THE JOURNAL OF COMPARATIVE NEUROLOGY 402:538–559 (1998)

Interhemispheric Connections of Somatosensory Cortex in the Flying Fox

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ABSTRACT

The interhemispheric connections of somatosensory cortex in the gray-headed flying fox (*Pteropus poliocephalus*) were examined. Injections of anatomical tracers were placed into five electrophysiologically identified somatosensory areas: the primary somatosensory area (SI or area 3b), the anterior parietal areas 3a and 1/2, and the lateral somatosensory areas SII (the secondary somatosensory area) and PV (pairetal ventral area). In two animals, the hemisphere opposite to that containing the injection sites was explored electrophysiologically to allow the details of the topography of interconnections to be assessed. Examination of the areal distribution of labeled cell bodies and/or axon terminals in cortex sectioned tangential to the pial surface revealed several consistent findings. First, the density of connections varied as a function of the body part representation injected. For example, the area 3b representation of the trunk and structures of the face are more densely interconnected than the representation of distal body parts (e.g., digit 1, D1). Second, callosal connections appear to be both matched and mismatched to the body part representations injected in the opposite hemisphere. For example, an injection of retrograde tracer into the trunk representation of area 3b revealed connections from the trunk representation in the opposite hemisphere, as well as from shoulder and forelimb/wing representations. Third, the same body part is differentially connected in different fields via the corpus callosum. For example, the D1 representation in area 3b in one hemisphere had no connections with the area 3b D1 representation in the opposite hemisphere, whereas the D1 representation in area 1/2 had relatively dense reciprocal connections with area 1/2 in the opposite hemisphere. Finally, there are callosal projections to fields other than the homotopic, contralateral field. For example, the D1 representation in area 1/2 projects to contralateral area 1/2, and also to area 3b and SII. J. Comp. Neurol. 402:538–559, 1998.

Indexing terms: corpus callosum; area 3b; area 3a; secondary somatosensory area; evolution

The corpus callosum is the largest fiber bundle in the forebrain of eutherian mammals. Its size varies as a function of the size of the cerebral cortex, and specific connectional relationships between cortical fields via this pathway vary considerably across species. There are also differential patterns of connections between parts of the representation of the receptor surface within a given sensory field. For instance, in the primary somatosensory area (SI or area 3b) of some mammals, the representations of distal body parts, such as the hand in primates, tend to be sparsely interconnected or acallosal, whereas the proximal and midline body part representations are densely interconnected (for review, see Innocenti, 1986). This observation, together with comparable findings in the visual cortex, have led some investigators to propose that callosal connections are involved in "fusing" the midline of sensory representations (e.g., Manzoni et al., 1989; Guillemot et al., 1992; for review, see Innocenti, 1986). Another possibility is that it is the use of the body part in question that dictates the pattern of connectivity. For instance, the hand plays an important role in fine sensory discriminations in primates. In the primary somatosensory area (3b), and area 1, the hand representation is mostly free of callosal connections. In primates, the transfer of informa-

Grant sponsor: Australian Research Council; Grant sponsor: NH&MRC.

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Received 14 March 1997; Revised 28 July 1998; Accepted 4 August 1998

tion from the hand representation occurs via area 2, posterior parietal cortex (Killackey et al., 1983; Manzoni et al., 1984; Iwamura et al., 1994), and the second somatosensory area (SII; Manzoni et al., 1984). Related to the second hypothesis is the proposition that in species with a large number of cortical fields, the indirect transfer of information on distal parts through "higher order" fields may reflect necessary extra step(s) of processing, linked to their specialized roles (Cusick and Kaas, 1986; Ledoux et al., 1987; Kaas, 1995a). Thus, this hypothesis suggests that the number of cortical fields present in a particular species also contributes to the differences in the pattern of interhemispheric connections observed in different mammals.

In previous work in flying foxes (Calford et al., 1985; Krubitzer and Calford, 1992; Krubitzer et al., 1993), complex somatosensory cortical organization has been described, and three topographic representations are recognized in anterior parietal cortex, areas 3b, 3a, and 1/2, and three in lateral somatosensory cortex, the second somatosensory area (SII), the parietal ventral area (PV), and the ventral somatosensory area (VS). The reasons for undertaking the present investigation in the flying fox were twofold. First, it was part of a broader comparative effort in our laboratory to examine the organization and connections of somatosensory cortex in a number of diverse species. In this context, it was of interest to determine whether there are features of callosal connectivity that are highly conserved in mammals. It was also of interest to examine the validity of the different proposals that attempt to account for the observed patterns of connections in the flying fox, particularly the specialization hypothesis. The flying fox is of special interest because its wing is a modified hand incorporating digits 2–5. Digit 1 (D1), however, is free of membrane attachments and is used in non-aerial locomotion (crawling and climbing) and in grasping actions.

The second reason for undertaking these experiments stemmed from studies in macaque monkeys and flying foxes in which we observed interhemispheric transfer of receptive field changes (namely, rapid unmasking of larger receptive fields) induced by denervation of D1, or cooling its representation in area 3b or area 1/2 (Calford and Tweedale, 1990; Clarey et al., 1996). Because area 3b representations of the digits in the two hemispheres are not interconnected in monkeys, at least one additional cortical field must have been involved in transferring these effects across the hemispheres. As it is possible that additional fields are also involved, we were interested in examining interhemispheric connections of the D1 representation in areas 3b and 1/2 in this species.

To address the above issues, different fluorescent tracers were injected in the matched body part representations in different fields of anterior parietal cortex in the same animal, so that similarities and differences in callosal connections of different fields could be directly compared. In addition, multiple tracers were placed into different body part representations of the same field in order to assess their relative contribution to the pattern of connections with the opposite hemisphere. Given the general proposals on the function of the corpus callosum (midline fusion and specialized body part use), and our specific interest in the connectivity of the D1 representation, injections were placed into either distal representations (D1, wrist, toes) or midline representations (trunk, shoulder, face structures). In some of these same animals, the hemisphere contralateral to the injected hemisphere was explored electrophysiologically to determine which body part representations in the different fields were connected via the callosum.

We also examined the connections of electrophysiologically identified somatosensory fields lateral to SI. Patterns of ipsilateral connections indicate close interactions between anterior parietal and lateral fields. For instance, we have shown that ipsilateral interconnections are dense between SII and area 1/2 and between PV and area 3b (Krubitzer et al., 1993). We were therefore interested to see whether this pattern would also be reflected in the callosal connections, especially because lateral fields are considered to be involved in more complex and global aspects of stimulus analysis (see Krubitzer, 1996, for review).

Abbreviations

Cortical fields in the flying fox

1	caudal somatosensory area (cutaneous)
2	caudal somatosensory area (deep)
3a	rostral somatosensory area (deep)
3b	primary somatosensory area (SI)
4	primary motor area, M or MI
LP	lateral parietal area
PV	parietal ventral area
SI	primary somatosensory area (3b)
SII	second somatosensory area
VS	ventral somatosensory area

Body parts

AM	arm membrane
B	body
CK	cheek
CN	chin
CNV	chin vibrissae
D1–D5	digits 1–5
DFL	distal forelimb
dig	digits
ER	entorhinal cortex
F	foot
FA	face
FL	forelimb
FM	finger membrane
H	head
HL	hindlimb
L	lips
LL	lower lip
LT	lower trunk
M	mouth
N	naris
NE	neck
P	pinna
PFL	proximal forelimb
PW	prowing
SH	shoulder
SN	snout
SNV	snout vibrissae
T	toes
T1–T5	toes 1–5
TE	teeth
TM	toe membrane
TO	tongue
TR	trunk
UL	upper lip
ULV	upper lip vibrissae
UT	upper trunk
V	vibrissae
W	wrist

MATERIALS AND METHODS

Interhemispheric connections were investigated in eight gray-headed flying foxes (*Pteropus poliocephalus*) in which 15 injections of anatomical tracers were placed into electrophysiologically identified locations in areas 3b, 3a, 1/2, SII, and PV. Flying foxes are large frugivorous bats. The animals used in the present study weighed 500–700 g and had wingspans on the order of 1.2 m. The brain of the flying fox is about twice the size of that of an adult rat, and the cerebral cortex of flying foxes is well developed with a prominent lateral sulcus, but otherwise relatively lissencephalic. At the beginning of each experiment, the animal was anesthetized with ketamine hydrochloride (40 mg/kg IM) and xylazine (4 mg/kg IM), and was subsequently kept areflexive with supplemental doses of approximately half of the initial dose of ketamine. In some animals, diazepam (1 mg/kg IM) or pentobarbitone sodium (12 mg/kg IM or SC) were administered to supplement the ketamine. Animals were allowed to recover for the period required for tracer transport (2–7 days) and were given amoxycillin (7.5 mg/kg) pre- and postoperatively. All surgical procedures for chronic portions of the experiments were done under sterile conditions. After the animal was anesthetized, it was placed in a stereotaxic frame, the scalp was cut, the skull above the area to be injected was removed, the dura was retracted, and the opening was filled with silicone oil. An enlarged print was made of the exposed cortex so that the location of electrode penetrations could be recorded relative to cortical vasculature.

Electrophysiological recordings were made with tungsten-in-glass electrodes (approximately 1 MΩ at 1 kHz) which were lowered 700–1,000 μm into the cortex with a stepping-motor controlled microdrive. The electrode was moved in X/Y coordinates with a micromanipulator attached to the stereotaxic frame. Neural responses were amplified, filtered and viewed on an oscilloscope, and heard through a loudspeaker. A receptive field was defined as that area of the body surface that when stimulated produced a time-locked neural response, usually from multiple cells. Cutaneous stimulation consisted of light brushing of hairs and glabrous skin, whereas light pressure, taps, and manipulation of joints were used to stimulate deep receptors. Receptive fields were obtained for neurons at a number of sites, and when the area of interest was defined, injections of anatomical tracers were placed into particular body part representations in a cortical field. In most cases, microlesions (10 μA for 6 seconds) or probes were placed at physiological boundaries and marked on the photograph for later identification in histologically processed tissue.

In some of these experiments, one injection was placed in a single field (e.g., FF 186; Fig. 13), and in others, injections of different tracers were placed in a number of different fields (e.g., FF 260; Fig. 2), or in several different body part representations in the same field (e.g., FF 183; Fig. 8). In one case in which the aim was to determine the total pattern of callosal connections, a number of closely spaced injections were made to create one large injection that filled most of area 3b (FF 245; Fig. 5). Several different anatomical tracers were used. Single 0.05-μl injections of 0.1% wheat germ agglutinin conjugated to horseradish peroxidase (WGA-HRP: Sigma, St. Louis, MO) were made in three animals. These animals were allowed to recover for 2 days. Fluorescent tracers included fast blue (FB), diamidino yellow (DY), fluorogold (FG), and fluoroscein green beads (GB), and survival times for animals in which these anatomical tracers were used was 5–7 days. Small crystals (approximately 10–20 μm in diameter) of FB or DY were placed into electrophysiologically identified locations in somatosensory fields, after which plugs of gelfoam were placed into the crystal holes to prevent the tracer from escaping and spilling onto the cortex. Injections of 3% fluorogold (0.2–0.3 μl) and fluoroscein green beads (0.4 μl) were made by using a microsyringe, and injection holes were plugged with gelfoam.

The spread of the injected tracer ("injection site") ranged from 300 μm to 2.5 mm for both fluorescent tracers and WGA-HRP. In the case in which a number of injections of WGA-HRP were made to create a large region of tracer uptake (Fig. 5), the extent of the injection site was very large (2.5 mm × 6.5 mm). The injection sites illustrated in the results section represent the full extent of either the "halo" around the fluorescent tracer deposit or the full extent of the WGA-HRP reaction product (excluding immediately adjacent regions that contain transported tracer, i.e., densely labeled axons and cell bodies). These illustrations probably represent an overestimation of the effective uptake zone of most of the tracers used. In the case of FB and DY, Condé (1987) has shown that the uptake zone is restricted to the region of mechanical damage produced by the injection. Similarly, green beads tend to show very little diffusion from the injection site (e.g., Katz and Larovici, 1990); this is verified by our observations in these experiments (Fig. 1A). It is also widely assumed that the effective injection site of HRP (and its conjugate to WGA) is the densely staining central region and that little uptake occurs from the diffuse surrounding zone of the injection (e.g., Mesulam, 1982; but see Ahlsen, 1981). The final tracer used in this study, FG, tended to show the greatest spread (Fig. 1A); it is unknown how the effective uptake zone relates to the visible spread of this tracer.

When injections were complete, a sterile soft contact lens was placed over the cortex, the dura was pulled over the contact lens, a thin piece of gelfoam was placed across the opening, and the piece of skull was secured in place with acrylic, or a new piece was made from dental acrylic. The muscles and skin were sutured, and the animal was allowed to recover. In two cases, after the appropriate survival time, the animal was anesthetized as described above, and electrophysiological recordings were made in somatosensory cortex in the opposite hemisphere. At the end of all experiments, the animal was given a lethal dose of pentobarbitone sodium and transcardially perfused with 0.9% saline followed by 2% paraformaldehyde, and then 2% paraformaldehyde in 10% sugar phosphate buffer (1 M, pH 7.4). After perfusion, the brain was removed from the cranium, and the cortices were gently pried away from the brainstem and thalamus, flattened between glass slides, and left to soak overnight in 30% sugar phosphate buffer.

