

Microelectrode Maps, Myeloarchitecture, and Cortical Connections of Three Somatotopically Organized Representations of the Body Surface in the Parietal Cortex of Squirrels

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ABSTRACT

Microelectrode mapping methods and anatomical procedures were combined in the same animals to reveal the cortical connections of three architectonically distinct representations of the body surface in the somatosensory cortex of grey squirrels. In individual experiments, microelectrode multiunit recordings were used to determine the somatotopic organization of regions of the cortex and to identify sites for injections of the anatomical tracer, wheat germ agglutinin conjugated to horseradish peroxidase. After the brains were perfused, the cortex was separated from the brainstem, flattened, and cut parallel to the flattened surface to facilitate comparisons of areal connection patterns, physiological data, and architectonic subdivisions.

Recordings in the primary (S-I) and secondary (S-II) somatosensory fields confirmed earlier descriptions of the somatotopic organization of these fields (Sur et al.: *J. Comp. Neurol.* 179:425-450, '78; Nelson et al.: *J. Comp. Neurol.* 184:473-490, '79). In addition, recordings in the cortex caudal to S-I and ventral to S-II revealed a third representation of the body surface in parietal cortex, the parietal ventral area (PV). Neurons in PV were responsive to light tactile stimulation of skin and hairs. Multiple unit receptive fields of neurons in PV were larger than those for neurons in S-I but similar in size to those for neurons in S-II. PV represented the contralateral body surface in a somatotopic manner that can be roughly characterized as an inverted "homunculus" with the limbs directed medially, the trunk located ventrally, and the face congruent with the representations of the upper lip and nose in S-I. Neurons in some electrode penetrations in PV were also responsive to auditory clicks.

Microlesions placed at physiologically determined borders allowed all three somatic representations to be related to myeloarchitectonically defined fields. S-I was architectonically distinct as a densely myelinated region. Within S-I, a lightly myelinated oval of the cortex between the representation of the hand and face, the "unresponsive zone" (Sur et al.: *J. Comp. Neurol.* 179:425-450, '78), was an easily recognized landmark. S-II and PV corresponded to less densely myelinated fields. Other subdivisions such as motor cortex, primary auditory cortex, and visual areas 17 and 18 were distinguished.

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Connections were revealed by placing injections within S-I, S-II, or PV. Injections in S-I demonstrated reciprocal ipsilateral connections with the motor cortex, S-II, PV, a parietal medial (PM) zone along the caudal border of S-I, and a parietal rhinal (PR) zone ventral to PV and dorsal to the rhinal fissure. Injections placed in different parts of S-I suggested that connections with S-II, PV, PM, and the motor cortex are somatotopic. Callosal connections were with somatotopically equivalent parts of S-I. In one case where the unresponsive zone (UZ) was involved in the injection site, more extensive callosal connections included the motor cortex, S-II, PV, PR, PM, and UZ. Injections placed in S-II revealed ipsilateral interconnections with S-I, PM, PV, PR, and the cortex caudal to S-II. There were no significant connections with the motor cortex. Callosal connections were with S-II. Injections in PV demonstrated ipsilateral connections with S-I, S-II, PR, PM, and the motor cortex and callosal connections with PV, S-I, S-II, PR, and PM.

The results led to two major conclusions. First, the parietal cortex in squirrels and possibly other rodents has at least three, and possibly as many as five, interconnected representations of the body. Second, PV and S-II are so similar to each other in size, responsiveness, and location relative to S-I that if both S-II and PV exist in other rodents or in other mammals, the two fields could be confused with each other from study to study.

Key words: primary somatosensory cortex, motor cortex, corpus callosum, architectonics

The brain is intriguing, in part, because it is so variable in structure and function across vertebrate species. Brain diversity is highly apparent in mammals, where, as an obvious example, the amount of neocortex varies from being a small cap on the forebrain in an insectivore such as the hedgehog to the expanded bulk engulfing most of forebrain in humans. In addition to such vast differences in relative size of the neocortex, there are almost certainly profound differences in organization. A traditional and currently supportable view of forebrain organization is that mammals with little neocortex, such as the hedgehog, have few subdivisions of functional significance, while species with considerable neocortex have many subdivisions (see Merzenich and Kaas, '80; Kaas, '82). Since mammals with expanded neocortex evolved independently in a number of lines of descent, it follows that increases in the complexity of cortical organization occurred independently a number of times. However, our understanding of the evolution of advanced brains and the corresponding wondrous changes in mental abilities has been limited by a lack of accurate information on how the cortex is organized in different mammals. Most studies of cortical organization have been on cats, several species of monkeys, and rats, and even in these mammals only a few subdivisions of the cortex have been defined with certainty. However, modern methods of microrecording, microstimulation, histochemistry, and the tracing of connections allow subdivisions of the brain and their connections to be reliably defined, and great progress in understanding cortical organization is now possible.

