less vigorous. Responses to somatosensory stimuli deep to S2 in the region of VSr (Coq et al., 1998) and VSc (area VS of other reports; Cusick et al., 1989; Krubitzer et al., 1995; Qi et al., 2002) were not obtained (Fig. 9C-2), although we made few attempts to do so.

Cortex caudal to S2 has been referred to as the retroinsular area or region (Robinson and Burton, 1980a,b; Friedman et al., 1986). A few of our recordings were in this region, and neurons were responsive to light taps on the skin (Fig. 9C-2). The receptive fields were large, and neurons did not consistently respond to repeated stimuli. Our recordings were not extensive enough to reveal any clear somatotopy.

Architectonic characteristics of somatosensory areas. Our recordings were related to the architecture of cortex, in brain sections either cut in the coronal plane or cut parallel to the surface of flattened cortex. Results are only briefly noted here, because the architectonic characteristics of areas 3b, 3a, and 1–2 have been described before after borders were identified electrophysiologically (Sur et al., 1980; Wu et al., 2000), and the cytoarchitecture of frontal and parietal cortex has been illustrated in detail (Preuss and Goldman-Rakic, 1991b).

In brief, area 3b was consistently identified in the experimental material. In Nissl-stained sections, area 3b was characterized by densely packed, small neurons in layer IV (granular cells), whereas this feature was less pronounced in areas 3a and 1–2. Area 3a was also distinguished by larger layer V pyramidal cells, as was area 1–2. In myelin-stained sections, area 3b was denser in the middle layers than adjoining areas; these middle layers were also darker in cytochrome oxidase (CO) preparations.

Fig. 7. Flattened brain sections showing distributions of label after injections made into area 3b of cases 95-14 (A) and 95-18 (B). The types of tracers used and the locations of injections in the physiologically identified body parts are indicated in the upper right corner. Dashed lines indicate the borders of areas defined by physiological recordings and patterns of myelination. C: Darkfield photomicrographs show WGA-HRP injection sites in cases 95-14 and 95-18. A single injection results in two patches of label, one immediately rostral (i.e., area 3a) and one caudal to area 3b (i.e., area 1/2). D: Top: WGA-HRP injection site within the physiologically identified foot representation of area 3b in case 95-69. Label from this injection is charted in Figure 10. Bottom: Darkfield photomicrograph showing labeled axon terminals and neurons in S2 in the deeper portion of the upper bank of the lateral sulcus resulting from an injection into the area 3b foot representation. Conventions as in Figure 2. Scale bar in A = 5 mm (applies to A,B), in C = 500 μ m (applies to C,D).

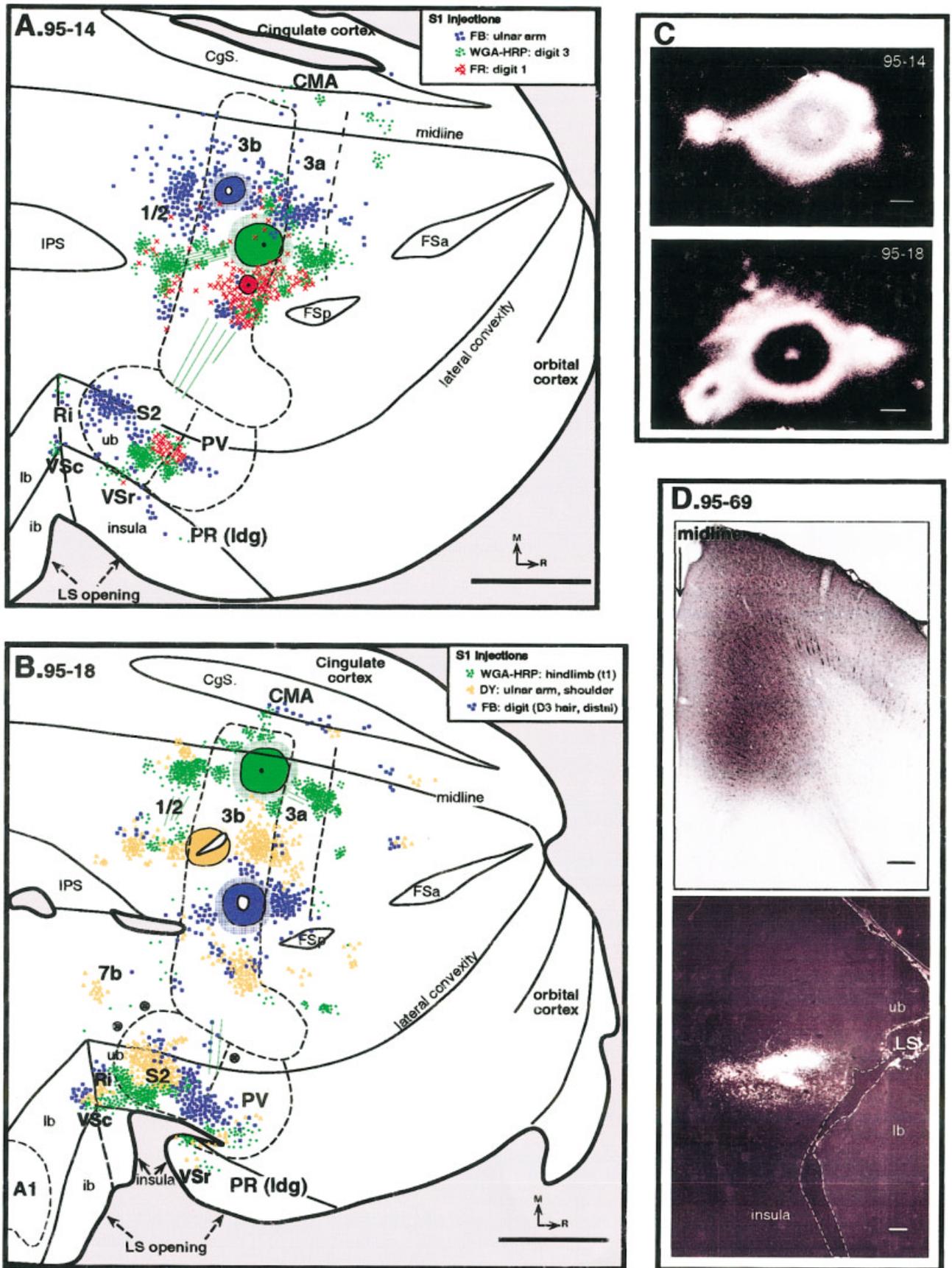


Figure 7

Areas S2 and PV were easily distinguished from area 3b by having a less pronounced layer IV, as well as less dense myelin and CO, but the two areas were not notably different from each other. Slight differences between S2 and PV and adjoining fields in the lateral sulcus were apparent, but we did not attempt to delimit these fields architectonically or describe them fully.

Corticocortical connections

The connections of subdivisions of somatosensory cortex were studied by placing injections of different tracers into physiologically identified locations in area 3b, S2, PV, and inferior parietal cortex (presumptive area 7b; Preuss and Goldman-Rakic, 1991a). Results are based on a total of 15 injection sites in nine galagos (Table 1). Distributions of ipsilateral cortical connections are described here. Regions of parietal and frontal cortex were labeled, but none of the injections labeled portions of occipital or temporal cortex.

Connections of area 3b. Injections in area 3b revealed topographic patterns of dense connections with four other areas of somatosensory cortex, areas 3a, 1–2, S2, and PV (Figs. 7–10). The injections also revealed local patterns of intrinsic connections within area 3b (Fig. 7C). The topographic patterns are most easily appreciated in cases in which the cortex was flattened and cut parallel to the surface (Figs. 7A,B, 8A), whereas laminar distributions of labeled neurons are better appreciated in brain sections cut in the coronal plane (Figs. 10, 11). All injections labeled neurons projecting to the injection site; the WGA-HRP injection also labeled axon terminations in target areas (e.g., Fig. 7D). All clusters of neurons that were densely labeled by the WGA-HRP injections also had overlapping foci of labeled terminals.

The basic features of the somatotopic pattern of connections were revealed by three injections in a mediolateral sequence in area 3b of galago 95-14 (Fig. 7A). The most medial injection of FB in the arm representation in area 3b labeled the most medial locations in areas 3a and area 1–2; the more lateral WGA-HRP injection in the representation of digit 3 labeled more lateral locations in areas 3a and 1–2; and the most lateral injection of FR in the representation of digit 1 labeled the most lateral locations in area 3a and area 1–2. In each of these bordering zones, the densest foci of labeled neurons followed the same mediolateral sequence as the injection sites, arguing strongly that these bordering fields form representations that parallel area 3b in overall somatotopic organization. Nevertheless, the distributions of labeled neurons overlap somewhat, indicating that the feedback connections to area 3b from these labeled neurons is somewhat mismatched somatotopically.

Topographic patterns of connections were also apparent in S2 and PV. Foci of labeled neurons were adjoined along the S2/PV border for the D1 injection and nearly so for the D3 injection, but the results are consistent with the premise of two adjoining representations, mirroring each other in somatotopic organization along the joined representations of the hand. The results indicate that digit 3 is represented "lateral" to digit 1 in both areas (lateral in flattened cortex, but deeper in the sulcus). The foci of labeled neurons related to the arm injection in area 3b indicate that the arm is represented caudal to the hand in S2 and rostral to the hand in PV. Thus, the results from this case (95-14) with three injections in area 3b provide

compelling evidence for two representations in cortex adjoining lateral area 3b and areas S2 and PV.

A few neurons in other regions of cortex were labeled by the area 3b injections in case 95-14 (Fig. 7A). Some of these neurons were rostral to area 3a in M1 or area 4 (Wu et al., 2000), in cingulate motor areas of the medial wall of the cerebral hemisphere (Wu et al., 2000), just caudal to area 1–2 in parietal cortex, caudal to S2, or adjoining S2 and PV in insular cortex in the depths of the lateral sulcus. These regions apparently have sparse, and possibly variable, connections with area 3b, and they indicate the locations of additional somatosensory and sensorimotor fields.