The cortices were cut tangential to the pial surface on a freezing microtome at 40 μm, and alternate sections were stained for myelin (Gallyas, 1979), reacted for HRP using tetramethylbenzidine (Mesulam, 1978; as modified by Gibson et al., 1984), and/or mounted for fluorescence microscopy. For sections reacted for HRP or mounted for fluorescence microscopy, the entire series of sections was drawn using a camera lucida. The drawings included the outline of the sections, injection sites, labeled cell bodies

and/or terminals, blood vessels, microlesions, and tissue artifacts. For both injections of WGA-HRP and fluorescent tracers, the reconstructions reflect a qualitative judgement of density differences in labeled cell bodies, not quantitative cell counts. Details of reconstruction of patterns of labeled cell bodies and axon terminals in flattened sections have been provided elsewhere (Krubitzer et al., 1993). Drawings were also made of the myelin-stained sections and include injection sites, architectonic boundaries, blood vessels, microlesions, and tissue artifacts. To obtain cortical field boundaries, the entire series of myelin-stained sections was reconstructed. The drawings of architectonic boundaries and labeled cell bodies and axon terminals were superimposed and related to electrophysiological recording sites by matching injection sites, blood vessels, and lesions to the enlarged photographs. In this way, comprehensive reconstructions of the injection areas and the location of labeled axon terminals and/or cell bodies in the opposite hemisphere could be made. Details of ipsilateral cortical connections resulting from some of the cases presented here and preliminary results of this study have been presented elsewhere (Krubitzer et al., 1993 and 1992, respectively). All experimental procedures were approved by the University of Queensland Animal Experimentation Ethics Committee (UAEEC).

RESULTS

The present investigation was designed to examine the interhemispheric connections of areas 3b, 3a, 1/2, SII, and PV in the flying fox. The connections described in these results are attributed predominantly to the corpus callosum, because we could trace labeled axons from the injection site through the corpus callosum. However, the possibility that some connections are achieved through an alternate route, such as the anterior commissure, was not specifically tested. In three cases (Figs. 2, 8, 9), multiple anatomical tracers were injected into different body part representations of the same field (e.g., the trunk and D1 representations in area 3b in case 260; the shoulder, D1, and snout representations in area 3b in case 183, and the toes and D1 representation in area 3b of case 184). In one case (Fig. 2), different anatomical tracers were placed in similar body part representations in different fields (e.g., the D1 representation in areas 3a, 3b, and 1/2 in case 260). In another case, multiple injections were placed in a single field and the injection sites were fused, whereas in four cases (Figs. 10–13), single injections were made in one field only. In all cases, electrophysiological recordings were used to accurately place the injections in the body part representation within the field of interest. The physiological data were later correlated with the myeloarchitecture of tangentially sectioned cortex and the injection site, as defined by the extent of the fluorescent "halo" or WGA-HRP reaction product (Figs. 1, 2).

In six animals, the location of labeled cell bodies and/or terminals in the opposite hemisphere was related to cortical myeloarchitecture. In two animals, on the day of perfusion, electrophysiological recordings were made from neurons in somatosensory cortex in the hemisphere opposite to that injected, and topographic "maps" of body part representations were generated for individual fields. In these cases, the location of labeled cell bodies and terminals was related to both myeloarchitecture and electrophysiological recording results (e.g., Figs. 3, 4). Because we have used various combinations of injections in the different fields and have correlated interhemispheric connections with physiological maps in some cases, but not others, we describe the following results case by case.

The myeloarchitectonic appearance of somatosensory areas, as correlated with electrophysiological maps, has been described in detail elsewhere (Krubitzer and Calford, 1992; Krubitzer et al., 1993) and will only be related briefly here. The primary somatosensory area, SI or area 3b, was defined by its dense staining for myelin (Fig. 1B), topographic representation of the body surface, neuronal response properties, and stimulation preferences of neurons. Neurons in area 3b responded vigorously and consistently to cutaneous stimulation and generally had smaller receptive fields than neurons in surrounding fields (Fig. 2B,C,E). Area 1/2, located caudal to area 3b, contained neurons that habituated to repetitive cutaneous stimulation, or responded to stimulation of deep receptors in circumscribed zones. Cutaneous receptive fields in area 1/2 were well defined in extent and usually slightly larger than in area 3b (see Krubitzer and Calford, 1992). As described previously, lightly myelinated regions of cortex interdigitated with area 3b, and these were considered portions of area 1/2 rather than modules within area 3b, because the architecture of these regions was continuous with that of area 1/2. Responses of neurons in these regions habituated to repetitive stimulation of cutaneous or deep receptors, as did neural responses throughout area 1/2. A further consideration for including this region within area 1/2 is that without this invaginated portion, area 1/2 would not contain a complete representation of the body surface.

A topographically organized field rostral to area 3b that stained lightly for myelin and contained neurons that were responsive to stimulation of deep receptors, manipulation of joints, and occasionally cutaneous receptors was termed area 3a in preliminary reports (Finnigan et al., 1992). Some sites rostral to area 3a contained neurons that were responsive to stimulation of deep or cutaneous receptors or manipulation of body parts. These sites were contained within a moderately myelinated region designated as primary motor cortex (MI) or area 4 (Kennedy, 1991). Physiological descriptions of areas 3a and 4 are beyond the scope of this study and will be detailed in subsequent reports; here they will only be considered in terms of their interhemispheric connections.

Three fields located lateral to areas 3b and 1/2 could also be identified: SII, PV, and VS. These fields contained complete representations of the body surface, and their neurons were responsive to stimulation of cutaneous receptors (Krubitzer and Calford, 1992). SII and PV stained more moderately for myelin than area 3b, but darker than area 1/2; VS stained very lightly for myelin.

Interhemispheric connections of anterior parietal fields 3a, 3b, and 1/2

Case FF 260. The injection of multiple fluorescent tracers in case FF 260 allowed a comparison of the interhemispheric connections of the digit 1 (D1) representation in areas 3a, 3b, and 1/2 and a comparison of the connections of the area 3b digit and trunk representations. All injection sites were electrophysiologically identified, and three different tracer injections were centered in the D1 representation of areas 3a, 3b, and 1/2 (Figs. 1, 2A). FG was injected in area 3a, FB was placed in area 3b, DY was

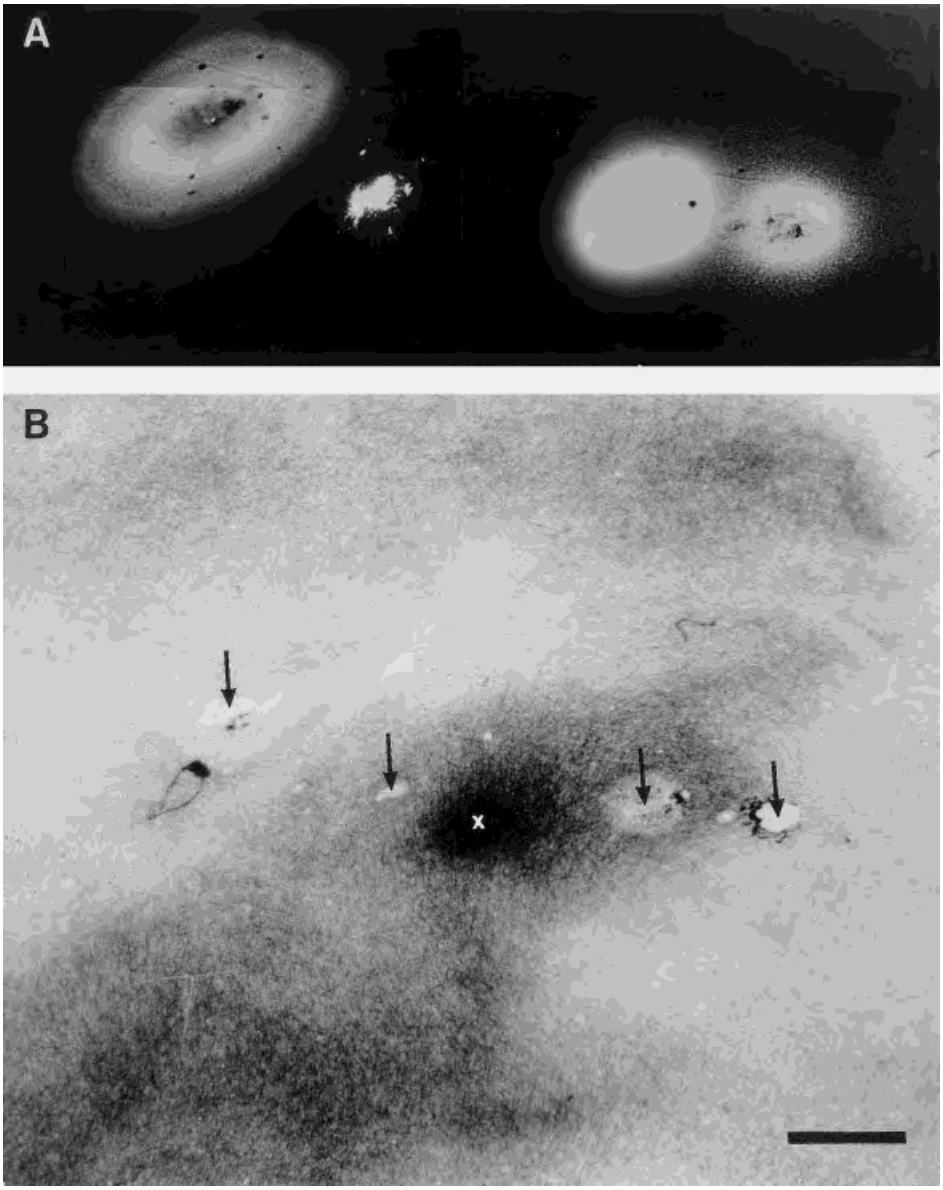

Fig. 1. **A:** A montage of the injection sites in FF 260. Cortex has been flattened and sectioned tangentially in this and all following cases. Injections of anatomical tracers include FG in area 3a (far left), green beads and FB in area 3b (two middle injections), and DY in area 1/2 (far right; see Fig. 2 for further details). The injections were restricted to the field of interest and did not spread into adjacent injection sites. **B:** Lightfield photomicrograph of the same region of cortex taken at the same magnification as A. This section has been stained for myelin and shows the location of the injection sites with arrows. Regions of dark myelin staining correspond to area 3b. The very dark staining (x) within area 3b is white matter, and is revealed in this particular section because of slight irregularities in brain flattening. Rostral is to the left and medial is to the top. Scale bar = 1 mm.

placed in area 1/2, and a fluoroscein GB injection was centered in the trunk representation of area 3b (Fig. 2). Correlation of injection sites, mapping, and myeloarchitecture in the ipsilateral hemisphere (Figs. 1, 2) demonstrates that the injections were restricted to the area of interest, and, except for the injection of FG, that there was little spread into adjacent representations within the field.

Labeled cell bodies in the opposite hemisphere (Fig. 4) were related to patterns of myeloarchitecture, and to fine grain electrophysiological maps of areas 3a, 3b, and 1/2 obtained 5 days after injections (Fig. 3). Several recordings were also made in cortex lateral to area 3b, in areas SII, PV, and VS. The correlation between electrophysiological recording results and myeloarchitectonic boundaries was good and conformed with previous descriptions of somatosensory cortex as described above.