The present study is part of a larger effort to determine further the basic organization of the neocortex in mammals and how this organization has been modified in the major lines of descent. The grey squirrel was chosen as an easily obtained rodent with the advantages of a larger brain and generally more distinct architectonic subdivisions than the commonly used rats and mice. Our investigation of the somatosensory cortex is paralleled by similar studies of the visual cortex (Hall et al., '71; Kaas et al., '72; Cusick et al.,

'80) and the auditory cortex (Merzenich et al., '76; Luethke et al., '85) in squirrels. Previous studies of the somatosensory cortex in squirrels have used microelectrode mapping methods to define the primary (Sur et al., '78) and secondary (Nelson et al., '79) somatosensory representations. In addition, the overall pattern of callosal projections of these two fields has been described (Gould and Kaas, '81). The initial goal of the present study was to use the sensitive tracer wheat germ agglutinin conjugated to horseradish peroxidase (WGA-HRP) to determine the cortical connections of S-I, and S-II. Because a major projection zone of S-I, and S-II was demonstrated in the ventral parietal cortex, we extended the original studies to map and further determine additional connections of a previously unknown representation of the body surface. An abstract of some of the results has appeared elsewhere (Krubitzer et al., '85).

METHODS

Multiunit recording methods were used to investigate subdivisions of the somatosensory cortex in 17 adult grey squirrels (*Sciurus carolinensis*). In the same animals, cortical connections were determined by injecting the anatomical tracer wheat germ agglutinin conjugated with horseradish peroxidase (WGA-HRP) into electrophysiologically defined locations. Physiological and anatomical results were later related to the cortical architecture in sections cut parallel to the cortical surface of artificially flattened cortex. Microelectrode recording techniques were adopted from Sur et al. ('81), the anatomical procedures correspond to those outlined in Sesma et al. ('84), and the methods of flattening cortex are described in Gould and Kaas ('81) and Sesma et al. ('84).

At the start of each experiment, the squirrel was initially anesthetized with 0.3 cc ketamine hydrochloride (130 mg/kg; see White et al., '82) and 0.1 cc of acepromazine (4.3 mg/kg). In addition, 0.1 cc of 2% xylocaine hydrochloride, a local anesthetic, was injected subcutaneously where ear bars entered the auditory meatus and where the scalp was

to be cut. Maintenance doses of 0.15 cc of ketamine, supplemented in some cases with 0.025 cc of nembutal (5.4 mg/kg), were given as needed to maintain a surgical level of anesthesia. After the animal was deeply anesthetized, a portion of the skull was removed, and the dura was retracted to expose most or all of the somatosensory cortex. An acrylic dam was built around the opening and filled with silicone fluid, which protected the brain from desiccation. The head was tilted in a plane that allowed the electrode to penetrate the cortex perpendicular to the surface of the cortical area of interest. Prior to recording, the exposed cortex was photographed so that the blood vessel pattern could be used to mark the location of electrode penetrations.

Recordings were made with low-impedance tungsten microelectrodes (0.9–1.2 M Ω at 1,000 Hz) with tip exposures designed to record from small clusters of neurons. Electrodes were advanced with a stepping microdrive. Recording depths were approximately 500–1,000 μ m from the pial surface, although better recordings of auditory responses from neurons in the parietal ventral area (PV) were obtained at deeper depths (see Results). To obtain the receptive fields for neurons in a given penetration, the body surface was stimulated with fine wires and glass probes to find the location where stimuli maximally activated the neurons. Stimulation consisted of light tapping on the glabrous surface of the skin, displacement of hairs and vibrissae on the hairy surface of the skin, or lightly scratching the hairy or glabrous surface of the skin. The somatotopic organization of a region of cortex was determined from receptive fields for a number of closely spaced recording sites.