Finally, the injections reveal aspects of the pattern of intrinsic connections within area 3b. Labeled neurons from each injection clustered around the injection site and tended to distribute more in a rostrocaudal than a mediolateral direction. Some overlap of the distributions of labeled neurons from different injections occurred, and some small foci of somatotopically mismatched connections were apparent. Most notably, the injection in the representation of the upper arm in case 95-14 (Fig. 7A) labeled some neurons lateral to the representation of the hand in area 3b (and in area 1–2), nearly 5 mm from the injection site. These displaced foci of labeled neurons are not completely surprising, however, as the representation of the arm is split in galagos, with the posterior arm medial and the anterior arm lateral to the hand representation (Sur et al., 1980). Thus, these long intrinsic (and in area 1–2) connections relate to adjoining skin surfaces on the arm.

The conclusions based on the results of case 95-14 (Fig. 7A) are supported and extended by similar results from other cases. Case 95-18 (Fig. 7B) differs from case 95-14 in that the three injections were in area 3b locations representing one similar and two different body parts. The injection at the similar location, representing the ulnar side of the arm, again labeled neurons in rostrally adjacent cortex across the width of area 3b and more laterally in 3b roughly where the radial side of the arm is represented lateral to that of the hand. The mediolateral sequence of three injections again produces matching sequences of foci of labeled neurons in area 3a and area 1–2 (although there was little label in area 1–2 from the D3 injection), a large D3 focus (hand) at the S2/PV border, a more caudal S2 focus and a more rostral PV focus for the arm injection, and deeper S2 and PV locations for the hindlimb injections. These are the expected topographic patterns based on the proposed somatotopic organizations of these four fields. In addition, the three regions of labeled neurons in Ri suggest the location of another somatotopic representation proceeding from foot to arm to hand away from the caudal S2 border. Finally, a few labeled neurons were again located in M1, cingulate motor areas, and parietal cortex caudal to area 1–2.

Results from a third case (95-51) with four injections involving area 3b confirm the overall pattern and provide additional findings (Fig. 8A). First, the medial injection in cortex devoted to the hindlimb produced a distribution of labeled cells very much like the distribution produced by the other hindlimb injection in case 95-18 (Fig. 7B). Second, the injection in cortex responsive to the upper lip labeled neurons in areas S2 and PV but not elsewhere (except for few neurons in area 3a). A second injection, involving the lower lip in area 3b, labeled neurons mainly in PV, with a few in S2, but also a large number in area 3a.

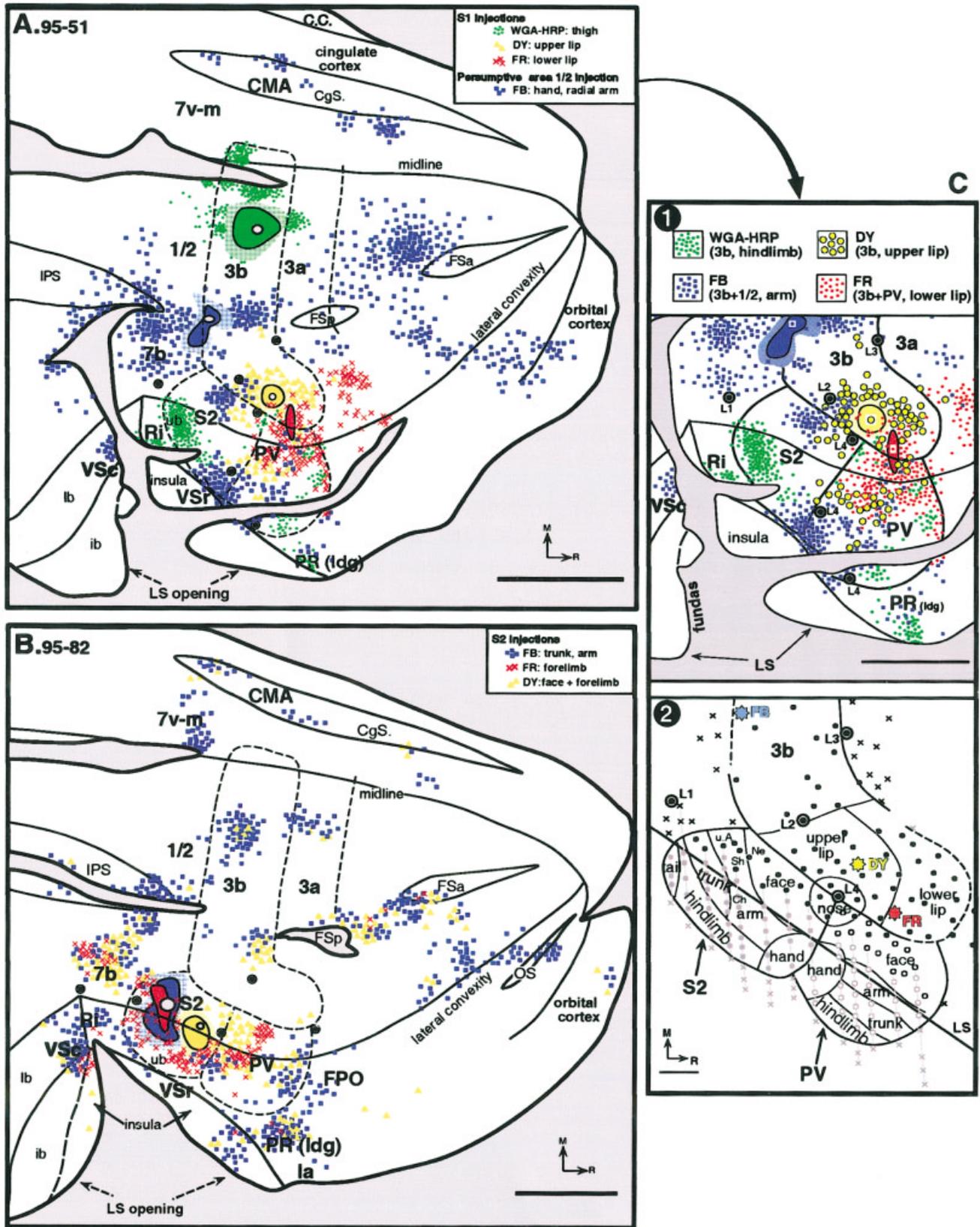


Fig. 8. Distributions of transported label after injections into area 3b in case 95-51 (A) and injections into S2 in case 95-82 (B). Note that S2 injections result in more label in the cortex near the lateral sulcus. C1: Enlarged view shows transported label in the lateral sulcus in case 95-51. C2: Recording sites and cortical somatotomy near the vicinity of lateral sulcus in case 95-51. Solid lines indicate the areal

boundaries of the physiological maps, and dashed lines indicate the boundaries of the myelination maps. A comparison of C with D shows that the locations of label are in good agreement with the somatotomy obtained from the physiological map. Conventions as in Figure 2. Scale bar in A = 5 mm (applies to A,B), in C1 = 3 mm, in C2 = 1 mm.



Fig. 10. Series of coronal sections through parietal cortex in case 95-69 demonstrating the connections of 3b following injections into different body parts. The upper left panel shows the recording map and the location of injections. The lower right panel shows the sym-

bol for the transported labels. The injection cores are indicated. Marker lesions are numbered on the surface view (box) and on the coronal brain sections. The 40- μ m sections are numbered from caudal to rostral (inside each section). Scale bar = 1 mm.

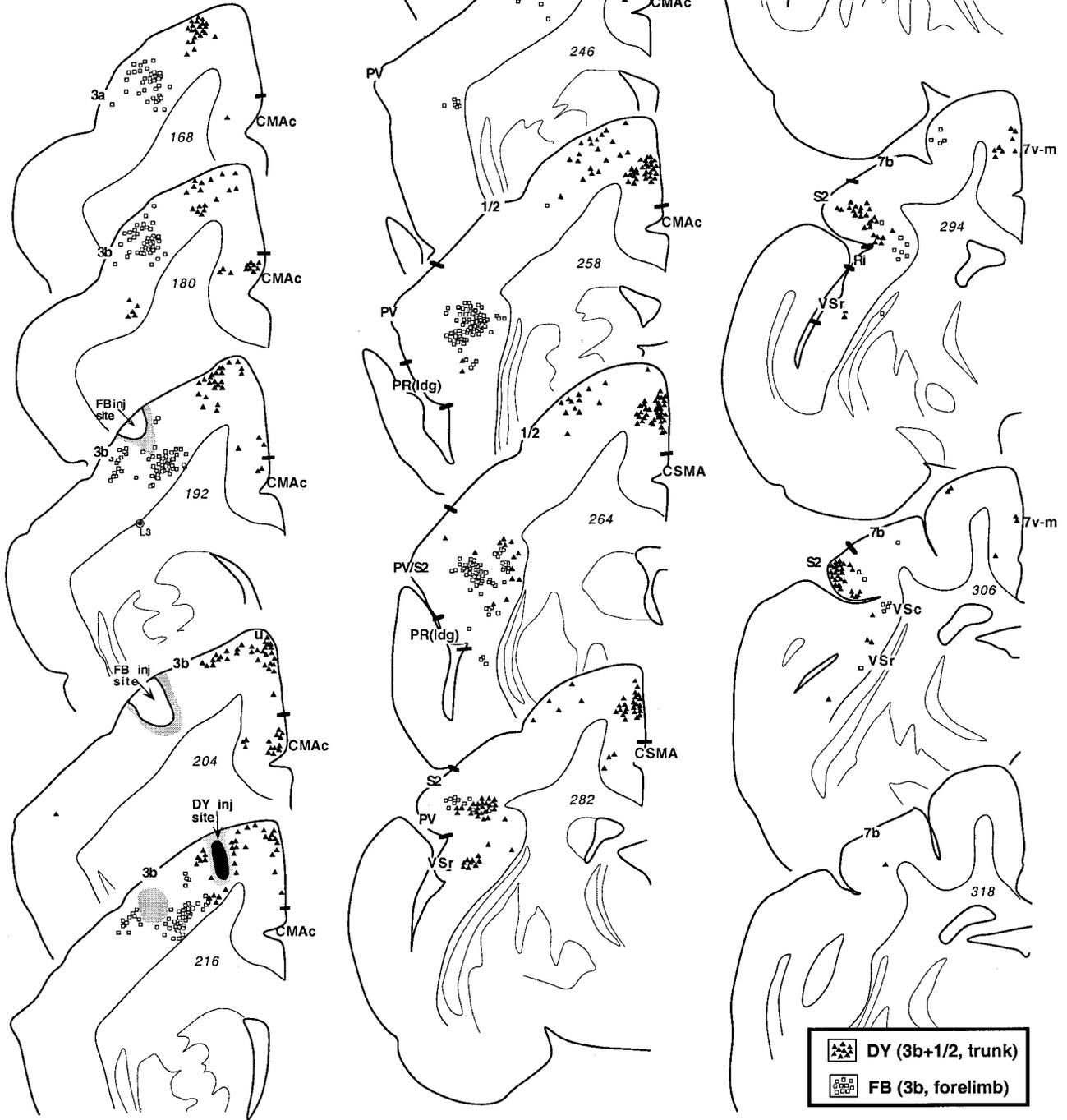
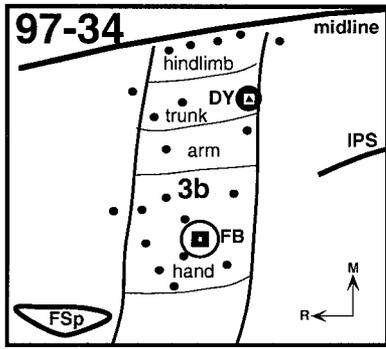