There were a number of important features of the pattern of labeled cells with respect to the somatotopic maps (Figs. 3, 4). First, no cell bodies labeled with FB were observed in the hemisphere contralateral to the injection sites, indicating that the area 3b D1 representation did not receive callosal input from the contralateral D1 representation in area 3b. In contrast to the lack of interhemispheric connections between the D1 representation in area

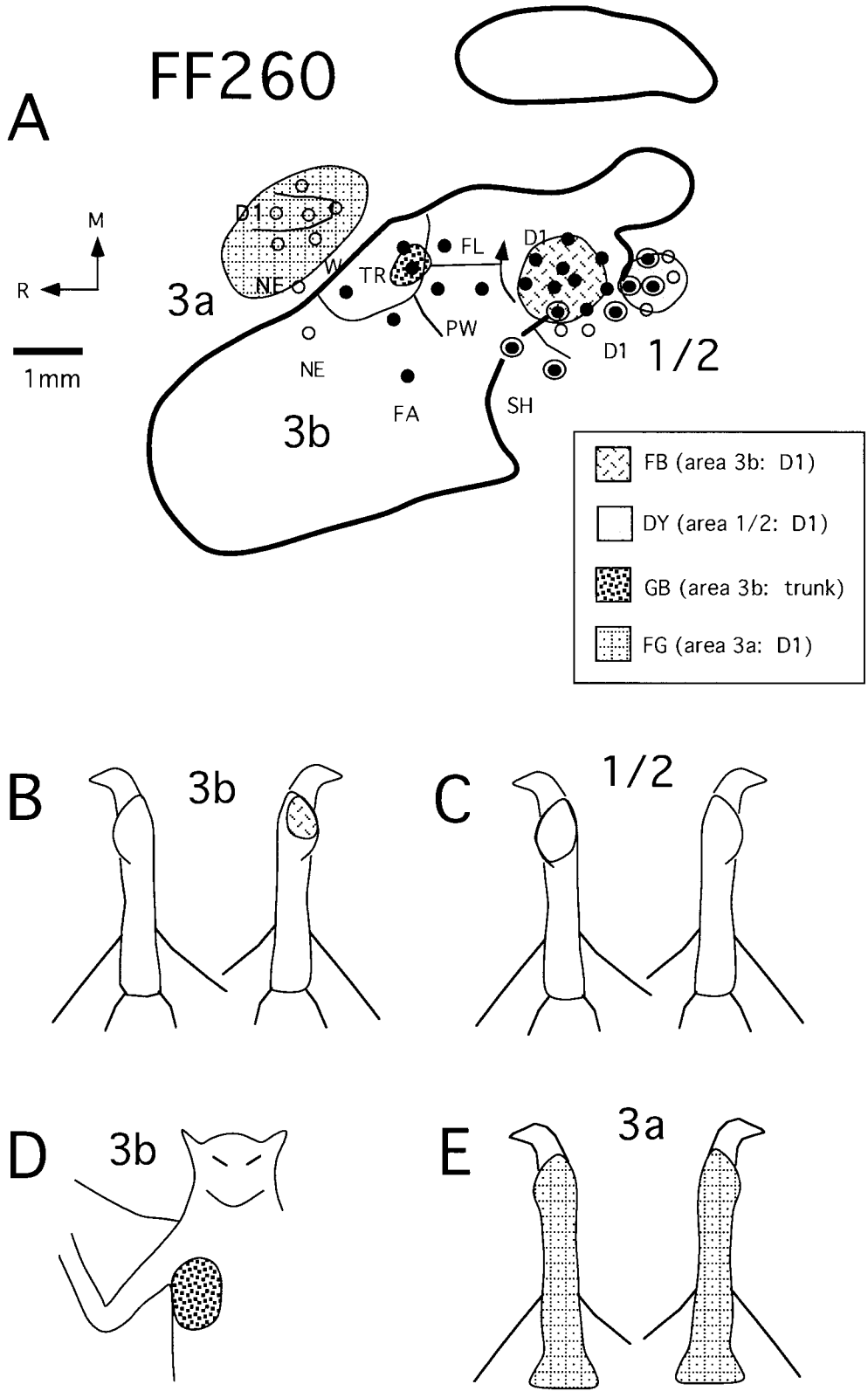

Fig. 2. The location of injection sites in relation to physiological recordings in the left hemisphere of FF 260 (**A**). The thick lines enclose regions of dense myelin staining (Fig. 1B) and correspond to the physiologically defined borders of area 3b. The thin lines indicate borders between representations of different body parts. Electrode penetrations in which neurons responded to cutaneous stimulation and did not habituate with repeated stimulation are indicated by solid circles, whereas those in which neurons habituated to repeated cutaneous stimulation are indicated by encircled solid circles. Electrode penetrations in which neurons responded to deep stimulation are indicated by open circles. The most caudal injection of DY was centered in the digit 1 (D1) representation of area 1/2, whereas an injection of FB was centered in the D1 representation of area 3b. An injection of GB was centered in the trunk representation of area 3b but spread slightly into the forelimb representation. The most rostral injection of FG was centered in the D1 representation of area 3a but spread into the adjacent representation of the wrist. **B–E:** The receptive fields of neurons located at each of the injected sites (see key). Scale bar = 1 mm.

3b in both hemispheres, the D1 representation in area 1/2 received substantial callosal input from the D1 representation in area 1/2 of the opposite hemisphere (Fig. 4), indicating topographically matched interhemispheric connections with respect to both body part representation and field. Labeled cell bodies were also located in representations of the prowing, forelimb, wrist, head, neck, and face of area 1/2; these were topographically mismatched to the representation injected. A smaller number of labeled cell bodies were found in the representation of the digits in area 3b (only two cells were found in the D1 representation) and in the representation of D1 in SII. A few labeled cell bodies were located adjacent to the caudal border of SII and medial to area 3a.

The representation of D1 in area 3a also received substantial callosal input (Fig. 4), but not from a topographically matched location in the opposite hemisphere. In this case, the injection of the tracer FG extended into cortex in which neurons responded to stimulation of the wrist (Fig. 2A). Labeled cell bodies in the opposite hemisphere were concentrated in the medial portion of area 3a, in regions representing the trunk, shoulder, forelimb, arm membrane, prowing, and hindlimb. Labeled cell bodies were denser in area 4 than in area 3a in the contralateral hemisphere and were found in representations of the trunk, shoulder, forelimb, hindlimb, and also regions where neurons were unresponsive to somatosensory stimulation. There were no labeled cell bodies within the small D1 representation in area 3a. Thus, more proximal body part representations in areas 3a and 4 project to distal body part representations (i.e. wrist and D1) in area 3a in the opposite hemisphere.

The injection of GB into the trunk representation of area 3b (Figs. 1A, 2A) resulted in labeled cell bodies in the trunk representation of areas 3b and 3a in the opposite hemisphere, although there were more labeled cell bodies in area 3a than area 3b (Fig. 4). Labeled cell bodies were also located in representations of other body parts in both fields, particularly in area 3a. Shoulder, forelimb, wing, neck, and even hindlimb and chin vibrissae representations in area 3a contained labeled neurons, whereas only the trunk, neck, and chin vibrissae representations in area 3b contained labeled neurons. A few labeled neurons were also observed in the physiologically identified trunk/hindlimb representation of SII and the approximate location of the trunk representation in PV. Finally, labeled neurons were observed rostral to area 3a, in the forelimb, shoulder, trunk, and face representations in area 4.

Case FF 245. To examine the larger pattern of connections of the primary somatosensory area, a number of small injections of WGA-HRP were placed along the mediolateral extent of area 3b, and the estimated uptake zones fused to form a large strip that encompassed representations of the chin vibrissae, digits, and prowing of area 3b, and the interdigitating strip of area 1/2 that included representations of the shoulder and pinna (Fig. 5). Two days after the placement of these injections, the hemisphere contralateral to the injection site was explored electrophysiologically (Fig. 6), and the boundaries of areas 1/2, 3b, and 3a were defined and related to myeloarchitecture and patterns of connections (Figs. 6, 7). Dense patches of anterograde and retrograde label were found in areas 3b, 3a, 1/2, SII, and PV of the contralateral hemisphere (Fig. 7), and sparser connections were observed with area 4, cortex medial to area 3b, and cortex caudal to area 1/2 (Fig. 7). In area 3b, numerous labeled cell bodies and axon terminals were observed in the representations of the snout vibrissae and tongue, although it is unlikely that the representation of the tongue was included in the injection. Sparse connections were observed with the forelimb, upper trunk, and finger membrane representations in area 3b, and very few labeled cell bodies and axon terminals were observed in the digit representations. Finally, a very large patch of label was observed far laterally, in the presumed location of the tongue tip representation in area 3b.

Labeled cell bodies and axon terminals were observed in abundance in area 3a (Fig. 7). Dense interhemispheric connections were found with the representations of the shoulder and genital representation, somewhat sparser connections were observed with the vibrissae, upper trunk, wrist, and finger and arm membrane representations, and far fewer labeled cell bodies and axon terminals were observed in the digit and tail membrane representations in area 3a. In area 1/2, the densest patch of transported tracer was observed in the portion of area 1/2 that interdigitates between the hand and face representation of area 3b, and represents the prowing, head, and snout/vibrissae representations, and much sparser anterograde and retrograde label was scattered across representations of the wrist, prowing, finger membranes, D1, forelimb, and shoulder representations.

Dense patches of labeled cell bodies and axon terminals were observed throughout most of the rostral and medial portions of areas SII and PV. Although only a few recording sites were located in this region, based on previous maps (also see Fig. 3) it is likely that the labeled cell bodies and axon terminals were in the representations of the face and forelimb, but not in representation of the trunk. The transported tracer observed in area 4 was in the wing, forelimb, and finger membrane representations (Fig. 6). Only labeled cell bodies were observed caudal to area 1/2, and only labeled axon terminals were observed medial to areas 3b and 3a. The patterns of anterograde and retrograde label observed in this case were not completely reciprocal in that some regions contained only labeled cell bodies (e.g., caudal to area 1/2, face representation of area 3a), or axon terminals (e.g., medial to area 3b and area 3a). Finally, a patch of labeled cell bodies and axon terminals was also observed in entorhinal cortex.

Case FF 183. In this case, different tracers were placed in different body part representations in areas 3b and 1/2 so that topographic differences in interhemispheric connections between fields could be appreciated. In case FF 183 (Fig. 8), an injection of FB was centered in the wrist representation in area 3b, but spread into the adjacent D1 representation. An injection of WGA-HRP was also placed in the snout/vibrissae representation of area 3b. Both injections were limited to physiological and architectonic boundaries of area 3b. An injection of DY was centered in the shoulder representation of area 3b, but spread into the naris representation of area 1/2. Only a small patch of WGA-HRP–labeled cell bodies and terminals was observed in the opposite hemisphere in a location similar to that injected, in the presumed location of the snout vibrissae/face representation of area 3b (Fig. 8). The lack of label from the FB and DY injections is unlikely to be due to lack of transport because labeled cell bodies in the ipsilateral cortex and thalamus were identified. The lack of FB-labeled cells is consistent with the results of case FF 260 in which no labeled cells were observed in the contra-

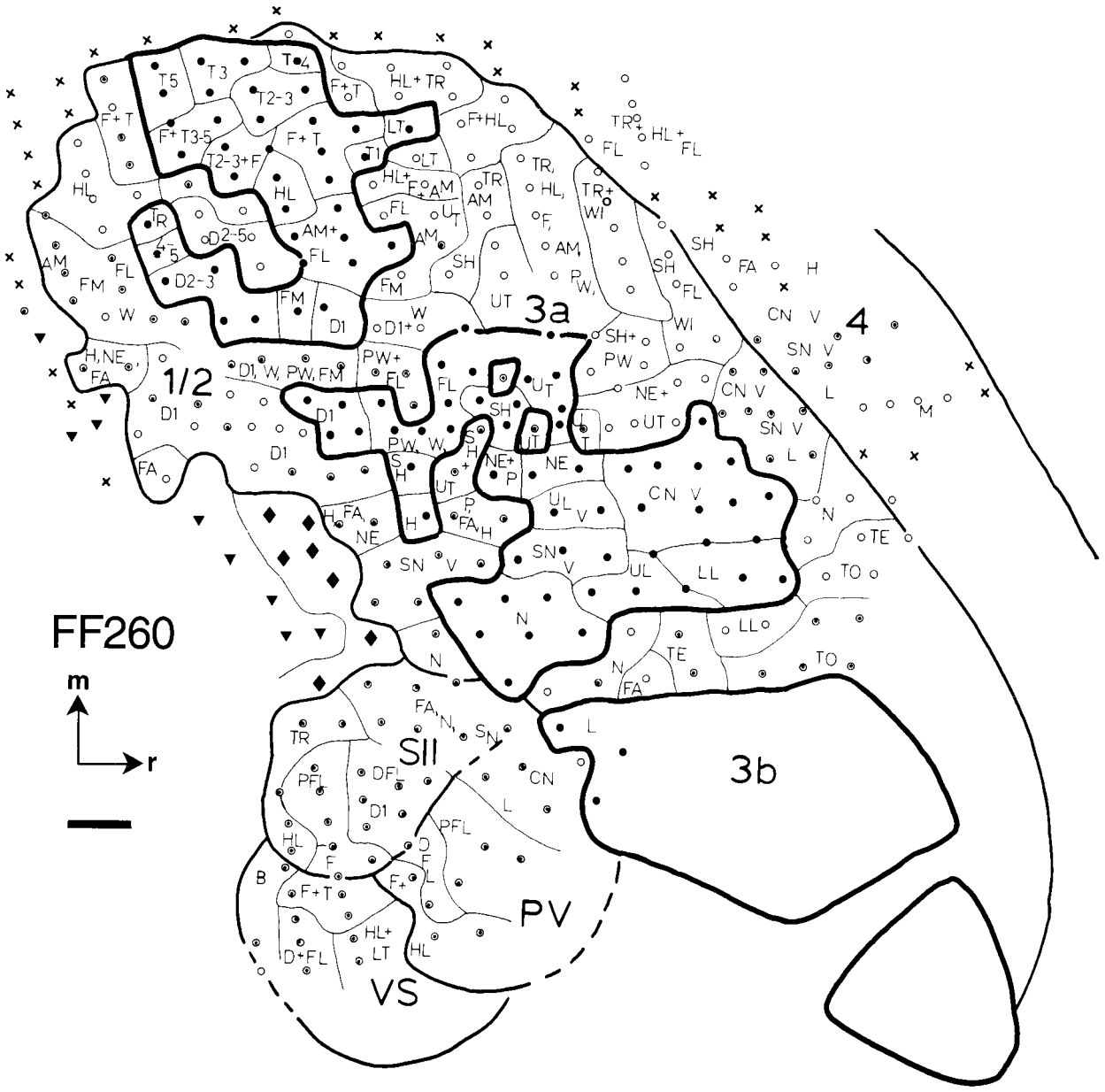

Fig. 3. The extent and organization of somatosensory cortex in the right hemisphere of FF 260. Area 3b was defined by dense myelin staining (areas enclosed by thick lines), and the presence of neurons responsive to cutaneous stimulation that did not habituate with repeated stimulation (solid circles). Thin lines mark the architectonic boundaries of other cortical fields such as areas 1/2, 3a, 4, the second somatosensory area (SII), the parietal ventral area (PV), and the ventral somatosensory area (VS), whereas the very fine lines delimit body part representations and other physiological borders (e.g., caudally an area containing visually responsive neurons [triangles] is distinguished from an area containing neurons responsive to somatosensory and visual stimulation [diamonds]. Broken lines indicate uncertainty as to the location of a border or a portion of it. Sites in which neurons were not responsive to stimulation of any body part are indicated by "x." Other conventions as in Figure 2. For abbreviations, see list. Scale bar = 1 mm.

lateral hemisphere after an injection in, or involving, the D1 representation of area 3b. However, the lack of labeled cells from the injection of DY centered in the shoulder representation is inconsistent with the results from case FF 245 and is difficult to interpret.