After detailed mapping of a given area (the primary, S-I, and secondary somatosensory areas, S-II, or PV) was completed, marker lesions were made at electrophysiologically defined borders in S-I (Sur et al., '78), S-II (Nelson et al., '79) and PV so that physiological boundaries could be subsequently related to brain sections reacted for HRP or stained for myelin. Next, an anatomical tracer was injected at one or more electrophysiologically identified sites. Over a period of 20 minutes, 0.05–0.1 μ l of 0.5% WGA-HRP was injected through a calibrated glass pipette into the representations of various body parts in S-I, S-II, or PV. Upon completion of the injection, the exposed cortex was covered with an acrylic cap, and the skin opening was closed. After 2 days, the animal was deeply anesthetized and perfused through the heart with 0.9% saline followed by 1.5% glutaraldehyde and 1% paraformaldehyde in phosphate buffer (pH 7.4). The fixed brain was removed, and the cortex was dissected from the brainstem, flattened between glass plates, and left to soak for approximately 24 hours in 30% sucrose phosphate buffer. The flattened cortices were frozen and cut into 40- μ m sections in a plane parallel to the cortical surface. Two in four sections were reacted for HRP with tetramethylbenzidine (TMB) (Mesulam, '78). The remaining adjacent sections were stained for myelin with the Gal-lyas ('79) silver procedure. Sections reacted for HRP were sometimes stained with cresyl violet for cytoarchitecture, but these sections were less useful than the myelin preparations for revealing architectonic boundaries.

For each case, drawings were made from several sections of tissue where the reacted anatomical tracer was most apparent. These drawings included the injection site, anterogradely labeled axons and terminals, retrogradely labeled cell bodies, and marker lesions. Drawings of

individual sections were aligned by using blood vessels and tissue artifacts and compiled into one comprehensive reconstruction. Architectonic borders determined from myelin stained sections were superimposed on the reconstructions.

RESULTS

In the present experiments, multiunit recording procedures were used to reveal boundaries and features of somatotopic organization of two previously defined subdivisions of somatosensory cortex, the primary somatosensory area, S-I (Sur et al., '78) and the secondary somatosensory area, S-II (Nelson et al., '79). In addition, the somatotopic organization of a third and previously unknown field, the parietal ventral area (PV), was determined. Ipsilateral and contralateral cortical connections of these three subdivisions of the brain were determined in the same animals by injecting WGA-HRP into electrophysiologically identified locations. The electrophysiological and connectional results were related to myeloarchitectonic subdivisions of cerebral cortex of the same animals. Correlation of structural and electrophysiological data was facilitated by artificially flattening the cerebral hemispheres and cutting cortical tissue parallel to the flattened surface.

The myeloarchitecture of cortex

Myeloarchitectonic differences reliably identified the boundaries of a number of cortical areas in brain sections cut parallel to the cortical surface. While parts of boundaries are obvious in single sections (Figs. 1–3), boundaries are better determined by examining a series of sections, since the flattened cortex may not always be cut in a plane exactly parallel to the cortical surface and the myelination pattern of cortical subdivisions changes throughout the cortical layers. Figure 1 illustrates the fact that many architectonic borders are apparent in single sections of flattened cortex. The first visual area, V-I or area 17, is most easily identified in the supragranular layers since it is more densely myelinated in these layers than the adjoining second visual area, V-II or area 18 (Hall et al., '71; Gould, '84). Thus, the 17/18 border is more distinct caudally in Figure 1 because it is slightly more superficial than the rostral portion of these visual areas. At favorable laminar levels, the outer boundary of area 18 is identified by a decrease in myelination density (caudal arrows in Fig 1). In temporal cortex, the densely myelinated temporal posterior region (TP) is distinct. This region has been reported to have darkly staining fiber bands in layers III and V (Kaas et al., '72). Since TP is surrounded by lightly myelinated cortex, all of its boundaries are pronounced. Rostrally in the temporal cortex, the temporal anterior region, TA (Kaas et al., '72), which includes the primary auditory field A-I (Merzenich et al., '76; Luethke et al., '85), is more heavily myelinated in deeper cortical layers than most adjoining cortex. Because of the level of the section, only part of A-I is evident in Figure 1. In parietal and frontal cortex, subdivisions of somatosensory cortex and motor cortex are also apparent. The architectonic characteristics of somatosensory areas and how they relate to the physiological and anatomical findings are described in more detail below. Architectonic features of neocortex in general have been described by Kaas et al. ('72), while the architecture of the visual (Hall et al., '71), auditory (Merzenich et al., '76), and somatosensory cortices (Nelson et al., '79; Sur et al., '78) has been described in more detail in other papers.