Fig. 11. Series of coronal sections in case 97-34 demonstrating the connections of 3b following different tracers injected into the trunk and forelimb representations. Compare with Figures 15 and 16 for the location of transported neurons following injections made into the same body representations of PV and S2. Sections are numbered rostral to caudal. Conventions as in Figure 10. Scale bar = 1 mm.

Because this second face injection also included the bordering portion of PV, the labeled neurons in area 3a may reflect projections to PV. The results from these two face injections suggest a lateral face representation in area 3a, as expected (without evidence of connections related to the upper lip), but they provide no evidence for representations of the lips in lateral 1–2. Third, the injection in cortex activated by the hand and radial arm labeled somatotopically appropriate locations in areas 3a, 1–2, S2, and PV, but also somatotopically mismatched locations in face portions of areas 3b and S2. Fourth, the results from the injection in the hand-arm cortex, by involving the bordering portion of area 1–2, suggest that area 1–2 has a pattern of connections that differs from that of area 3b by involving more of posterior parietal cortex, more strongly relating to M1, and involving orbital frontal cortex. Fifth, the results provide further evidence for a somatotopic pattern in Ri, with the hindlimb adjoining S2 and the arm more distant on the lower bank of the lateral sulcus. Likewise, separate arm and leg representations are suggested for PR.

The brains from the other two cases with area 3b injections were cut coronally. Results from these cases were used to reveal laminar patterns of connections and further demonstrate the interconnections between area 3b and areas S2, PV, 1–2, 3a, Ri, and PR (Figs. 10, 11). In area 3b, most of the neurons labeled by area 3b injections were in the superficial layers, especially as the neurons were more distant from the injection site. Labeled neurons in S2, PV, 1–2, and 3a included both superficial and deep layers, mainly layers I–II and V. Terminals labeled by the WGA-HRP injections in 3b were concentrated in layer IV in areas S2 and PV (Fig. 7D). Therefore, inputs from 3b to these areas exhibit the feed-forward connection pattern (Felleman and Van Essen, 1991). The topographic patterns approximated those expected from the somatotopies of areas. Thus, the forelimb injection in 3b labeled S2 and PV neurons closer to the 3b border than the trunk injection (Fig. 10); the face injection in 3b labeled neurons in S2 and PV along the 3b border; and hand, arm, and hindlimb injections labeled S2 and PV neurons progressively more distant from this border (Fig. 9).

Connections of S2. One to three injections of different tracers were placed at physiologically identified sites in S2 of six galagos. Connections were revealed with all three subdivisions of anterior parietal cortex, several areas of the lateral sulcus, lateral parietal cortex tentatively termed area 7b, motor cortex, and orbital frontal cortex, as described further below (Figs. 8B, 9A,B). Because of the small size of S2, it was difficult to confine injections to the representations of single body parts. However, the placement of injections in different portions of S2 did provide useful information on the somatotopy of other somatosensory areas. The surface-view distributions of neurons labeled by S2 injections were most accurately revealed in three cases in which cortex was flattened and cut parallel to the surface.

The intrinsic connections of S2. The injections in S2 labeled neurons scattered over much of S2. Some injections labeled more widespread distributions than others. A good example is the FR injection in the forelimb representation of galago 95-82 (Fig. 8B). Labeled cells extended across the deeper half of S2 devoted to the body, while avoiding the portion adjoining area 3b that represents the face. Similar widespread connections were revealed by the

FR injection in the body representation of S2 in case 96-88 (Fig. 9B), whereas somewhat less broad distributions were seen with other injections (Figs. 8B, 9A). Except for labeled neurons immediately deep to injections in S2, labeled neurons in other parts of S2 tended to be in layer III (Figs. 12, 15).

S2 connections with anterior parietal cortex. Injections in S2 typically labeled foci of neurons in areas 3b, 3a, and 1–2, with densest foci in area 3b (Figs. 8B, 9A,B). The somatotopic locations of labeled neurons tended to correspond to those of the S2 injection sites for areas 3a and 3b, but this was less apparent for area 1–2. In case 95-82 (Fig. 8B), for example, the FB injection in S2 trunk and arm labeled medial locations (also see Fig. 15) in 3a and 3b corresponding to the trunk and arm, and a few such neurons in area 1–2, but other labeled neurons were found in the more lateral portion of 1–2. The injection of DY in the face-forelimb portion of S2 (Fig. 8B) also labeled medial locations in 3a and 3b, presumably because of the forelimb involvement, and more densely a lateral location in 3b where the face is represented. As the anterior arm is represented lateral to the hand in galagos, a smaller lateral focus of labeled neurons from the FB trunk and arm injection may be somatotopically appropriate. An FR injection in the body representation in S2 (Fig. 9B) also labeled neurons in medial locations in areas 3b and 3a and over more scattered locations in area 1–2. Less confined injections in face, arm, and trunk portions of S2 (Fig. 9A) labeled neurons over larger portions of areas 3b, 3a, and 1–2 (also see Fig. 15).

Neurons labeled by S2 injections were mainly located in layer III of areas 3a, 3b, and 1–2 (Fig. 15). Along with the evidence from injections placed in 3b (i.e., terminations from 3b to S2 were restricted to layer IV), the connection patterns indicate that the areas of anterior parietal cortex provide feed-forward projections to S2, while receiving feedback projections (Felleman and Van Essen, 1991).

S2 Connections with PV and other areas of the lateral sulcus. One of the areas with the densest interconnections with S2 was PV. S2 and PV mirror each other in somatotopic organization, but this was not always obvious in the connection patterns because injections involved large portions of S2, and connections were not completely somatotopic. In case 95-82 (Fig. 8B), for example, a rostral DY face-forelimb injection and a caudal FR forelimb injection in S2 labeled caudal and rostral regions of PV, as expected from somatotopy, but labeled DY neurons were also in rostral positions. The large FB injection in the arm area-trunk region labeled PV neurons more rostrally than expected, and also in an unexpected caudal focus. Other injections in S2 labeled cells over large portions of PV (Fig. 9A) or sometimes labeled few cells in PV (Fig. 9B). The labeled neurons in PV were in both superficial and deep layers (Figs. 12, 15).

In addition to labeling neurons in PV, injections in S2 labeled neurons in cortex adjoining S2 deeper in the lateral sulcus (Figs. 8B, 9A,B). Cortex in this region has been called the ventral somatosensory area (VS), with caudal (VSc) and rostral (VSr) divisions adjoining S2 and PV, respectively. Although foci of label varied with the locations of the injections in S2, there was much scatter across this small region of cortex, and no obvious somatotopic pattern. Many of the labeled neurons were in deep cortical layers (Fig. 12), although some were in superficial layers