Case FF 184. In case FF 184 (Fig. 9), an injection of diamidino yellow was centered in the toe 2–3 (T2–3) representation in area 3b. An injection of FB was centered in the D1 representation but spread into adjacent forelimb representations in areas 3b and 1/2. Finally, an injection of FG was placed in the face representation of area 1/2 and spread into portions of the snout, chin, and neck representations in area 3b. Labeled cell bodies from all three injections were observed in the contralateral area 1/2 (Fig. 9). These cells were largely restricted to a myelin-light interdigitating strip of area 1/2, in the approximate location of the trunk, forelimb, face, and digit representations in this area (see Figs. 3, 6). The injection into the D1

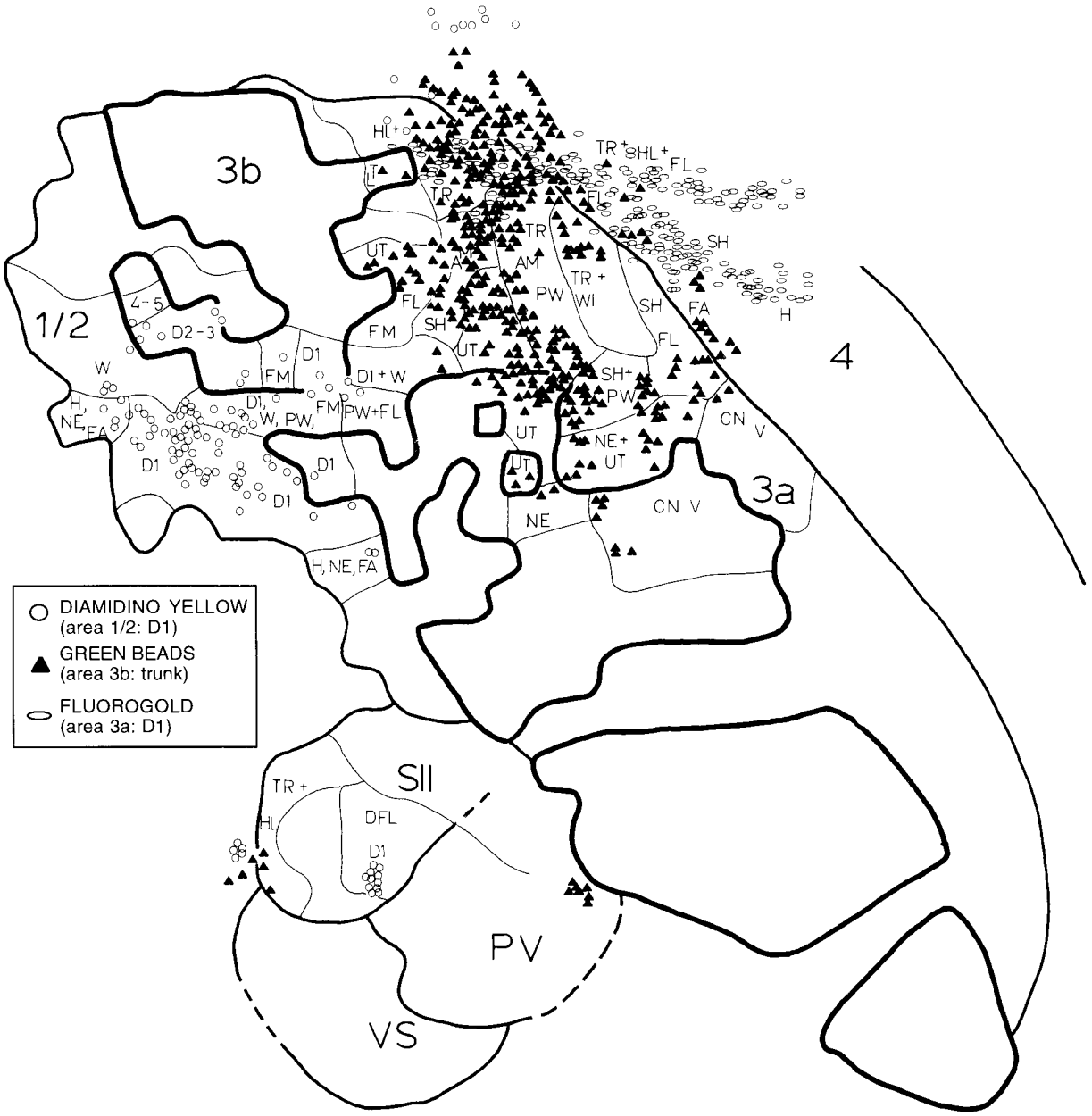

Fig. 4. Simplified map of somatosensory cortex in the right hemisphere of FF 260 showing the location of cell bodies labeled with three different fluorescent dyes (see key). There were no cell bodies labeled with FB (see also Fig. 2). Scale, orientation, and conventions are the same as in Figure 3.

representation in area 3b resulted in two discrete patches of labeled cell bodies, one rostral and one caudal. The caudal focus could be confidently assigned to area 1/2. However, because the boundary between areas 3a and 1/2 in the invaginating region is difficult to define, the rostral focus may have been in area 3a.

Case FF 258. In this case an injection of WGA-HRP was centered in the naris representation in area 3a, and spread into adjacent representations of the shoulder, and slightly into the naris representation in area 3b (Fig. 10). Resulting anterograde and retrograde label (Fig. 10) was in a matched location in the opposite hemisphere (see Figs. 3, 6).

Summary of connections of areas 3a, 3b, and 1/2. Taken together, the results from injections in anterior parietal fields indicate that area 3b is differentially interconnected with somatosensory areas in the opposite hemisphere as a function of the body part representation injected (see Table 1). The face representation in area 3b receives and projects to the face representation in area 3b (and in one case area 1/2) in the opposite hemisphere. The D1 and T2–3 representations in area 3b have no callosal connections with area 3b in the opposite hemisphere, but do receive very sparse input from area 1/2 in the opposite hemisphere. Finally, the trunk representation in area 3b received input from the trunk representation in area 3b,

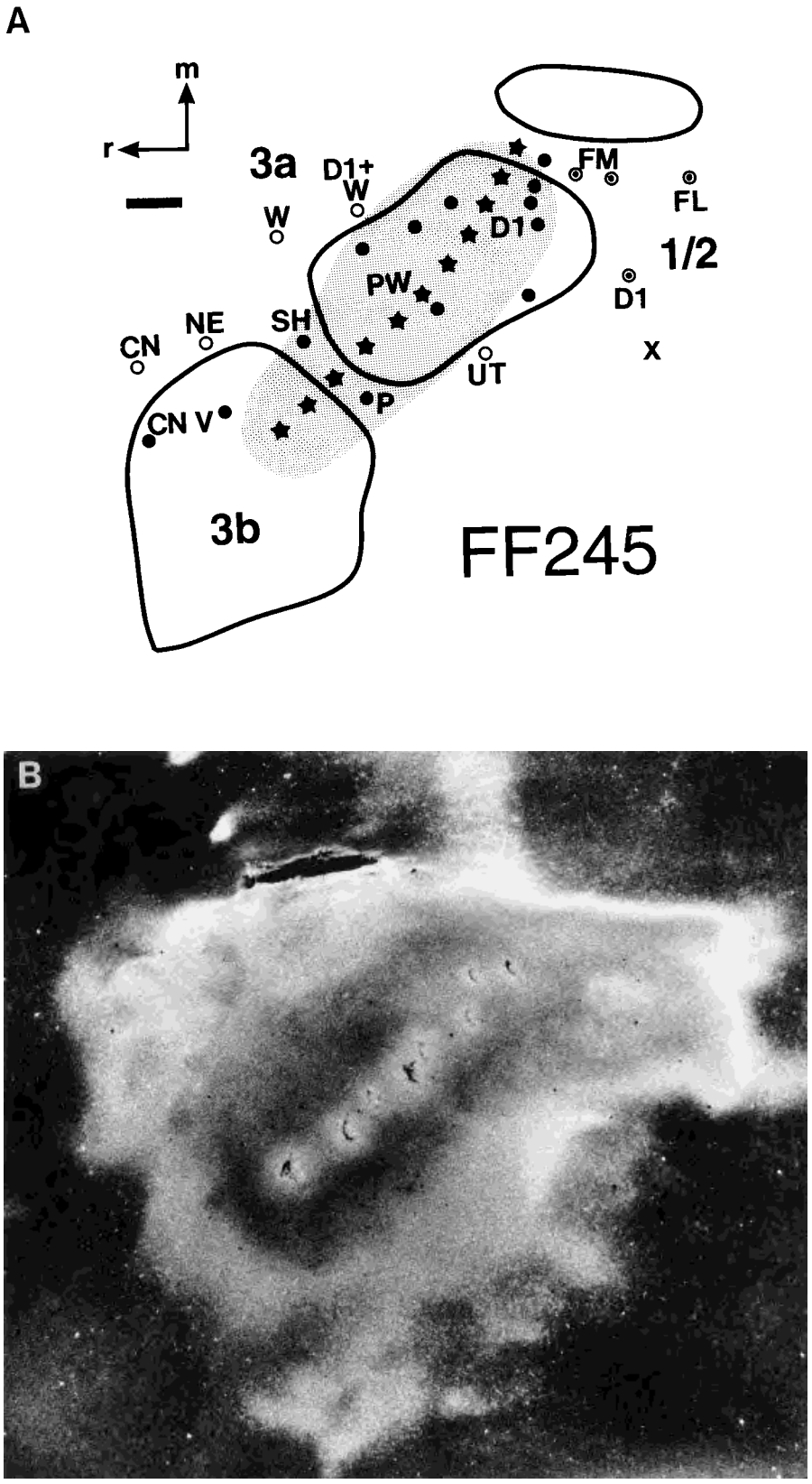

Fig. 5. **A:** An illustration showing the location of electrode penetrations and the spread of WGA-HRP (shading) resulting from the multiple injections (stars; 0.1 ml at each site) in area 3b and spreading into portions of area 1/2 in FF 245. **B:** Darkfield photomicrograph taken at the same magnification as the illustration above of the injections illustrated in A. Note that the individual injections fuse to form a single strip injection. Conventions as in previous Figures. Scale bar = 1 mm in both A and B.

from related representations in area 3a, and also from similar representations in areas SII and PV in the opposite hemisphere. Unlike for area 3b, interhemispheric interconnections were observed between the area 1/2 D1 representations. In addition, the D1 representation of area 3a received input from related representations in areas 3a and 4, but not from matched representations of the opposite hemisphere, whereas more proximal representations in area 3a were interconnected with proximal representations in area 3a of the opposite hemisphere. The majority of interhemispheric projections to areas 3b and 1/2 emanate from that portion of area 1/2 that interdigitates between the hand and face representations of area 3b.

Interhemispheric connections of lateral somatosensory fields SII and PV

Cases FF 199 and FF 188. Injections of anatomical tracers in SII resulted in transported tracer in several fields in the opposite hemisphere. An injection of DY centered in the cheek representations in SII (Fig. 11), but spreading into the forelimb representation, resulted in labeled cell bodies in the approximate location of the forelimb and face representation of SII in the opposite hemisphere. Labeled cells in PV were in the presumed location of the digits. Labeled cells in an interdigitating strip of area 1/2 were also identified in the opposite hemisphere in the approximate location of the representations of the forelimb, digits, and face. No labeled cell bodies or axon terminals were observed in area 3b.

In case FF 188, an injection of WGA-HRP centered in the digit representations in SII and, spreading into snout, shoulder, hindlimb, and trunk representations (Fig. 12), resulted in labeled cell bodies and axon terminals in the approximate location of the trunk and shoulder representations in SII in the opposite hemisphere. No transported tracer was observed in PV or area 1/2 in this case.

Case FF 186. In this case, an injection of WGA-HRP was centered in the forelimb representation of PV and spread into the adjacent representations of the neck, trunk, and hindlimb (Fig. 13). Labeled cell bodies and axon terminals were observed in PV, SII, and VS in the opposite hemisphere, in the approximate location of the forelimb representation in all three fields (Krubitzer et al., 1993; but see Fig. 4). An additional focus of label was observed caudal to VS, in the lateral parietal area (LP).