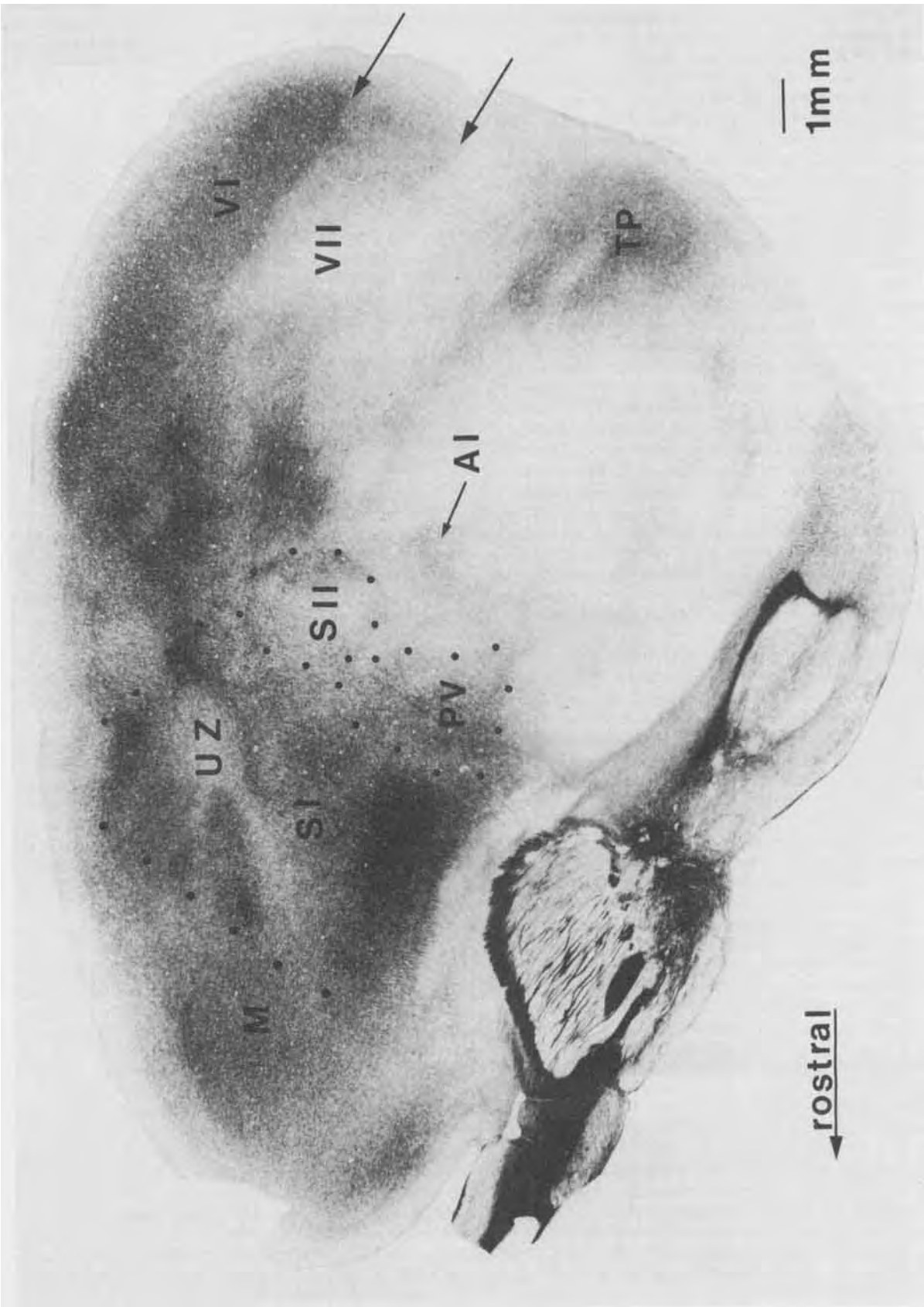


Figure 1

Myeloarchitecture of S-I, S-II, and PV

S-I is architectonically distinct from S-II, PV, and surrounding regions of cortex. It occupies a large region and is the most extensive representation of the body surface in the squirrel cortex. Its rostral extent is readily determined since S-I is more heavily myelinated than the neighboring motor cortex (Fig. 1, 2A). The caudal boundary of S-I is also easily identified since S-I is more densely myelinated throughout most of the cortical layers than the parietal medial zone (PM), S-II, and PV, all of which abut S-I caudally (Fig. 2A). At its lateral border, S-I is bounded by lightly myelinated cortex. Within the densely myelinated S-I, there are regions that are lightly myelinated. A 1-mm oval of very lightly myelinated cortex is coextensive with a portion of S-I that has been described as unresponsive to light cutaneous stimulation (Sur et al., '78). This "unresponsive zone," the UZ (Figs. 1, 2A), is also characterized by a less granular layer IV (Kaas et al., '72; Sur et al., '78). Two lightly myelinated strips of cortex extend rostrally and rostrolaterally within S-I from UZ. The cortex lateral to the unresponsive zone contains a cutaneous representation of the upper and lower lips. This large portion of S-I occupies approximately a 4×3 mm expanse of the cortex. Caudolateral to the unresponsive zone, a moderately myelinated region is coextensive with the nose representation in S-I. Immediately caudal to the unresponsive zone, another region of moderately myelinated cortex is coextensive with the vibrissae representation. The portion of S-I just medial to the unresponsive zone tapers into a moderately myelinated region of the cortex that contains representations of the forelimb, trunk, and hindlimb in a lateral to medial cortical progression from UZ.

Several fields border S-I. Motor cortex (M), just rostral to S-I, is less myelinated than S-I. Although the motor cortex becomes more myelinated in deeper cortical layers, it remains less myelinated than S-I. Thus, the S-I/M border is distinct in almost all sections (Figs. 1, 2A, 3A). A lightly myelinated strip of the cortex, the parietal medial area (PM), is immediately caudal to S-I and medial to S-II. The border between S-I and PM is most apparent in superficial layers of the cortex (Fig. 2A). In deeper cortical layers, PM is more heavily myelinated so that the S-I/PM border is less