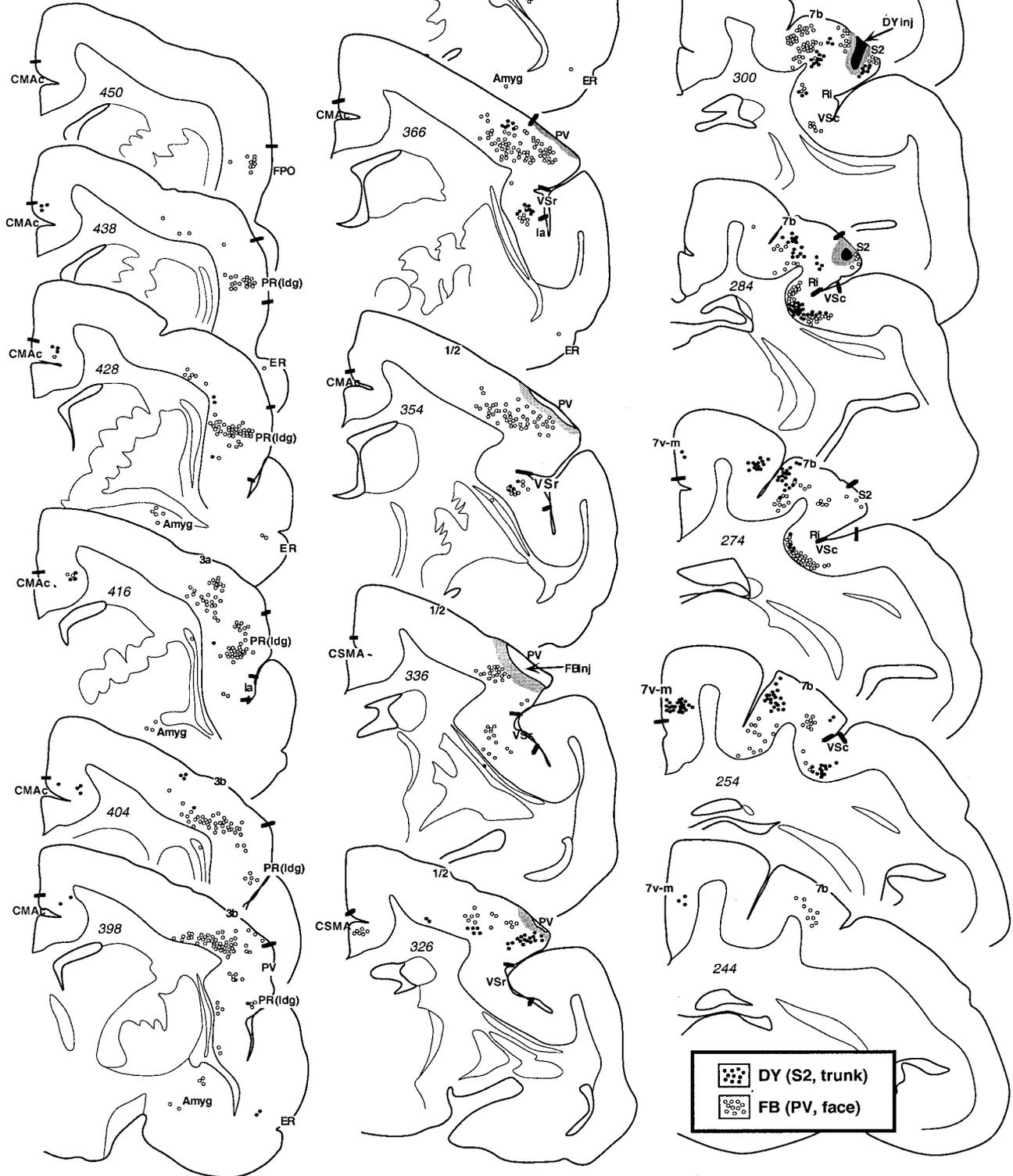
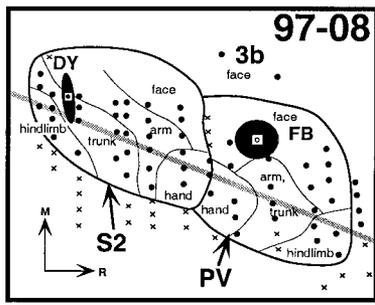


Fig. 12. Series of coronal sections in case 97-08 showing the distributions of label for injections placed in the trunk portion of S2 and the face portion of PV. Conventions are as in Figure 10. Note that S2 and PV share common connections with a majority of areas. However, only S2 is connected with 7 v-m, whereas only PV is connected with the amygdala and entorhinal cortex. Scale bar = 1 mm.

(Fig. 14). Labeled neurons were also located in the Ri region caudal to S2 and the PR region rostral to PV.

S2 connections with inferior parietal cortex (7b), motor cortex, and orbital-frontal cortex. The region of cortex just caudal to area 1–2 and ventral to the intraparietal sulcus in galagos has been referred to as area 7b (Preuss and Goldman-Rakic, 1991a). Dense patches of labeled neurons were found in area 7b and adjoining cortex (Figs. 8B, 9A,B). The distributions of neurons for different injections overlapped, and there was no clear somatotopic pattern. Labeled neurons were in both infragranular and supragranular layers, with more neurons in layer III (Figs. 12, 15). Other distributions of labeled neurons were located in primary motor cortex (M1) in the region representing the forelimb between the anterior (FSa) and posterior (FSp) frontal sulci (Figs. 8B, 9B), as well as in more lateral locations (Fig. 9B). These neurons were concentrated in the superficial layers (Figs. 12, 15). A few labeled neurons were in cingulate motor cortex and cingulate sensorimotor cortex of the medial wall (see Wu et al., 2000 for motor areas of galagos). Finally, patches of labeled neurons were distributed across regions of orbital cortex (described as area 14VL by Preuss and Goldman-Rakic, 1991b), with no obvious somatotopic pattern.

Connections of PV. One or two different tracers were injected into physiologically identified locations in PV of four galagos. The connections of PV were widespread, and they resembled those of S2. Following injections in PV, dense foci of labeled neurons were located in areas 3b, 3a, and 1–2 of anterior parietal cortex, S2 and other areas of the lateral sulcus, inferior parietal cortex, M1 and cingulate motor areas, and orbital frontal cortex. As for S2, the intrinsic connections were widely distributed in PV, and they largely involved layer III cells.

PV Connections with anterior parietal cortex. Examples of areal distributions of labeled neurons after injections in PV are shown in Figure 9A and B. In case 96-32 (Fig. 9A), an injection of FR was placed in the face and forelimb region of caudal PV. Dense distributions of labeled neurons were in hand and face portions of areas 3b, 3a, and 1–2, with labeled cells being more densely and more broadly distributed in area 3b and more sparsely in area 1–2. Similar results were obtained in case 96-88 (Fig. 9B), in which two different tracers involved face and forelimb portions of PV. These injections were less effective in labeling neurons than the injection in case 96-32, neurons that were labeled were located in face portions of areas 3b, 3a, and 1–2. Area 3b had additional labeled neurons in forearm and hand regions. Other injections in PV also labeled neurons in these three areas (Figs. 12, 13, 15, 16, 17). The labeled neurons were in both superficial and deep layers, and terminations revealed by a WGA-HRP injection (Fig. 13) and a BDA injection (Fig. 16) were in overlapping regions in both superficial and deep layers, while avoiding layer IV. Thus, the projections of PV to anterior parietal cortex were of the feedback type.

PV connections with S2 and adjoining areas of the lateral sulcus. Injections in PV usually (Figs. 9A, 12, 13, 15, 16), but not always (Fig. 9B) labeled large numbers of neurons in S2. The labeled neurons were both supragranular and infragranular, and terminations in S2 were colocalized in the same layers. Thus, PV appears to provide feedback connections to S2. Other labeled neurons were in the VSr region deep in the sulcus (Fig. 14E), just rostral to PV in the PR region, and caudal to S2 in the Ri

region (Fig. 14F). Projections overlapped the same regions and showed a mixed pattern, with terminations often involving superficial and deep layers, but also involving layer IV in VSc and possibly in PR (Figs. 13, 14B,F, 16).

PV connections with inferior parietal and motor cortex. Injections in PV also labeled neurons in the 7b region just caudal to area 1–2 (Figs. 9A,B, 14C), with labeled neurons and terminals in both superficial and deep layers (Figs. 13, 15). Other labeled neurons were found in primary motor cortex, M1, and just rostral to M1 in the location of the ventral premotor area (PMV; Fig. 9A,B). Motor cortex located on the medial wall of the cerebral hemisphere, including caudal subdivisions of the cingulate motor (CMac) and cingulate sensorimotor areas (CSMA; Wu et al., 2000), also displayed connections with PV (see coronal sections of Figs. 9A,B, 11, 12, 13, 14A). Labeled neurons and terminals were in both superficial and deep layers.

PV connections with orbital cortex, perirhinal cortex, and amygdala. The orbital frontal cortex (area 14VL of Preuss and Goldman-Rakic, 1991) was densely labeled after PV injections, possibly more so than after S2 injections (Fig. 9A,B). Retrogradely labeled neurons and terminals were in superficial and deep layers. Some retrogradely labeled neurons, but not terminals, were in perirhinal cortex (area 35) and in the amygdala (Fig. 18). The labeled neurons were in the deeper layers of perirhinal cortex and mainly in the medial dorsal nucleus but also the lateral nucleus of the amygdala (Fig. 18). The existence of connections between PV and limbic systems and the denser connections between PV and orbital cortex mark the different functional role of PV from S2.

PV connections with 7b Injections in the region of 7b (Fig. 14D) were made in two cases. A large FB injection (Fig. 9A) medial and caudal to S2 labeled neurons in S2, PV, Ri, VSc, and adjoining parts of parietal cortex. Other labeled neurons were in area 1–2, and a few were in area 3b. A greater number of labeled neurons were scattered across the lateral frontal lobe. A few labeled neurons were in cingulate motor cortex. A very restricted injection in the 7b or lateral extreme of area 1–2 (Fig. 9B) labeled a few neurons in S2, PV, posterior parietal cortex, and cortex near the tip of the lateral sulcus.

DISCUSSION

Our present results provide the first comprehensive description of the organization and connections of somatosensory cortex of any prosimian primate (Fig. 19). Primates emerged with the major radiation of Eutherian mammals over 60 million years ago (Purvis, 1995), and they soon diverged into three major branches of prosimian or strepsirrhine primates, tarsoids, and anthropoid primates (New World monkeys, Old World monkeys, apes, and humans). Prosimians include lemurs, lorises, and galagos. These prosimian primates are varied in body size, ecological specializations, and behavior (Fleagle, 1988). However, they all have small brains relative to those of other primates (Radinsky, 1974), and this alone suggests that they may have retained more brain features from a preprimate past than the more derived anthropoids. Our studies were on galagos, because they are an available prosimian that breeds very successfully in captivity.