DISCUSSION

We examined the details of callosal connections of five somatosensory fields in the flying fox by combining neuroanatomical techniques with electrophysiological recording techniques and architectonic analysis. In the following discussion, we first consider some methodological issues that bear on interpretation of our results. Second, we compare our findings for each of the somatosensory fields with those observed in other mammals in an effort to determine common features of interhemispheric connections. Finally, we address the issues posed at the beginning of this study regarding the relationship between callosal connections and specialized peripheral morphology, and the use of the specialized structure. We consider whether our results are consistent with current theories that attempt to account for the patterns of interhemispheric connections observed in mammals.

Methodological issues

A number of studies have shown that tracers differ in their sensitivity, i.e., reveal different numbers of cells in a specific afferent region (e.g., Horikawa and Powell, 1986; Craig et al., 1989). Although this aspect of using multiple tracers has implications for comparing the density of a connection, it has less relevance for considerations of the existence of a particular connection as determined by the presence or absence of labeled cells in a given contralateral field or body part representation. Of importance in the present study is knowing whether the lack of labeled cells following a tracer injection does indeed reflect the absence of callosal connections with that cortical site, and not a general failure of transport or specific failure of transport in the interhemispheric pathway. In two cases, FB was injected into the area 3b representation of a distal body part (D1 and D1/wrist in FF260 and FF183, respectively; see Table 1), and there were no labeled cells in the opposite hemisphere. In both cases, labeled cells were observed in the thalamus and in ipsilateral somatosensory cortex; therefore, there was not a general failure of transport. The possibility remains that there was a selective lack of transport in the callosal pathway; differential pathway-specific transport of FB has been reported from the chicken thalamus by Güntürkün et al. (1993). However, it is unlikely that our results reflect an inability of FB to be transported through callosal fibers and/or to accumulate in sufficient quantities in cell bodies in the opposite hemisphere because 1) we observed labeled FB cells in area 1/2 following an injection into contralateral area 3b in one case (FF184, Fig. 9), 2) there are reports in the literature of interhemispheric cortical connections using this tracer (e.g., Miceli et al., 1985; Cipolloni and Pandya, 1989), and 3) the pattern of interconnection observed with FB was supported by the case in which a large WGA-HRP injection was made into area 3b (Fig. 7: the contralateral area 3b D1 representation was largely devoid of labeled cell bodies and axon terminals).

In one case (FF183, Fig. 8), we did not observe labeled cells following an injection of DY into the shoulder representation of contralateral area 3b, which spread into area 1/2. In other fields and in other body parts (see Table 1) there was successful interhemispheric transport of this tracer. In addition, this particular outcome is difficult to explain because 1) we observed labeled cells in the thalamus and ipsilateral cortex, 2) we observed labeled cells following injection of other tracers into the area 3b representation of a proximal body part (e.g., GB into the trunk representation in FF260, Fig. 4), and 3) the general expectation based on the findings of other studies (see below) is that the representations of proximal body parts are densely interconnected.

A related problem regarding our injection sites is the spread of the injection site into adjacent body part representations. Our interpretation of interhemispheric connections is that they are both topographically matched and mismatched. If our tracer spread into adjacent body part representations, a connection that is described as mismatched may actually be due to the spread of the injection in an adjacent, but mismatched, body part representation.

There is only one injection in one case in which this may be an issue. In case FF260, our injection of FG that was centered in the digit 1 representation of area 3a was large, and clearly spread outside of the representation that was mapped (Fig. 2A). Thus, the resulting transported tracer in the trunk representation in area 3a in the opposite hemisphere may be the result of the spread of the injection

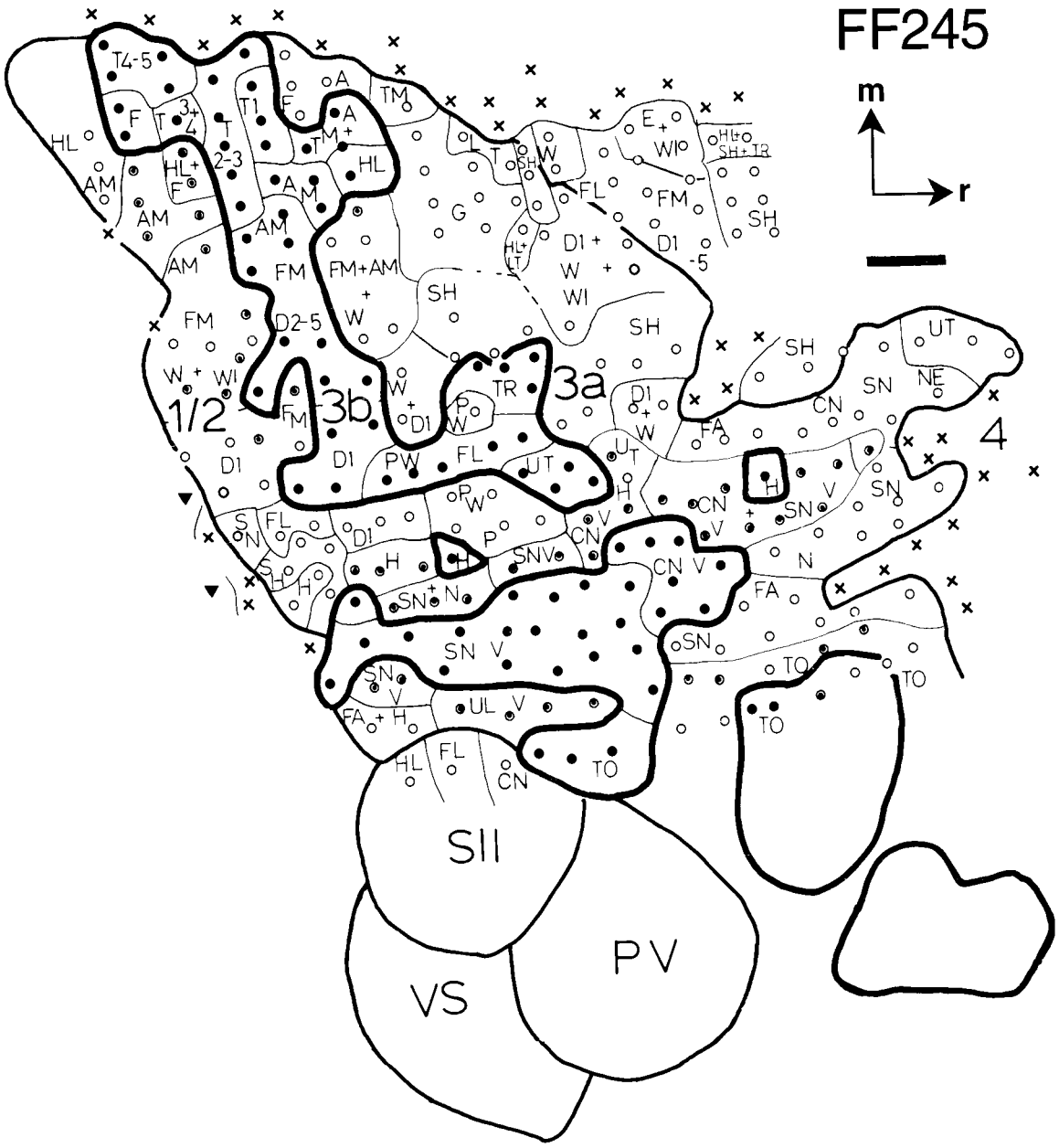

Fig. 6. The extent and organization of somatosensory cortex in the right hemisphere of FF 245. Conventions as in Figure 3. Scale bar = 1 mm.

into the trunk representation. The other injections in this case were either very small and/or restricted to the region in which electrophysiological recordings were made. Therefore, we could accurately assess the representations into which the injections had spread.

Interhemispheric connections of somatosensory fields in mammals

The primary somatosensory area, SI or area 3b. In the flying fox, the trunk representation in area 3b (SI) received inputs from similar representations in areas 3b, 3a, 4, SII, and PV, and from mismatched locations in areas 3b, 3a, and 4 in the contralateral hemisphere. The snout representation received inputs only from the snout representation in area 3b in the contralateral hemisphere. The representations of most distal body parts were sparsely interconnected or acallosal. There was no evidence for interhemispheric connections between the D1 representations in area 3b of each hemisphere, but the D1–D5 representations of area 3b did project extremely sparsely to the D1 representation of area 1/2 in the opposite hemisphere.

To date, interhemispheric connections of SI or area 3b have been examined in a variety of eutherian mammals including rodents, carnivores, lagomorphs, tree shrews,


3b
1/2
3a
4
AM
FM
AM
FM
FM
D2-5
SH
SH
W
W
FL
D1
D1
D1
D1
UT
UT
FA
PW
H
SN V
H FA
TO
SII
PV
VS
ER

Figure 7

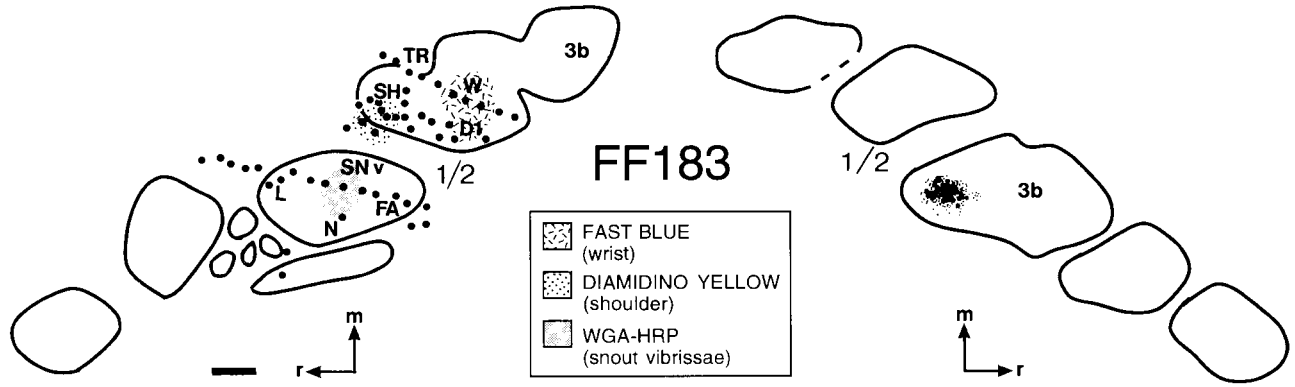

Fig. 8. **Left:** Location of electrode penetrations (dots) and spread of injected tracers (see key) relative to densely myelinated area 3b (areas enclosed by lines) in FF 183. The injection of FB was centered in the wrist representation of area 3b but spread into the adjacent D1 representation. The injection of DY was centered in the shoulder representation of area 3b but spread into lightly myelinated cortex containing neurons responsive to stimulation of the naris (either area 3a or area 1/2). The injection of WGA-HRP was centered in the representation of the snout vibrissae. **Right:** The extent of area 3b as revealed by dense myelin staining in the hemisphere opposite to that injected with tracers. There were no cell bodies labeled with either FB or DY. A patch of cell bodies (large dots) and axon terminals (small dots) labeled with WGA-HRP was located in area 3b in a similar mediolateral location to that injected in the expected location of the snout vibrissae representation. Scale bar = 1 mm (bottom left) and pertains to both panels.

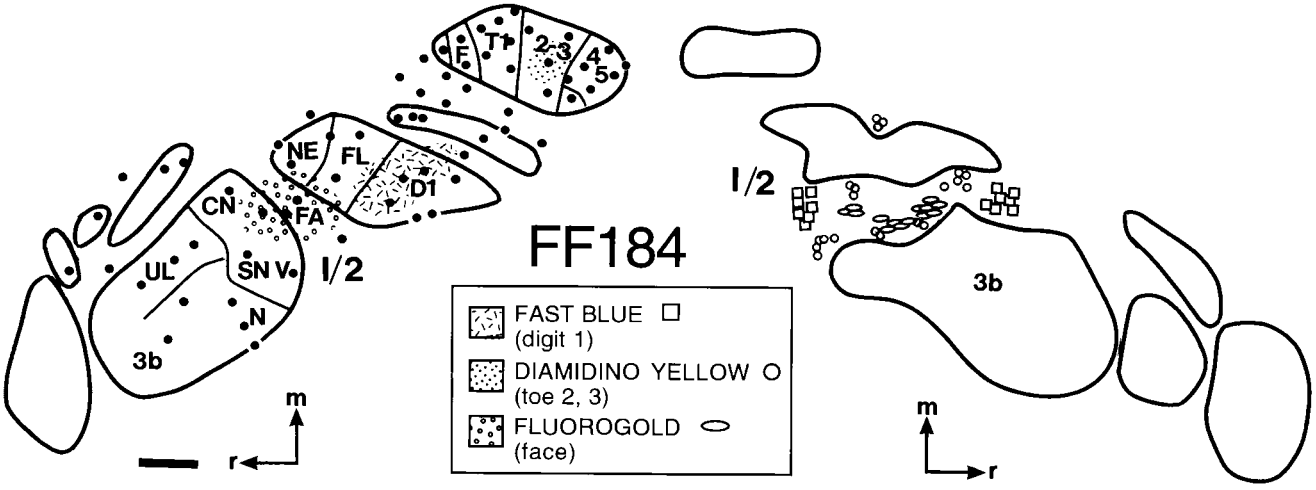

Fig. 9. **Left:** Location of electrode penetrations (dots) and spread of injected tracers (see key) relative to densely myelinated area 3b (areas enclosed by lines) in FF 184. The injection of FB was centered in the D1 representation of area 3b. The injection of DY was centered in the representation of toes 2 and 3 in area 3b. The injection of FG was centered in the representation of the chin and snout in area 3b but spread medially into myelin-light cortex and the edge of the neck and forelimb representations of area 3b. **Right:** The extent of area 3b as revealed by dense myelin staining in the hemisphere opposite to that injected with tracers. Clusters of cell bodies labeled with the various tracers (see key) were located in myelin-light regions corresponding to area 1/2 and possibly portions of area 3a. Conventions as in previous figures.