obvious. S-II is in a lateral portion of the cortex that is poorly myelinated in superficial cortical layers so that the boundary with the well-myelinated S-I is unambiguous (Fig. 2A). S-II is moderately myelinated in the middle cortical layers (Fig. 2B) and is bordered laterally and caudally by lightly myelinated cortex, making the caudolateral perimeter distinct. Like S-II, PV is less myelinated than S-I in more superficial cortical layers so that the boundary between S-I and PV is clearly visible (Fig. 2A). In successively deeper layers of the cortex, PV is first moderately myelinated (Fig. 3A) and then densely myelinated (Fig. 3B). PV is bounded medially and laterally by lightly myelinated cortex, and caudally by a moderately to heavily myelinated area of cortex (Fig. 3A,B) that is coextensive with the physiologically defined A-I (Merzenich et al., '76; Luethke et al., '85).

PV is also apparent in brain sections cut in the frontal plane. Figure 8 of Nelson et al. ('79) shows frontal brain sections through S-II with the borders of S-II marked. The cortex just ventral to S-II in the photomicrographs is PV. In these frontal sections, PV can be seen to have moderately dense myelination in the middle layers, and moderately dense packing of small cells in layers III and IV.

Representations of the body surface

Multiunit recordings revealed three systematic representations of the body surface in the parietal cortex of squirrels, S-I, S-II, and PV. Our recordings from S-I were limited, since the larger size of the area (Sur et al., '78) made it easy to place restricted injection sites in the identified locations within the field. However, recording results from S-I are briefly described to show consistencies with previous findings. Because the smaller size of S-II made it more difficult to confine injections to that area, we mapped it more extensively in order to identify and lesion all boundaries before injecting the anatomical tracers. In two experiments, more detailed results on the internal organization of S-II were obtained than those previously published for squirrels (Nelson et al., '79).

S-I. Neurons in S-I were highly responsive to somatosensory stimuli across the middle cortical layers where most recordings were obtained. The general characteristics of the neurons in S-I were like those previously described for the squirrel (Sur et al., '78). As noted previously, neurons in S-I responded to light cutaneous stimulation and the receptive fields were small and on the contralateral body surface. Representations of restricted body parts were usually continuous, and the general orientation of the body representation was inverted.