Previous studies of somatosensory cortex in prosimians have involved microelectrode maps and the architecture of the S1 region of several species of galagos (Sur et al., 1980;

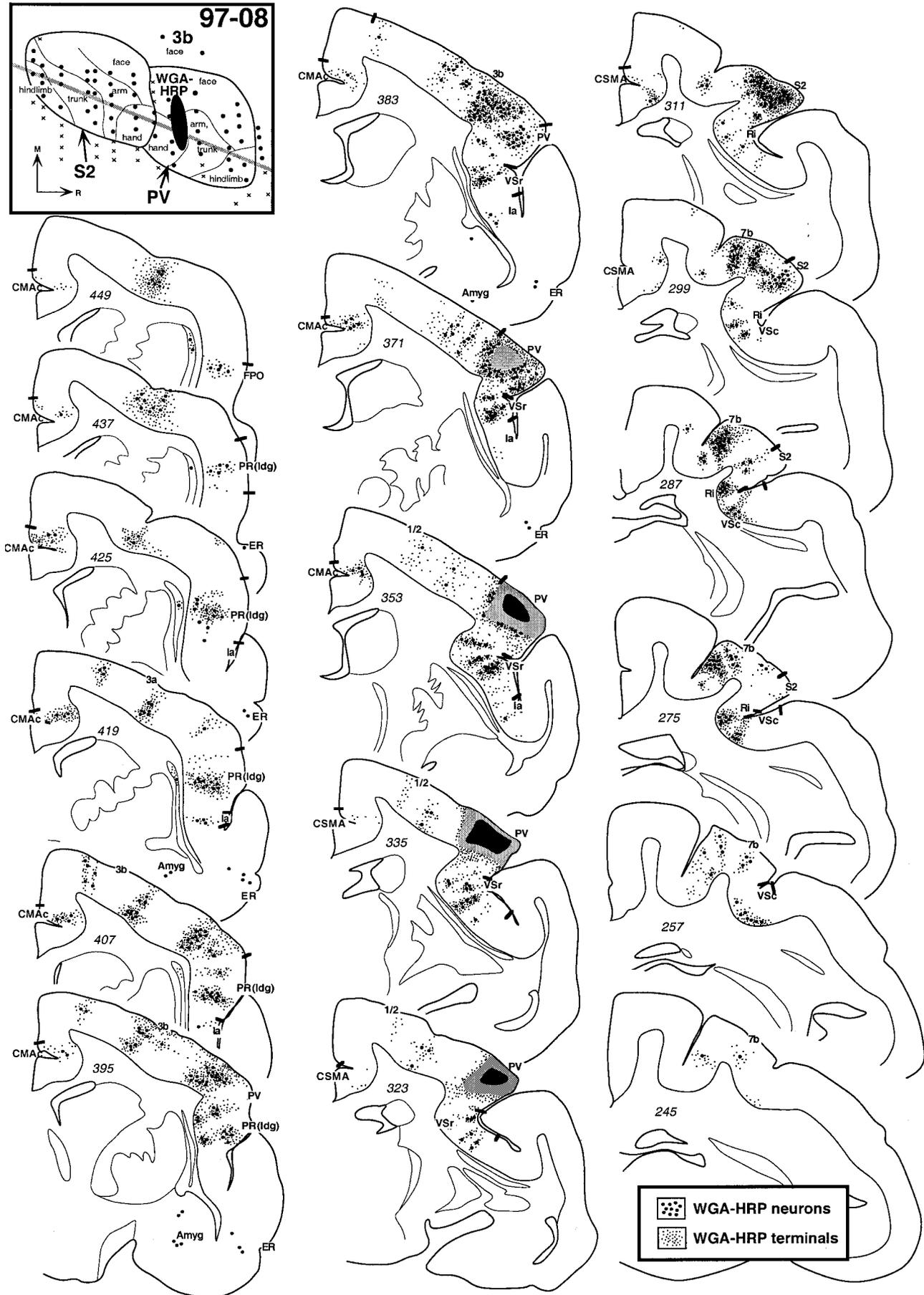
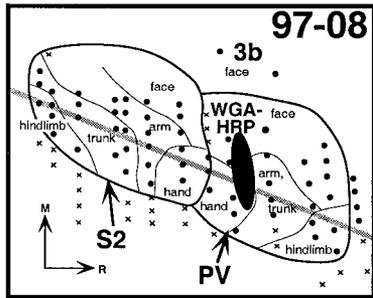


Fig. 13. Series of coronal sections in case 97-08 showing the labeled terminals (small dots) and neurons (large dots) following a WGA-HRP injection into the forelimb representation of area PV. The injection core is shown in black. Conventions as in Figure 11. Scale bar = 1 mm.

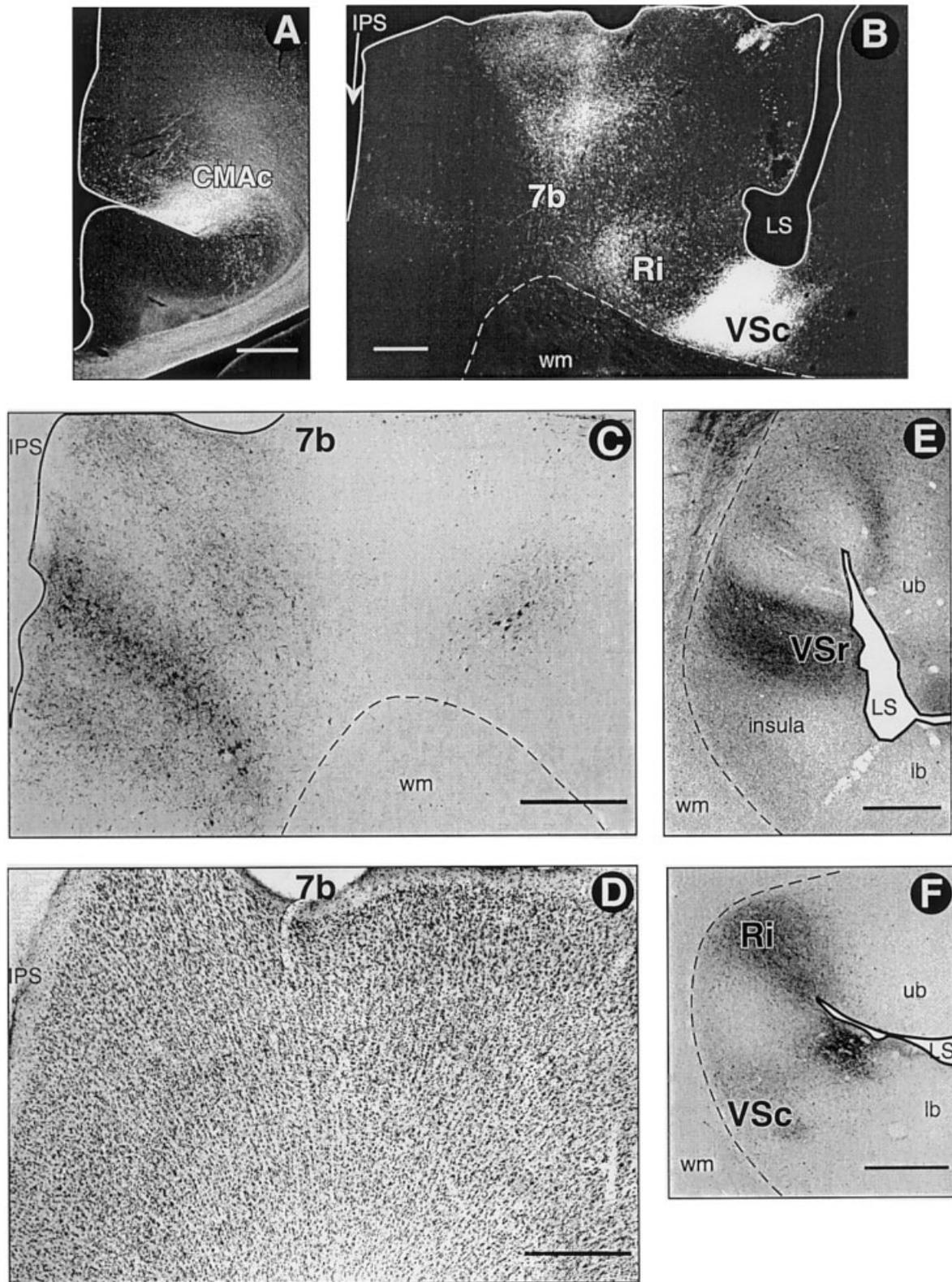


Fig. 14. Photomicrographs showing the transported label following a WGA-HRP injection into the forelimb region of PV in case 97-08. **A,B:** Darkfield. **C-F:** Brightfield. Densely labeled terminals and neurons are located in the lateral sulcus, inferior parietal lobe, and upper

bank of the cingulate cortex. **D:** Nissl-stained section shows the cytoarchitecture of area 7b in relation to the locations of transported label in C. See also Figure 13. See list for abbreviations. Scale bars = 500 μm.



Fig. 16. Series of coronal sections in case 97-34 demonstrating the labeled terminals and neurons following a BDA injection into the face and upper arm representations of PV. All connections are reciprocal. Conventions as in Figure 10. Scale bar = 1 mm.