and primates (see Innocenti, 1986; Johnson, 1990, for review). Without exception, connections are observed between the primary somatosensory areas, and the density of these connections depends on the body part representation examined. In mammals such as raccoons (Ebner and Myers, 1965; Herron and Johnson, 1987), cats (Ebner and Myers, 1965; Shanks et al., 1975; Caminiti et al., 1979; McKenna et al., 1981), rats (Wise and Jones, 1976; Akers and Killackey, 1978; Olavarria et al., 1984; Koralek et al., 1990), mice (White and DeAmicis, 1977), squirrels (Gould and Kaas, 1981; Krubitzer et al., 1986), tree shrews (Cusick et al., 1985; Weller et al., 1987), and primates (Pandya and Vignolo, 1968; Jones and Powell, 1969; Karol and Pandya, 1971; Jones et al., 1975; Jones and Hendry, 1980; Killackey et al., 1983; Shanks et al., 1985; Conti et al., 1986; Krubitzer and Kaas, 1990; Beck and Kaas, 1994), only representations of proximal body parts within SI

Fig. 7. Simplified map of somatosensory cortex in the right hemisphere of FF 245. WGA-HRP–labeled cell bodies (large dots) and axon terminals (small dots) were located throughout a large part of the anterior parietal and lateral somatosensory fields. The distribution of cell bodies and axon terminals was not uniform, and some regions lacked labeled cell bodies and/or terminals (e.g., VS). A patch of labeled cell bodies and terminals was observed lateral to somatosensory cortex, in entorhinal cortex (ER). Labeled axon terminals were also located medial to areas 3a and 3b. Scale and orientation are the same as in Figure 7.

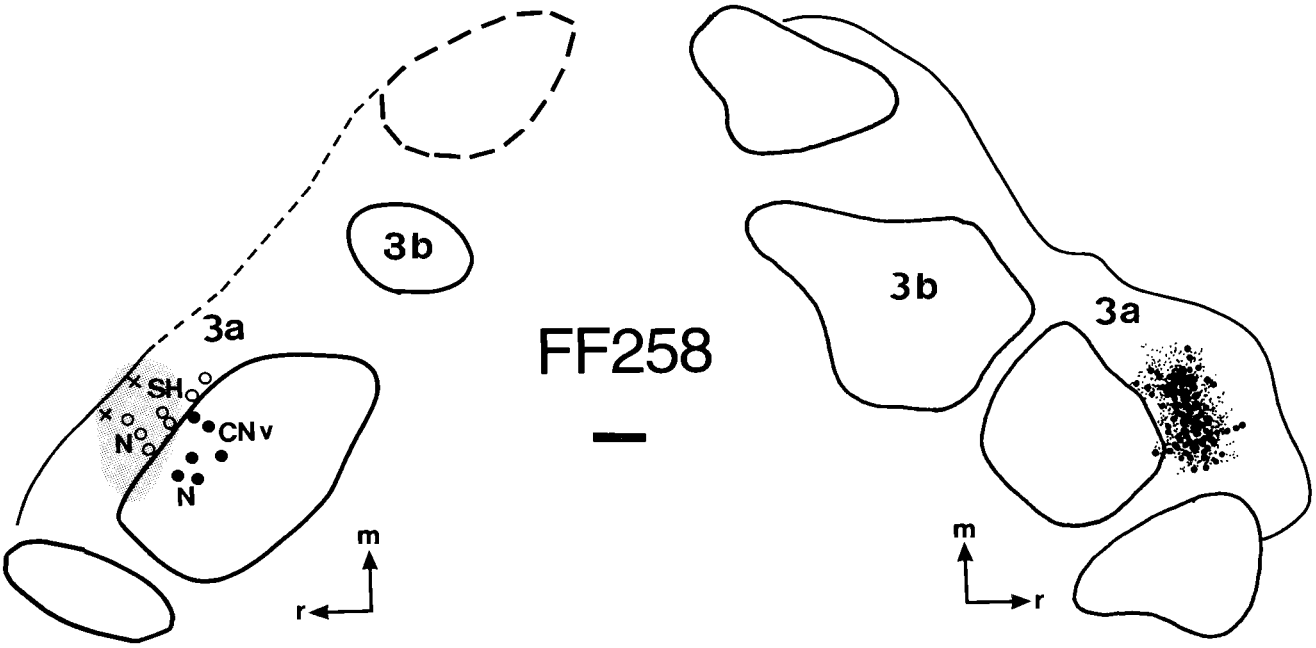

Fig. 10. **Left:** Location of electrode penetrations (dots and open circles) and spread of a WGA-HRP injection (shading) centered in the naris representation of area 3a in FF 258. WGA-HRP spread into cortex in which neurons were responsive to stimulation of deep receptors in the shoulder and slightly into the naris representation in area 3b. **Right:** A patch of WGA-HRP–labeled cell bodies (large dots) and axon terminals (small dots) was located at a similar mediolateral location to that injected and was largely restricted to myelin-light area 3a immediately rostral to area 3b. Conventions as in previous figures. Scale bar = 1 mm.

TABLE 1. Summary of Callosal Connections[1]

Case	Areas injected	Tracer	Contralateral fields								
			3a	3b	1/2	4	SII	PV	VS	ER	LP
260	3a(D1)	FG	x			x					
	3b (trunk)	GB	x	x		x	x	x			
	3b (D1)	FB									
	1/2 (D1)	DY		x	x		x				
245	3b (D1/pw, cn) 1/2 (sh/pw)	WGA-HRP	xo	xo	xo	xo	xo	xo		xo	
183	3b (sn v)	WGA-HRP		xo							
	3b (wrist, D1)	FB									
	3b, 1/2 (sh)	DY									
184	3b (T2-3)	DY			x						
	3b (D1)	FB			x						
	3b, 1/2 (sn v, face)	FG			x						
258	3a (naris)	WGA-HRP	xo								
199	SII (cheek)	DY			x		x	x			
188	SII (dig)	WGA-HRP					xo				
186	PV (fl)	WGA-HRP					xo	xo	xo		xo

x, labeled cell bodies; o, labeled axon terminals; DY, diamidino yellow; FB, fast blue; FG, fluorogold; GB, green beads.

[1]A summary of the callosal projection patterns revealed in each experiment indicating the sites of injections and of retrogradely labeled cell bodies (x) and anterogradely labeled axon terminals (o). The fluorescent labels diamidino yellow FB, FG, and GB are transported only retrogradely, whereas retrograde and anterograde transport is possible with WGA-HRP.

(area 3b) are densely interconnected via the corpus callosum, whereas the representations of distal body parts tend to be sparsely interconnected or acallosal. In other species, such as rabbits (Ledoux et al., 1987), callosal connections have been observed between distal body part representations. In mice (Jacobson, 1970; Yorke and Caviness, 1975; White and DeAmicis, 1977) and rats (Wise and Jones, 1976; Akers and Killackey, 1978; Olavarria et al., 1984; Koralek et al., 1990) the representations of the vibrissae in granular cortex are acallosal, whereas the equivalent, but nonspecialized, body area representations in primates, carnivores, and tree shrews appear to be callosally interconnected.

The lack of interhemispheric connections between the D1 representations in area 3b in the flying fox is thus similar to the projection pattern described for distal representations in most mammals. However, it should be noted that most early reports are not directly comparable to the present study because anterior parietal fields 3a, 3b, 1, and 2 in primates were often considered as a single field, SI, whereas only area 3b in species such as cats and primates is considered homologous to area 3b in the flying fox (see Kaas, 1983; Krubitzer and Calford 1992). Another issue to be considered is the heterogeneous nature of SI. For instance, in mice and rats, SI can be divided into granular and dysgranular zones, such that different body parts are represented in separate "granular" zones or islands (Woolsey and Van der Loos, 1970; Welker et al., 1984). Architectonic discontinuities in the form of interdigitating myelin dark and light regions have also been observed in rodents such as squirrels, tree shrews, and in New World and Old World primates (Cusick et al., 1985; Krubitzer et al., 1986; Krubitzer and Kaas, 1990; Jain et al., 1996; see Fig. 4 in Krubitzer, 1995). In addition, cytochrome oxidase (CO) dark and light regions have been shown in owl monkeys and galagos (Beck and Kaas, 1994). Thus, accumulating evidence indicates that heterogeneity in area 3b is a common feature across mammals. More importantly, the different subregions in area 3b have different patterns of interhemispheric connections. All studies that have considered these architectonic distinctions have demonstrated that the dysgranular zone in rodents, and the unmyelinated or CO-light portion of area 3b in other species, receive dense callosal inputs relative to the rest of area 3b (e.g., Wise and Jones, 1976; Akers and Killackey, 1978; Gould and Kaas, 1981; Olavarria et al., 1984; Cusick et al., 1985; Krubitzer et al., 1986; Krubitzer and Kaas, 1990). We have previously shown that

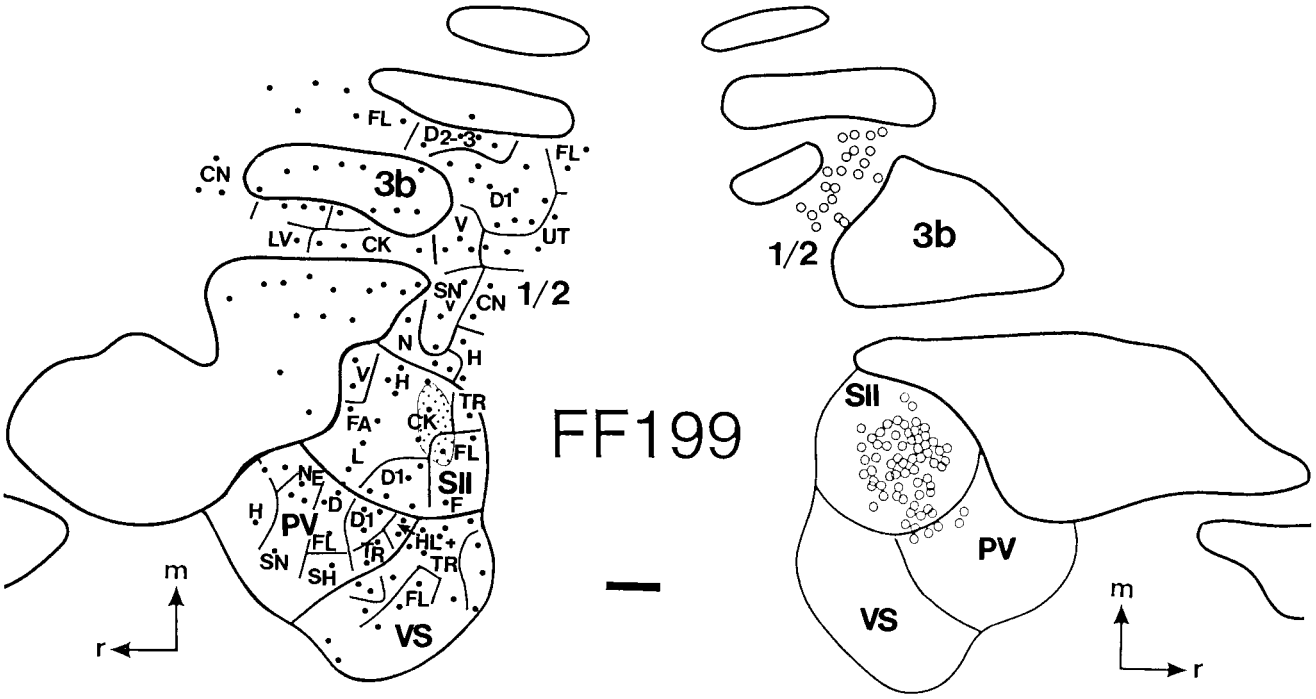

Fig. 11. **Left:** Location of electrode penetrations (dots) in the anterior parietal and lateral somatosensory fields, and the spread of a DY injection within SII in FF 199. The injection was centered in the cheek representation in SII and spread slightly into the representation of the forelimb. The thick lines enclose myelin dense area 3b, whereas the thinner lines indicate the myeloarchitectonic borders between the more moderately stained lateral fields. **Right:** Clusters of cell bodies labeled with DY (open circles) in somatosensory cortex in the opposite hemisphere were located in SII, near the SII/PV border, and in myelin-light cortex (area 1/2) located more medially. Scale bar = 1 mm.