Since S-I in the grey squirrel has already been mapped in detail (Sur et al., '78), recordings were limited to only parts of S-I in any given squirrel. In cases 84-76 and 84-54, where the forelimb representation was mapped, the physiological results were in good agreement with previous findings (Sur et al., '78). Thus, a double representation of the forepaw was found in the rostral portion of the forelimb representation of S-I, while the forearm and wrist were represented in the caudal portion of the forelimb representation. Another mapped portion of S-I represented the lips (cases 85-50, 84-57, 84-99, Figs. 10A, 11A). As in the earlier study, the present investigation identified a large lower lip representation at the rostral boundary of the face representation and a large upper lip representation immediately caudal to that of the lower lip.

Fig. 1. The myeloarchitecture of the neocortex in the grey squirrel. A section cut parallel to the surface of an artificially flattened cerebral hemisphere has been stained for myelin. The single section provides a view of the extents and locations of cortical areas that is comparable to a reconstructed lateral view of the brain. The advantages of the plane of section are that some architectonic boundaries can be followed over much of their extents in a single section and that reconstructions can be based on few sections. For example, the border of the primary (V-I) with the secondary (V-II) visual cortex is obvious over much of its caudal extent (arrow, upper right), and more superficial sections clearly revealed its rostral location. The lateral border of V-II (area 18) is also obvious caudally (between arrows on right). Rostrally, a sudden reduction in overall density of myelination marks the border between the primary motor (M) and the primary somatosensory (S-I) cortex (see the rostral row of mediolateral dots). Within S-I, the lightly myelinated unresponsive zone, the UZ, separates a medial representation of the forelimb from a lateral representation of the face. Lightly myelinated bands extend from UZ to the motor cortex. More caudally, the caudal borders of S-I, the second somatosensory area (S-II), and the parietal ventral somatosensory area (PV) are associated with sudden decreases in the density of myelination. These borders are more apparent when several brain sections are considered. The primary auditory area, A-I, is more densely myelinated than the surrounding cortex, but this is more apparent in deeper sections. Finally, the densely myelinated temporal posterior region, TP, is a useful reference. Rostral is right, and medial is upper in the section.