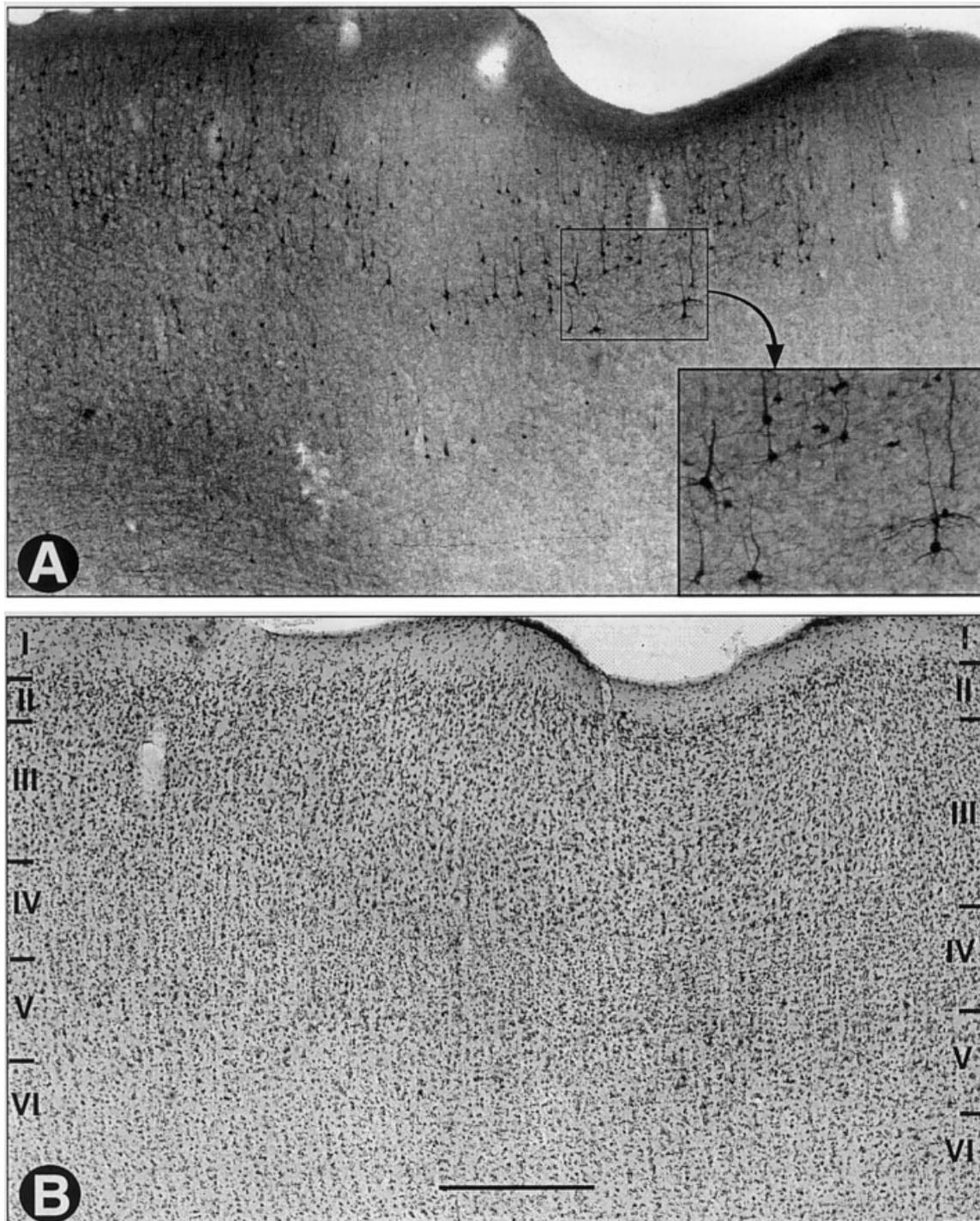


Fig. 17. **A:** Labeled neurons in area 3b following a BDA injection into PV in case 97-34 (Fig. 16) The box shows several of these neurons at a higher magnification. **B:** Adjacent Nissl section identifying area 3b. By comparing A and B, one can see that most of the labeled neurons are in layer III. Scale bar = 500 μm .

Carlson and Welt, 1980), slow loris (Krishnamurti et al., 1976; Carlson and Fitzpatrick, 1982), and potto (Fitzpatrick et al., 1982). In addition, the existence of a second somatosensory area, S2, was demonstrated by microelec-

trode mapping methods in galagos (Burton and Carlson, 1986; Garraghty et al., 1991). Finally, there have been a number of attempts to parcellate somatosensory and other regions of cortex in architectonic studies in several pros-

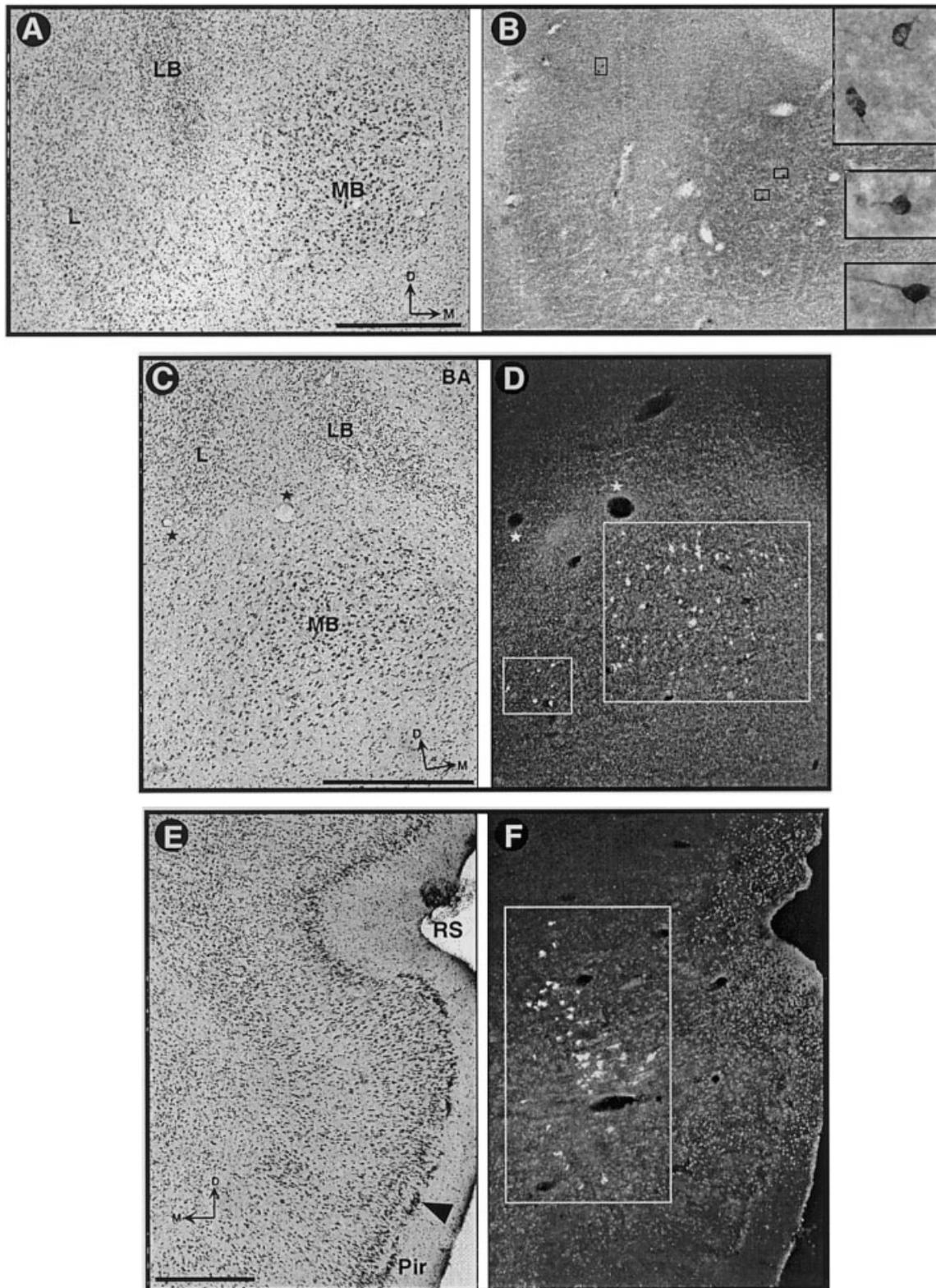


Fig. 18. Labeled neurons in limbic structures following an injection of BDA in PV in case 97-34 (see Fig. 16). Nissl-stained sections show nuclei of the amygdala (**A,C**) and borders of entorhinal cortex (**E**). These Nissl-stained sections are matched by adjacent sections processed for label on the right (**B,D,F**). **B**: BDA-labeled neurons in

brightfield. The labeled neurons in the small box are shown at higher magnification on the right. **D,F**: WGA-HRP-labeled neurons in dark-field. Boxes surround labeled neurons. Stars mark matching blood vessels in **C** and **D**. Scale bar = 500 μ m. See list for abbreviations.