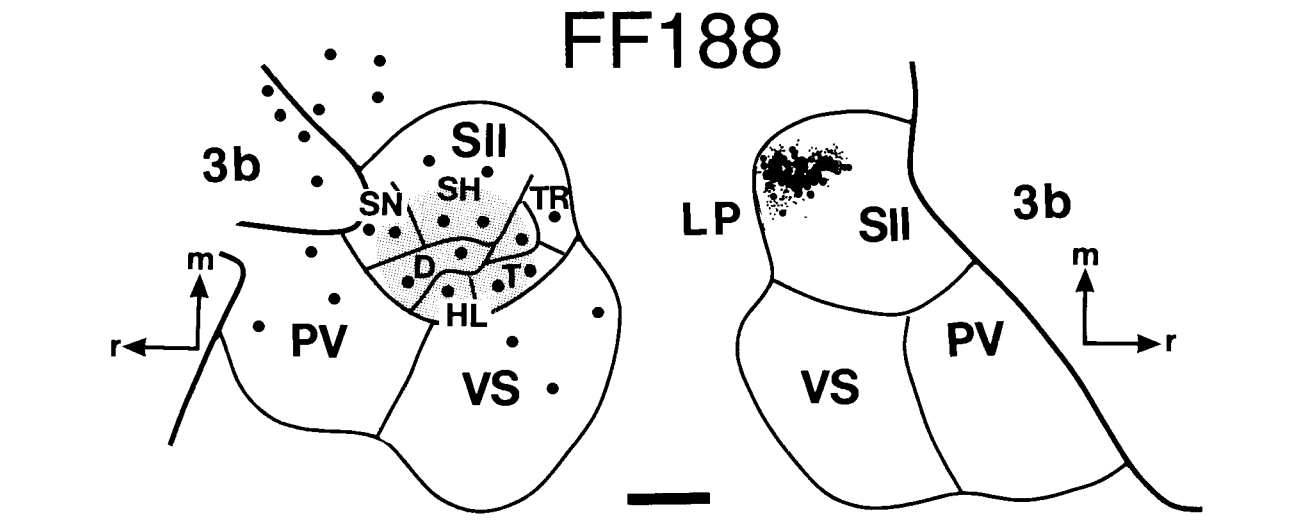

Fig. 12. **Left:** Location of electrode penetrations (dots) in the lateral somatosensory fields and adjacent areas, and the spread of a WGA-HRP injection within SII in FF 188. The WGA-HRP injection was centered in the representation of the digits in SII and spread into cortex in which neurons were responsive to stimulation of the shoulder, trunk, hindlimb, and snout. For clarity, body part representations have not been illustrated in area 3b, PV, and VS. **Right:** WGA-HRP–labeled cell bodies (large dots) and axon terminals (small dots) were restricted to SII in the opposite hemisphere. Conventions as in Figure 11. Scale bar = 1 mm.

area 3b of flying fox consists of myelin and CO-dense zones interdigitated by invaginations from the adjacent area 1/2 (Krubitzer and Calford, 1992; Krubitzer et al., 1993). In the present study, we demonstrate that the myelin-light, interdigitating zone in the flying fox (area 1/2) is the prominent interconnection zone with contralateral area 3b. We propose that the dysgranular zone in rats, the myelin-light portions of area 3b in squirrels, and area 1/2 in flying foxes are homologous and represent regions that interconnect most strongly across the hemispheres (Fig. 14). We

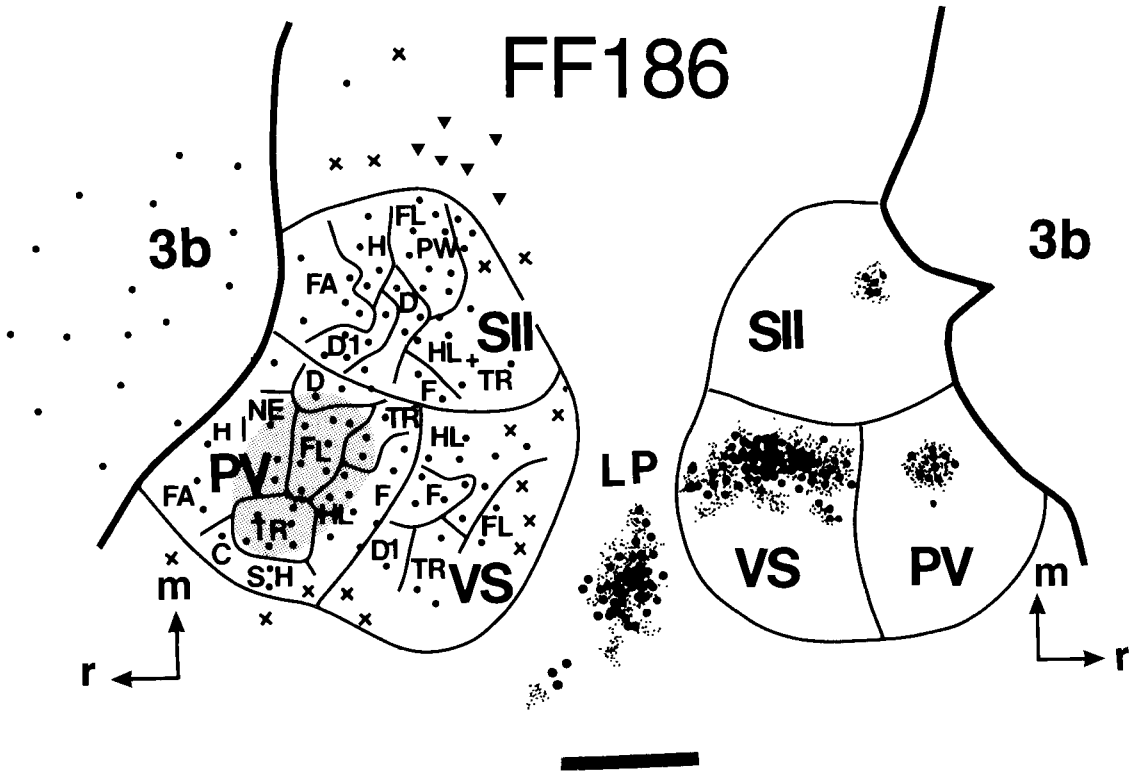

Fig. 13. **Left:** Location of electrode penetrations (dots) in the lateral somatosensory fields and adjacent areas, and the spread of a WGA-HRP injection within PV in FF 186. The WGA-HRP injection was centered in the forelimb representation and spread into cortex in which neurons were responsive to stimulation of the digits, neck, trunk, and hindlimb. For clarity, body part representations have not been illustrated in area 3b. **Right:** Patches of WGA-HRP–labeled cell bodies (large dots) and axon terminals (small dots) were located in SII, PV, and VS in the opposite hemisphere; an additional patch was located caudal to VS. Conventions as in Figure 12. Scale bar = 1 mm.

proposed in an earlier study (Krubitzer and Calford, 1992) that area 1/2 in the flying fox may be homologous with areas 1 and 2 in primates. Callosal connections of area 1/2 in the flying fox are more like those of area 2 in New World monkeys than like those of area 1, in which the hand representation is acallosal. However, because the marmoset has an unmyelinated, callosally connected strip between the representations of the hand and face in area 3b, it is difficult to determine whether area 1/2 in the flying fox is homologous with areas 1, 2, 1 and 2, or with this unmyelinated zone in primates.

Interhemispheric connections of individual cortical fields such as SI and SII have been described in several species. For instance, in squirrels, injections into the electrophysiologically identified face representation in SI resulted in retrograde and anterograde label in the contralateral SI. However, the transported tracer was most dense in the myelin-light region called the unresponsive zone and appeared to avoid the expected location of the vibrissae and lip representations (Gould and Kaas, 1981; Krubitzer et al., 1986). Injections into the face representation in SI in squirrels also resulted in extensive label in motor cortex, the parietal rhinal area, the parietal medial area, and areas SII and PV of the opposite hemisphere. Injections into the forelimb representation in SI resulted in more restricted patterns of callosal connections with only the forelimb representation in SI in the opposite hemisphere. A similarly designed study in the raccoon (Herron and Johnson, 1987) found that injections into the representation of the hindpaw or forepaw in SI resulted in no connections with SI of the opposite hemisphere, whereas injections into more proximal representations resulted in moderately dense connections with SI in the opposite hemisphere.

In a study of the tree shrew by Weller et al. (1987), injections were placed into electrophysiologically identified locations in SI and SII, and targets in SI and SII in the opposite hemisphere were explored electrophysiologically. These investigators found that whereas more proximal body part representations, including the naris, projected to similar representations in the opposite hemisphere, digit and toe representations in SI did not project to similar representations in SI in the opposite hemisphere. However, these representations received projections from more proximal body part representations in SI, and from distal and proximal representations in SII. These studies, like the present study, demonstrate that callosal connections of SI are differentially distributed, depending on the body part representation injected. They also demonstrate that connections are hetero- and homotopic within SI, and hetero- and homoareal.

Area 3a. Callosal connections of area 3a in the flying fox varied with respect to the body part representation injected: The snout representation in area 3a was interconnected only with the snout representation in area 3a in the opposite hemisphere, whereas the distal forelimb representation of area 3a received more broadly distributed, topographically matched and mismatched projections from areas 3a, 3b, and 4 of the opposite hemisphere. Studies in which the total pattern of callosal connections of anterior

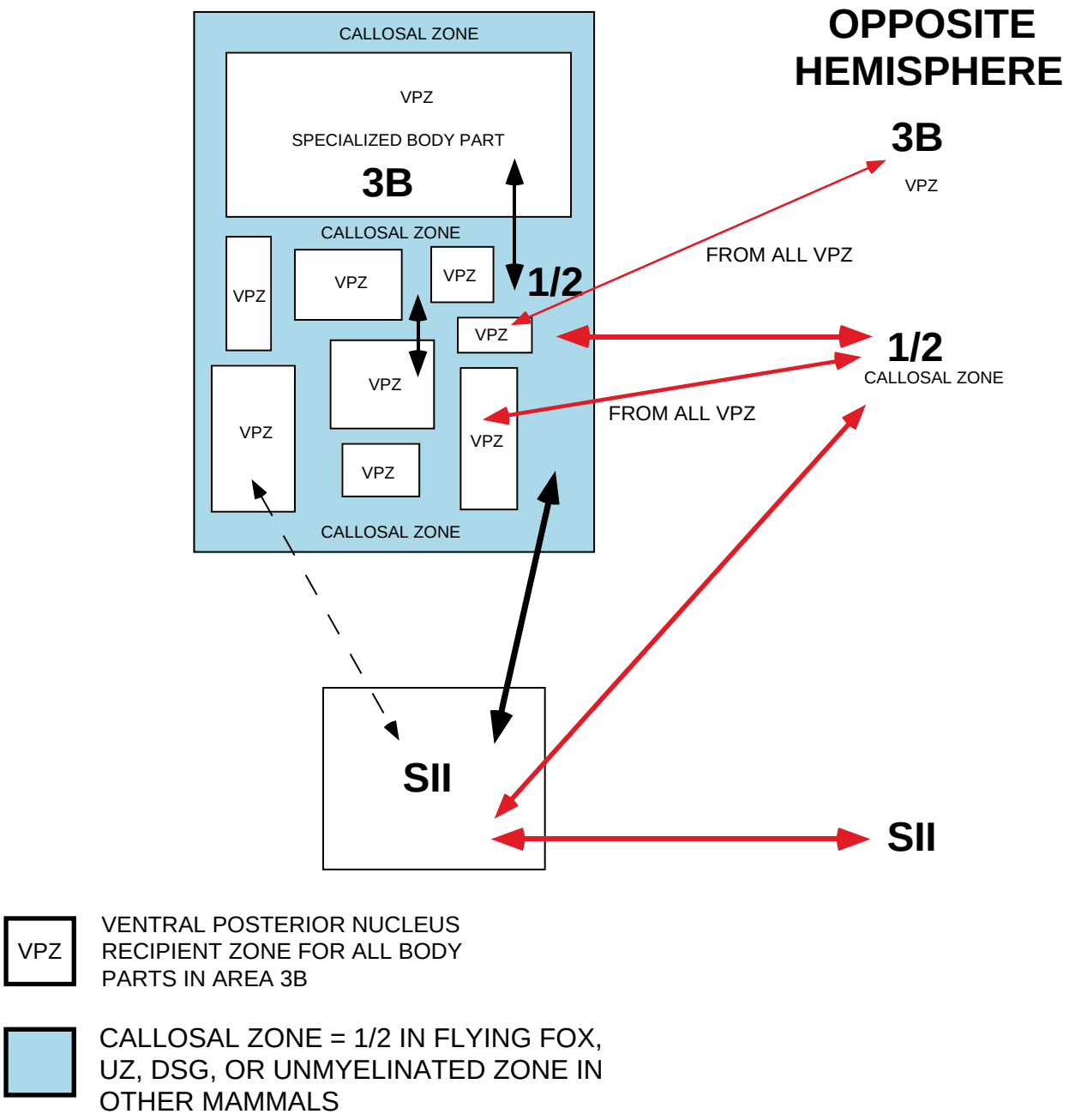

Fig. 14. A summary of the patterns of callosal connections in mammals. In this figure, the myelin-dense, ventral posterior nucleus recipient zones (VPZ) are shown as white squares. Although these regions are discontinuous, and are separated by myelin-light callosal zones (blue), they are considered as a single field. Some of the thalamic recipient zones are acallosal, especially the specialized body part representations. Some of the other VPZs do have sparse connections with similar zones in the opposite hemisphere (arrows are shone only for one of these squares, but all, save the specialized body part representation, project to 3b in the opposite hemisphere). There are parallel pathways across the hemisphere in that information from area 3b can reach the other hemisphere via direct connections between nonspecialized VPZs, through the callosal zone (which is area 1/2 in the flying fox), or through SII.

parietal cortex were examined indicate that in monkeys (Jones and Powell, 1969; Karol and Pandya, 1971; Jones et al., 1975; Jones and Hendry, 1980; Killackey et al., 1983; Shanks et al., 1985) and cats (Shanks et al., 1975; McKenna et al., 1981), area 3a receives projections from the opposite hemisphere, and that the density of input to different body part representations, to a large extent, reflects that of area 3b. Thus, in cats and monkeys, the paw/hand representation in area 3a had sparse or no connections with the opposite hemisphere.