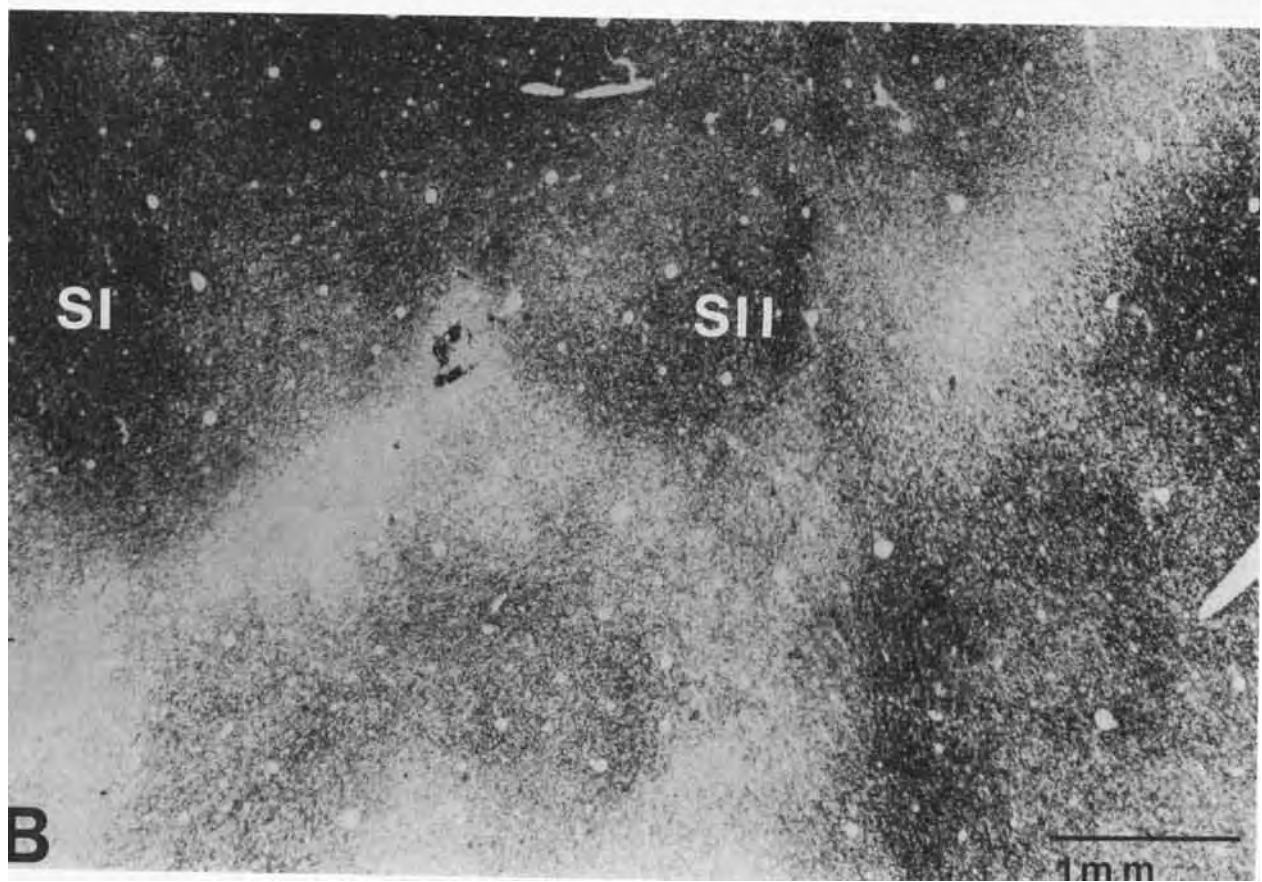
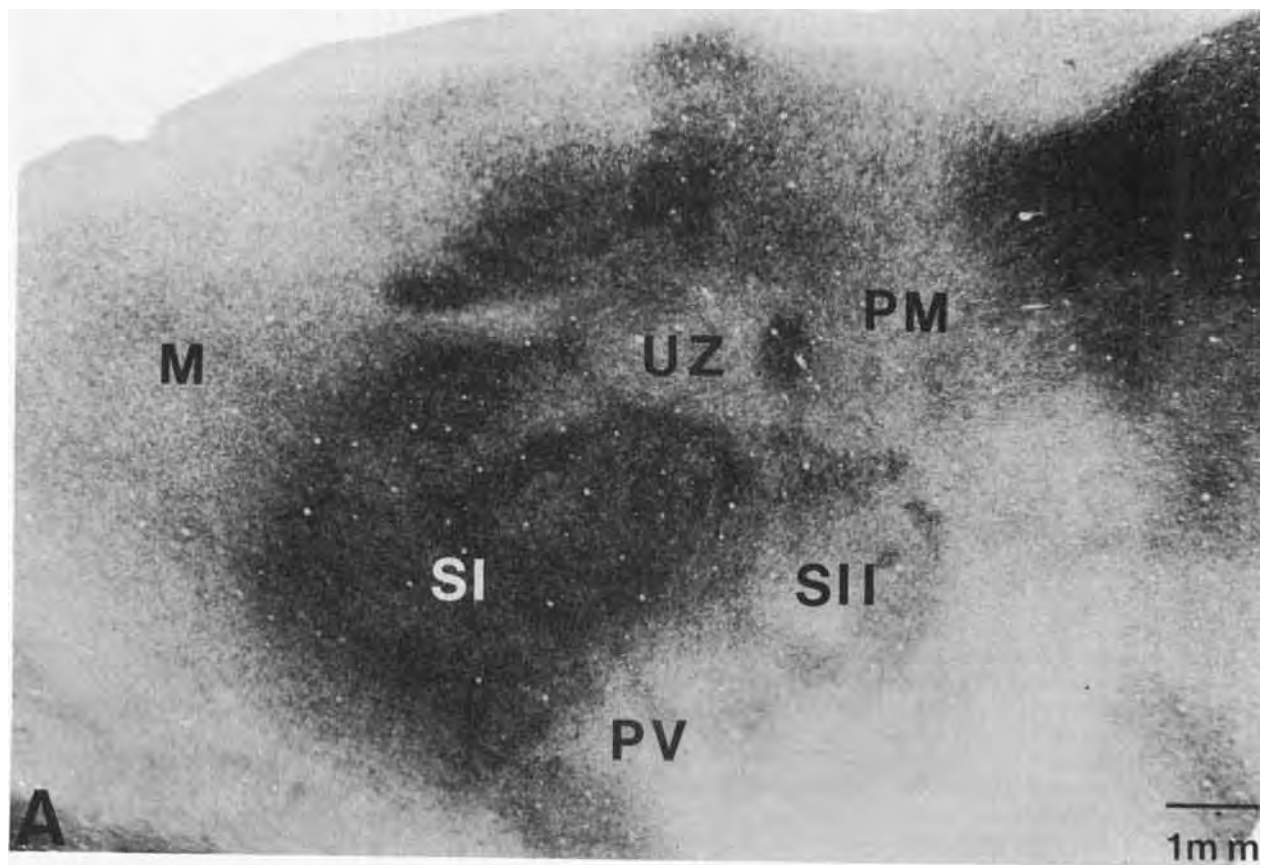