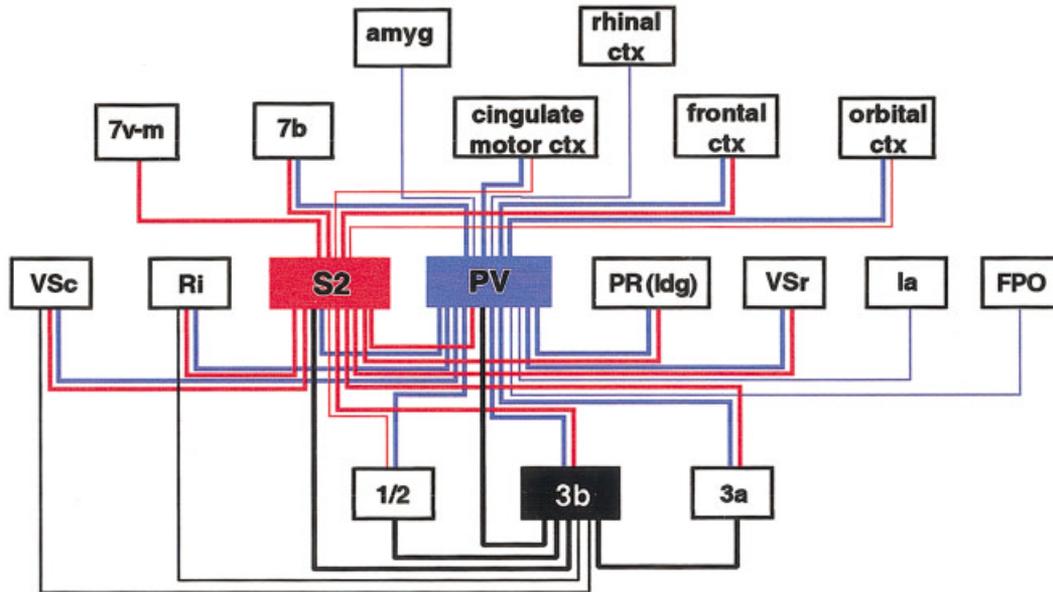


Fig. 19. Summary of corticocortical and corticolimbic connections of the somatosensory areas. Connections between all areas are reciprocal, except for the projections from entorhinal cortex and amygdala to PV. Thick lines represent strong connections, and thin lines repre-

sent weak connections. Black lines indicate connections between 3b and other areas; red lines indicate connections between S2 and other areas; blue lines indicate connections between PV and other areas. Note that S2 and PV relay somatic information to limbic structures.

imians, with varying results (Clark, 1931; Bonin and Bailey, 1961; Sanides and Krishnamurti, 1967; Zilles et al., 1979; Preuss and Goldman-Rakic, 1991a). The relationship of the present results to previous findings on prosimians, and to the much more extensive results on monkeys, are discussed below.

Somatosensory areas in prosimian Galagos

Anterior parietal cortex. We identified three areas in anterior parietal cortex of galagos: area 3b or S1 proper, a mediolateral strip of cortex along the rostral border of 3b that we tentatively identify as area 3a, and a mediolateral strip of cortex along the caudal border of 3b that we tentatively identify as a composite field, area 1–2. Area 3b contains a single, systematic representation of mainly the contralateral body surface (present results; Sur et al., 1980; Carlson and Welt, 1980), as it does in monkeys (Kaas et al., 1979). The basic somatotopy of area 3b in galagos and monkeys, with the digit tips (for example) along the rostral border, conforms to the basic organization of the primary somatosensory area, S1, in a wide range of mammals. Because of this similarity and others, the area 3b representation in monkeys has been referred to as S1 proper (see Kaas, 1983 for review).

Traditionally, S1 has been used to refer to cortex that includes areas 3a, 3b, 1, and 2 of monkeys and other anthropoid primates. However, each of these fields is now known to contain a separate representation of the body. As another confusing issue, area 3b of prosimians is not as distinctly differentiated as area 3b of monkeys, so the area has not been consistently identified as area 3b or somatosensory konicortex. Thus, Brodmann (1909) misidentified the present area 3b as area 1 in prosimians, and Clark (1931) considered the area to be a composite (area 1–3) of

three fields of monkeys (3a, 3b, 1), as did Zilles et al. (1979). Krishnamurti et al. (1976) provided the first extensive microelectrode map of S1 in any prosimian primate (slow loris), and a konicortical region (area 3b; Sanides and Krishnamurti, 1967) was recognized as co-extensive with S-1 (also see Preuss and Goldman-Rakic, 1991a, for 3b of galagos).

Although S1 in galagos has the overall somatotopy of area 3b of monkeys, galago S1 does retain some primitive features. In most mammals, the representation of the glabrous forepaw is rostral to that of the rest of the forelimb, but in anthropoid primates the greatly enlarged hand representation displaces the forelimb representation to cortex medial to that devoted to the hand, and cortex lateral to the hand represents the face (Sur et al., 1982). In galagos, the anterior arm is represented lateral to the hand to form a partial continuity with the neck and face representations (present results; Sur et al., 1980). In this regard, the somatotopic pattern in galagos is less derived than in monkeys, as is the cytoarchitecture.

The intrinsic connections of area 3b of prosimians have not been described before. The results resemble those from monkeys (Krubitzer and Kaas, 1990) in that connections are largely confined to the region of the injection site and tend to distribute more rostrocaudally across area 3b than mediolaterally across representational divisions. Some of the longer range intrinsic connections appear to unite the anterior and posterior arm representations on the lateral and medial sides of the hand representation.

Cortex immediately rostral and immediately caudal to S1 in galagos has generally been described as unresponsive to somatosensory stimuli (Sur et al., 1980). In contrast, area 3a, just rostral to area 3b, is responsive to muscle spindle receptor activation and (to a lesser extent)

cutaneous receptor activation in monkeys (Krubitzer and Kaas, 1990), whereas caudal to area 3b, area 1 has long been known to form a systematic representation of cutaneous receptors (Kaas et al., 1979). Thus, one of the important findings of the present experiments was clear evidence for such representations bordering area 3b in galagos. Although we did record a few responses to taps on the skin and other somatosensory stimuli in these bordering zones, and the results supported the concept of bordering parallel representations, these recordings were too few to be compelling. Instead, the injections of tracers in area 3b provided convincing evidence of separate representations along both borders, paralleling area 3b in somatotopy.

We refer to the more anterior field as area 3a because it is likely to be homologous with area 3a of monkeys. Cytoarchitecturally, this cortex has the thinner layer IV and the larger pyramidal cells of layers III and V (Wu et al., 2000) that characterize area 3a (Jones and Porter, 1980). Thus, the region was identified histologically as area 3a in galagos by Preuss and Goldman-Rakic (1991a) and in slow lorises by Sanides and Krishnamurti (1967). The connection pattern with area 3b matches that of area 3a of monkeys (Huffman and Krubitzer, 2001). In our investigation of motor areas of cortex in galagos, we found that electrical stimulation with microelectrodes in area 3a evoked movements in a somatotopic pattern from hindlimb, forelimb, to face movements in a mediolateral sequence, indicating that a movement map is in at least approximate register with the area 3b inputs. As movements can be elicited from area 3a of monkeys (Stepniewska et al., 1993, for owl monkeys; Wu and Kaas, 1999, for squirrel monkeys), this feature also suggests that the rostral region is correctly identified as area 3a in galagos. If so, we would also expect thalamic connections from the dorsal, proprioceptive portion of the ventroposterior complex (the ventroposterior superior nucleus; Cusick et al., 1985) in galagos.

The identity of cortex immediately caudal to area 3b in galagos is less certain. This cortex was relatively unresponsive to light touch, although it had dense connections with area 3b in a parallel topographic pattern. In most monkeys, area 1 is highly responsive to cutaneous stimulation (Merzenich et al., 1978; Kaas et al., 1979; Sur et al., 1982; Pons et al., 1985) and is densely connected with area 3b (Krubitzer and Kaas, 1990). In contrast, area 2 is activated by both deep receptor (muscle spindle) and cutaneous receptors and has much sparser connections with area 3b (Pons et al., 1985; Pons and Kaas, 1986). The caudal projection zone of area 3b in galagos is very much like area 1 of monkeys in relative size, position, and connections with area 3b, so a reasonable assumption would be that the field is area 1. If so, we would expect thalamic connections with the ventroposterior nucleus, rather than the ventroposterior superior nucleus, which projects to area 2 (Cusick et al., 1985). Although the responsiveness of the area in galagos is not like area 1 of monkeys, the responsiveness of area 1 of marmosets, a New World monkey, is often rather weak to cutaneous stimuli (Krubitzer and Kaas, 1990; Carlson et al., 1986).

Unfortunately, area 1 does not have a distinct enough architectonic appearance to make an identification of the area in galagos on histological criteria, and others have variously referred to the region as area 5 (Brodmann, 1909), area 2–5 (Preuss and Goldman-Rakic, 1991a), or

area 1–2 (Sanides and Krishnamurti, 1967). In this paper, we refer to the region as area 1–2 to reflect our uncertainty in identifying this cortex as either area 1 or area 2 of monkeys. However, all mammals appear to have similar caudal and rostral projection zones of S1 (Beck et al., 1996), and we suggest that the three basic subdivisions of anterior parietal cortex in prosimians have been retained from an early, non-primate ancestor.

Somatosensory areas of the lateral sulcus

Our results provided compelling evidence for two complete representations of the contralateral body surface in cortex of the lateral sulcus of galagos, areas S2 and PV, and also provided evidence for additional areas including the ventral somatosensory area (VS), the parietal rostral area (PR), and the retroinsular area (Ri). Evidence for S2 and PV was expected, because these areas have been identified in a number of species of monkeys (Krubitzer and Kaas, 1990; Cusick et al., 1989; Krubitzer et al., 1995; Qi et al., 2002) and in humans (Disbrow et al., 2000). Furthermore, S2 has been described in all mammals investigated, and more recently PV has been identified in a range of non-primate mammals (see Disbrow et al., 2000 for review). Thus, it seems reasonable to propose that both S2 and PV were present in early mammals and were retained in most or all subsequent lines of descent. In these mammals, S2 and PV are characterized as separate representations adjoining area 3b or S1 along its lateral border, with PV rostral to S2 (Fig. 1). Face representations in both areas adjoin the face representation of S1, whereas forelimb, trunk, and hindlimb activate locations progressively more distant from this border. S2 and PV mirror each other in somatotopy, reversing along representations of the face, forepaw, and hindlimb. S1 provides a major input to both areas.

In galagos, we identified S2 and PV in microelectrode mapping experiments by their expected somatotopic patterns and locations, as well as by topographic connections with area 3b. As expected from results in other mammals, receptive fields were larger for neurons in these areas than for neurons in S1, and the two areas responded in a similar manner to light contact on the skin and the movement of hairs.