Interhemispheric afferents and efferents of area 3a have been described only briefly for the marmoset (Huffman et al., 1996). In this study, the hindlimb/trunk representation in area 3a was interconnected most strongly with area 3a in the opposite hemisphere; however, interconnections were also observed with cortex immediately rostral to

area 3a, which corresponds to area 4 or primary motor cortex, and less densely with cortex in the location of the supplementary motor area. Sparse connections were also observed with areas 3b, 1, 2, and the medial portion of posterior parietal cortex. Our results from the flying fox are similar to those from marmosets in that the densest connections for any body part representation were with area 3a in the opposite hemisphere, and some body part representations such as the digits were interconnected with areas 3b and 4 of the opposite hemisphere.

Areas 1 and 2. Projections of area 1/2 in the flying fox were typically to matched body part representations in the contralateral areas 1/2, 3b, and SII. More limited projections were also observed with mismatched representations in the opposite hemisphere. For example, an injection in the D1 representation in case FF 260 resulted in labeled cell bodies not only in the D1 representation of area 1/2 in the opposite hemisphere, but also in representations of the wing, head, neck, and face in area 1/2. The only study of callosal connections in primates which differentiated parietal areas 1 and 2 electrophysiologically demonstrated that in both New World and Old World monkeys, the hand representation in area 1 was extremely sparsely interconnected or acallosal (Killackey et al., 1983). However, there appeared to be differences in the pattern of interhemispheric connections of area 2 between New World and Old World monkeys: In macaque monkeys, the hand representation in area 2 was sparsely connected or acallosal, whereas in owl monkeys the hand representation in area 2 was callosally connected. The flying fox appears to differ from Old World monkeys with respect to the interhemispheric connections of the representation of different body parts in area 1/2. As for area 2 in New World monkeys, the area 1/2 representation of distal body parts (i.e., D1) had moderate-to-dense inputs from the corresponding location in area 1/2 in the opposite hemisphere.

Lateral somatosensory fields, SII and PV. In the flying fox, SII received inputs from SII in the opposite hemisphere, and in one of two cases, SII also received inputs from the portion of area 1/2 in the opposite hemisphere that interdigitates with area 3b. In the single case in which interhemispheric connections of PV were examined, reciprocal connections were found with topographically appropriate regions of the contralateral lateral somatosensory fields (PV, SII, VS, LP).

Most studies of the total pattern of callosal connections to SII report a patchy and uneven distribution from throughout its contralateral counterpart (rats, mice, and hamsters: Koralek et al., 1990; Olavarria and Van Sluyters, 1995; squirrels: Gould and Kaas, 1981; macaque monkeys: Karol and Pandya, 1971). Other studies have examined the callosal connections of SII by using methods akin to the present work, by placing injections into electrophysiologically defined locations within the field. These studies confirmed a patchy distribution of callosally projecting cell bodies in SII (cat: Barbaresi et al., 1989; tree shrew: Weller et al., 1987; raccoon: Herron and Johnson, 1987; marmoset: Krubitzer and Kaas, 1990; macaque monkey: Manzoni et al., 1984). Given that PV has not been delineated from SII in each of these species, or not distinguished in some studies, it is probably the case that the present finding of reciprocal callosal interconnectivity between SII and PV seen in the flying fox is consistent with the the results of recent studies in other species. These projections were specifically described in the marmoset (Krubitzer and Kaas, 1990).

Interhemispheric projections to SII from the parietal somatosensory fields have been described in a number of species (cat: Caminiti et al., 1979; Barbaresi et al., 1989; tree shrew: Weller et al., 1987; raccoon: Herron and Johnson, 1987; marmoset: Krubitzer and Kaas, 1990; macaque monkey: Manzoni et al., 1984). The present study in flying foxes and the previous study in marmosets indicate that projections to SII and the contralateral parietal fields are from the zone between the hand and face representations of area 3b, which is considered part of area 1/2 in the flying fox and area 1 in marmoset. This projection parallels the strong ipsilateral interconnectivity of these fields. Unlike the interconnectivity of SII and area 1/2, the interhemispheric projection from SII to area 3b does not appear to be reciprocal.

Interhemispheric connections of PV have only been described previously in the squirrel and were reported to be with SI, SII, PV, the parietal rhinal area, the parietal medial area (possibly a division of posterior parietal cortex; Slutsky et al., 1996), the temporal anterior area, and cortex caudolateral to SII in entorhinal cortex (Krubitzer et al., 1986). Some of these connections are similar to those of PV in the flying fox: Connections were observed with PV in the opposite hemisphere, and these were formed by a single focus of labeled cell bodies and axon terminals. This contrasts with the pattern of interconnections of PV in the squirrel, which are patchy and widespread. In both species, connections were observed with cortex caudolateral to PV, which is termed VS in the flying fox and is termed the parietal rhinal area in squirrels.

Callosal connections, morphological specialization, and developmental constraints

Segregation of thalamic and callosal inputs to the primary sensory fields or segregated callosal territories (Fig. 14) has been observed in the cortex of a variety of mammals (Jones et al., 1975; Wise and Jones, 1976; Jones and Wise, 1977; Gould and Kaas, 1981; Olavarria et al., 1984; Krubitzer et al., 1986; Krubitzer and Kaas, 1990). Observations of a similar distribution of callosal connections in eutherian mammals and anterior commissure connections in metatherian mammals suggest that similar developmental mechanisms, which evolved early in mammalian evolution, construct these patterns of interhemispheric connections. Correlated activity of the different sources of input to the developing cortex (e.g., Olavarria and Li, 1995; see Constantine-Paton, 1982), or timing differences in the development of the interhemispheric (callosal or anterior commisure) and thalamic axons that occupy these territories, could account for initial segregation. Along with ipsilateral inputs to a field, thalamic and callosal inputs clearly compete for cortical space in developing mammals (see Lent et al., 1990). Disruption of one of these major sources of input during development affects the tangential distribution of the other sources and changes the allotment of cortical territory of the different sources of input (e.g., Innocenti and Frost, 1979, 1980; Rhoades and Dellacroce, 1980; Caminiti and Innocenti, 1981; Cusick and Lund, 1982; Rothblat and Hayes, 1982; Olavarria and Li, 1995; for review, see Innocenti, 1986). Changes that occur after the major sources of input have carved out their territory (Killackey and Chalupa, 1986) indicate that subcellular events (e.g., changes in synaptic efficacy) refine the amount of cortical territory that each source holds, and

maintenance of these patterns may be use dependent (e.g., Jenkins et al., 1990; Recanzone et al., 1992a,b). Apparently, this process of refinement and readjustment continues throughout adulthood, at least in the primary sensory and motor cortex (e.g., Donoghue et al., 1990; Kaas et al., 1990; Recanzone et al., 1993; Nudo et al., 1996; for reviews, see Kaas, 1995b; Calford et al., 1998).

Earlier in this discussion we reviewed a number of studies which demonstrate that callosal connections are patchy and that their distribution is usually associated with the representation of a body part that is considered to be specialized. The uneven distribution of callosal connections may be constructed initially by developmental processes similar to those described above and refined with the use of the specialized body part or sensory surface. A number of studies in developing mammals indicate that significant postnatal changes in callosal connections occur at the synaptic level (for review, see Innocenti et al., 1995; Innocenti, 1986). Within a species over time, selection may operate not only on the specialized body part to increase its size or receptor density, but also on the corresponding representation, at least in primary fields, to conserve discrete receptive fields created from thalamic inputs that are uninterrupted by callosal afferents and efferents (Fig. 14). This would allow for short, lateral, intra-areal connections and increased speed of transmission between inputs from immediately adjacent body part representations. This type of organization may be necessary to maintain the integrity of sensory discrimination derived from inputs from specialized body parts. A number of investigators have reported that regions of cortex in which receptive fields for neurons are small tend to be free of interhemispheric connections (e.g., McKenna et al., 1981; Herron and Johnson, 1987). Our data in the flying fox support the idea that these regions in cortex are usually associated with a peripheral specialization. In this regard, it is interesting to note that the parallel of sparse interhemispheric connections between D1 representations of areas 3b for the flying fox and distal forelimb in other species reflects a functional homology rather than a geometric homology. In the flying fox the neurons with receptive fields on D1 are found at the dorsal midline aspect of the representation in caudal area 3b (Calford et al., 1985), whereas, in other species the distal forelimb is represented with the ventral midline in rostral area 3b.

The pattern of interhemispheric connections of the wing and digit representations has implications for the suggestion that stronger callosal interconnectivity allows for fusion of the midline representations (Innocenti, 1986; Manzoni et al., 1989; Guillemot et al., 1992). The representations of the wing membranes and D2–D5 in areas 3b have a relatively high density of callosal interconnectivity. Although these are distal body parts, the use of the wing, as discussed below, may constitute a specialization that favors direct interconnectivity. In contrast, the dexterous use of D1 may constitute a specialization which, along with the digits in primates, favors lateralization of the representations. Thus, although the present study does not provide a clear interpretation of the differential pattern of callosal connections which would definitively support either the specialization hypothesis or the midline fusion hypothesis, it is easier to account for the data in terms of specialization-based considerations. Indeed, midline fusion may be considered as a specialization favoring direct interconnectivity.

Differential interconnectivity is not restricted to the area 3b representation. In the flying fox, there are dense projections from proximal forelimb representations of areas 3a and 4 to distal and proximal representations of the forelimb representation in area 3a of the opposite hemisphere, and more restricted patterns of area 3a interconnections for the face representation in area 3a in the opposite hemisphere. This may be a reflection of the adaptation of the forelimb for flight in the flying fox. Inputs from the specialized receptor assemblies in the bat wing (hair–dome complexes; Crowley and Hall, 1994), which respond to very small puffs of air, are unlikely to be involved in processing information related to object discrimination and identification. It may be important for each hemisphere to have access to cutaneous inputs that signal small changes in air pressure from both sides of the body and deep inputs that signal muscle stretch and limb position from both sides of the body, as well as access to motor representations on both sides controlling the limbs to make adjustments to the wing during flight. In contrast, the flying fox has no remarkable aspects in the use of, or representation of, the face and head.

Physiological results from work on short-term plasticity in flying fox area 3b indicate that regions with poor direct interhemispheric connectivity can still have significant functional interactions. It has previously been reported that partial peripheral denervation of D1, or digit amputation or local anaesthesia, in the flying fox produces rapid expansion of receptive fields in area 3b in the ipsilateral hemisphere—for neurons with fields on the mirror image body area to that directly affected (Calford and Tweedale, 1990). This phenomenon resulted in a balanced unmasking of increased responsiveness and larger neural receptive fields in matched locations of each hemisphere. Studies aimed at investigating the mechanism of this effect found, paradoxically, that blocking of afferents emanating from the homotopic location in the opposite hemisphere resulted in a rapid unmasking of larger neural receptive fields in area 3b. This effect was found for both D1 and wing representations in flying fox, and hand and foot representations in macaque monkey (Clarey et al., 1996). As for the macaque, the present results in flying fox indicate that the interhemispheric unmasking effects for specialized distal body part representations require the involvement of multiple somatosensory fields. It is conceivable for both species that this involves the ipsilateral area 3b to area 1 (1/2 in flying fox) projection, and callosal projections to the opposite area 1 (1/2). In addition, in the flying fox, the callosal projections from area 1/2 to distal body part representations in area 3b may fulfill this role. Preliminary work with deactivation at each of these stations in the proposed pathway supports this assertion (Clarey et al., 1993). An analogous pathway in humans, from S1 (area 3b) to areas 1, 2, or 5 ipsilaterally and areas 1, 2, and 5 to contralateral areas 1, 2, and 5, has been suggested as the basis for a number of callosally mediated psychophysical phenomena (Quinn and Geffen, 1986).

Our results, as well as observations in other mammals, suggest that the pattern of interhemispheric connections is likely to reflect a compromise between a number of factors including maintaining sensory discriminatory integrity of processing of inputs from specialized body parts (particularly in primary areas), developmental competition for cortical space, and the function of the body part for which the cortical representations are interconnected.

ACKNOWLEDGMENTS

We thank Kelly Huffman and Gregg Recanzone for helpful comments on this manuscript. L.K. received an Australian Research Council fellowship, and M.B.C. received a NH&MRC grant.

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