Previously, Burton and Carlson (1986) identified S2 in galagos and demonstrated a somatotopic organization very similar to the one reported here (also see Garraghty et al., 1991). In addition, they described connections between S1 and S2 that were somatotopically matched, as in the present study. Finally, their injections in S2 revealed inputs from both the ventroposterior nucleus (VP) and the ventroposterior inferior (VPI) nucleus of the somatosensory thalamus (also see Wu et al., 1996). The dense inputs from VP conform to a non-primate pattern, whereby VP independently activates both S1 and S2 (see Garraghty et al., 1991 for review). In monkeys, this dense input from VP to S2 is lacking (Krubitzer and Kaas, 1992), and S2 depends on areas 3b and 3a for activation (see Garraghty et al., 1990 for review). In galagos, lesions of S1 (area 3b) failed to deactivate S2 (Garraghty et al., 1991). Thus, galagos and probably other prosimian primates have retained a non-primate ancestral mode of activating S2 that has been lost in anthropoid primates.

Previous studies in galagos and other prosimians did not provide any evidence for a PV, either in microelectrode mapping attempts or in patterns of connections with S1,

possibly because no specific effort was made to identify PV or explore the PV region. Here we provide clear evidence for PV as a representation just rostral to S2. We also demonstrate that PV, like S2, is topographically connected with area 3b and that S2 and PV are densely interconnected. S2 and PV resemble each other architectonically and physiologically, although architectonic distinctions were made between cortex in the two locations by Preuss and Goldman-Rakic (1991a). In our material, PV appeared to have generally larger pyramidal cells in layer V than S2. Receptive fields were generally larger, and responses were less vigorous and less consistent after a repeated stimulus. Cortical connections were generally similar, but PV was more densely connected with frontal cortex and demonstrated connections with the amygdala and perirhinal cortex (Fig. 19).

The existence of a ventral somatosensory area (VS) in cortex along the ventral (deep in the sulcus) border of S2 and PV was suggested by our limited recordings in the region, and by connections with S2 and PV. Although the evidence for VS is only suggestive in galagos, there is more complete evidence of VS as another representation of the contralateral body in New and Old World monkeys (Cusick et al., 1989; Krubitzer et al., 1995; Qi et al., 2002). VS may constitute separate rostral (VSr) and caudal (VSc) representations along the borders of PV and S2, respectively, as recordings in titi monkeys suggest (Coq et al., 1998). VS appears to mirror PV and S2 in overall somatotopic patterns. As VS has been described in a non-primate, the flying fox (Krubitzer and Calford, 1992), this subdivision may be widely distributed in mammals. However, more complete mapping is needed to establish its existence in galagos.

Cortex immediately caudal to S2 in galagos was also responsive to tactile stimuli, and the region had connections with S2 and PV. This location has been called retroinsular cortex (Ri) in monkeys (Jones and Burton, 1976; Robinson and Burton, 1980a,b; Friedman et al., 1986; Burton et al., 1995; Krubitzer et al., 1995). Neurons in Ri have been described as responsive to somatosensory stimuli or to both somatosensory and visual stimuli (Robinson and Burton, 1980a,b; Krubitzer et al., 1995). Clearly this region of cortex is involved in somatosensory processing in galagos, but we are uncertain whether this region is Ri.

Cortex immediately rostral to PV has been described in monkeys on the basis of PV and S2 connections as the parietal rostral area (PR; Krubitzer and Kaas, 1990). In galagos, we found that cortex in the PR location also has connections with S2 and PV. In addition, neurons in galago PR responded to tactile stimuli in a rapidly habituating manner and had large receptive fields. These characteristics and the connections suggest that PR is a processing area at a level higher than PV and S2. The responsiveness of neurons in PR has not yet been studied in monkeys.

Inferior parietal cortex and the 7b complex

The functional organization of much of posterior parietal cortex in primates is not well understood. Traditionally, the more rostral part of the region has been divided into two broad zones, area 5 and area 7 of Brodmann (1909), with proposed subdivisions of each. In a prosimian lemur, Brodmann (1909) included in an area 5 much of the cortex we designate as 1–2 and more caudal parietal cortex in an area 7. More recently, Preuss and Goldman-

Rakic (1991a) parcellated cortex in galagos and included the rostral part of Brodmann's area 5 in a 2–5 region, closely matching our 1–2, while dividing the rest of posterior parietal cortex into six subdivisions of area 7. Here we refer to the region just caudal to S2 in inferior parietal cortex as area 7b and parietal cortex on the medial wall as 7v-m (Figs. 8, 9) after Preuss and Goldman-Rakic (1991a), while allowing that these are regions defined here by location rather than the usual stringent criteria for cortical areas. By location, area 7b in galagos corresponds to 7b of macaques, where neurons have been described as responsive to visual and somatosensory stimuli (Hyvarinen and Shelepin, 1979; Robinson and Burton, 1980a,b). Robinson and Burton (1980a,b) found evidence of a crude somatotopic organization in area 7b, with the head medial to the body (also see Krubitzer et al., 1995). Little is known about the functional properties of parietal cortex of the medial wall in monkeys.

In galagos, we found that injections in both S2 and PV revealed connections with the area 7b region, and S2 injections labeled connections with the area 7v-m region. Thus, both areas are implicated in somatosensory functions. An injection in rostral but not an injection in caudal 7b labeled neurons in S2, suggesting the existence of functional subdivisions in the region. Both area 7b injections labeled neurons more medially near the rostral tip of the intraparietal sulcus and in lateral frontal cortex, whereas the larger, more caudal injection also labeled neurons in 7v-m. These connections suggest that the rostral half of inferior parietal cortex has a role in somatosensory processing, as well as the 7v-m region of the medial wall.

Frontal cortex

Our injections in area 3b, S2, PV, and area 7b all labeled neurons in parts of the frontal lobe of galagos. In our previous study of motor cortex in galagos (Wu et al., 2000), we identified a primary motor area, M1, just rostral to area 3a, a sequence of four premotor areas just rostral to M1 (the ventral premotor area [PMV]; area 6 Ds; the dorsal-caudal premotor area [PMDc]; and the supplementary motor area [SMA]), a more rostral frontal eye field (FEF), a dorsal-rostral premotor area (PMDr), pre-SMA, and three cingulate motor or sensorimotor areas in cortex of the medial wall, the caudal and rostral cingulate motor areas (CMAc and CMAr), and the cingulate sensorimotor area (CSMA). More rostrally in galagos, Preuss and Goldman-Rakic (1991a) distinguished a granular frontal region and orbitofrontal opercular cortex. These regions have been considered to be prefrontal cortex in galagos as they receive inputs from the mediodorsal nucleus of the thalamus (Markowitsch et al., 1980; however, see Preuss and Goldman-Rakic, 1991a).

Our injections into area 3b of galagos indicate that this area is sparsely connected to primary motor cortex (M1) and cingulate motor cortex (CMAc), as in monkeys (Krubitzer and Kaas, 1990). Connections between area 3b and M1 in galagos have also been revealed by M1 injections (Wu et al., 2000). In monkeys, injections in M1 also reveal sparse connections with area 3b (see Stepniewska et al., 1993 for review; Darian-Smith et al., 1993). More connections with M1, as well as cingulate motor areas, were revealed by an injection in caudal area 3b that extended into area 1–2 (Fig. 8A). This result suggests that area 1–2 of galagos is more densely connected with M1, an interpretation that is consistent with the finding that areas 1

and 2 of monkeys project more densely to M1 (Stepniewska et al., 1993).

Injections in S2 and PV also revealed connections with M1, with PV having denser M1 connections than S2. In monkeys, such connections have been demonstrated by S2 and PV injections (Krubitzer and Kaas, 1990; Qi et al., 2002) and by M1 injections (Stepniewska et al., 1993). S2 and PV also have connections with cingulate motor cortex, prefrontal cortex, and orbital cortex in galagos. Sparse connections of S2 with cingulate motor cortex have been reported in marmosets (Krubitzer and Kaas, 1990), but it is uncertain whether S2 and PV project to prefrontal and orbital cortex in monkeys.

Finally, our large injection in area 7b of galagos labeled neurons in lateral premotor as well as prefrontal cortex (Fig. 9A). Similar results were reported by Preuss and Goldman-Rakic (1991c) after injection into inferior parietal cortex of galagos. Similar frontal lobe connections of area 7b have been described in macaque monkeys (see Preuss and Goldman-Rakic, 1991c for review).

The evolution of somatosensory cortex in primates

The comparative evidence reviewed above suggests that the mammalian ancestors of primates had at least five somatosensory areas: S1, rostral and caudal bordering strips, PV, and S2. S1, PV, and S2 were activated via projections from the ventroposterior nucleus of the thalamus, whereas PV and S2 also received feed-forward inputs from S1. The strips of cortex along the rostral and caudal borders of S1 also received activation inputs from S1. Architecturally, S1 was poorly differentiated. This basic system was retained in early primates. In addition, early primates either retained from a non-primate ancestor or evolved several additional somatosensory areas, probably VS, PR, Ri, and more caudal fields. These somatosensory areas projected to several motor, premotor, and frontal fields. With the emergence of the first anthropoid primates, S1 (area 3b) became much more "sensory" or konicortical in architecture, and adjoining areas 3a and 1 became more architecturally distinct and more responsive to thalamic inputs from muscle spindle receptors (area 3a) or cortical and thalamic inputs related to cutaneous receptors (area 1). A distinct area 2 with muscle spindle inputs from the thalamus and cutaneous receptor inputs from areas 3b and especially area 1 had become differentiated. The addition of other somatosensory areas in cortex of the lateral fissure may have occurred, but this is still uncertain.

ACKNOWLEDGMENTS

We thank Drs. C. Collins, S. Iyengar, and I. Stepniewska for helpful comments on the article and Drs. P. Beck and N. Bichot as well as Mrs. M. Feurtado for assisting in mapping sessions and surgeries. We are also grateful to Ms. J. Ives and L. Trice for histological assistance.

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