Figure 2

In addition to those regions of S-I that were systematically mapped, many recording sites were made near S-I/S-II and S-I/PV borders. Figure 4 illustrates penetrations near the S-I/S-II border in cortex devoted to the upper lip and nose in S-I. With the progression of recording sites across the S-I/S-II border, the receptive fields became large and reversed in somatic sequence to retrace the receptive field locations for neurons in S-I. Figures 6 and 7 illustrate receptive fields for neurons in penetrations extending from the representations of the lip and nose in S-I into PV. Again, receptive fields were smaller for neurons in S-I than those for neurons in PV. As for S-I/S-II border, a reversal in the receptive field sequence occurred as recording sites progressed from S-I into PV.

The entire physiological representation of the body surface in S-I was found to be coextensive with the myeloarchitectonically identified area described in the previous section, and some body parts could be related to subdivisions of the architectonic field. Thus, after injections of WGA-HRP, label in S-I could be assigned, not only to S-I, but to the representations of body parts within S-I on the basis of myeloarchitecture.

S-II The main purpose in mapping S-II in detail was to carefully determine boundaries so that injections of tracers could be placed and confined within the field. However, the mapping results also allowed comparisons with previously published maps of S-II in squirrels. As for S-I, present findings were in good agreement with previous findings. Figure 4 illustrates penetrations in representations of various body parts in S-II and their corresponding receptive fields. The physiologically defined S-II occupies a small expanse of the cortex (approximately 2 mm × 2 mm) that is adjacent to the nose representation in S-I. Penetrations 1-7 in Figure 4 illustrate receptive fields for a row of recording sites across S-I/S-II border. Receptive fields of neurons for progressively caudal electrode penetrations (from S-I into S-II) revealed a clear reversal sequence on the body surface (e.g., penetrations 1-7, Fig. 4). In addition, the size of the receptive fields for S-II were clearly larger than those for S-I. S-II was bounded medially, caudally, and laterally by cortex unresponsive to tactile stimulation. As previously reported, the basic orientation of the representation in S-II in the grey squirrel was an upright (noninverted) "homunculus." The head was represented rostromedially, and it occupied the greatest portion of S-II. The forelimb was represented caudolateral to the face representation. Within the forelimb representation, the upper arm was represented caudally, and the digits were represented rostrally. Cortex devoted to the trunk was caudolateral to the face and forelimb representations. Within the trunk region, the

dorsal trunk was caudal and the ventral trunk was rostral. The representation of the hindlimb was caudolateral to the representation of the trunk. Like the representation of the digits of the forelimb, the digits of the hindlimb were represented rostrally, and the upper hindlimb was represented caudally. The gluteal region and tail were represented in a small amount of cortex in the most caudolateral part of S-II.

Figure 4 illustrates some of the results from an extensive map in which receptive fields were determined for 39 electrode penetrations in S-II. The observations on the internal organization of S-II described above were based on this and other maps of S-II. Figure 5 illustrates summary maps from two other cases for comparison. The organization of these maps was much like that in the case illustrated in Figure 4, varying somewhat in the amount of cortical space allotted to a particular body part representation. When the proportions of S-II devoted to the head, trunk, forelimb, and hindlimb were calculated, not only for the three maps illustrated in this paper (Figs. 4, 5), but also for the three cases illustrated in the paper of Nelson et al. ('78), the head was found to occupy an average of 47% of S-II, the trunk 23%, the forelimb 14%, and the hindlimb 16%. These average values were very close to those obtained for four of the six individual cases. In the two remaining cases, the proportions varied with the head occupying as much as 64% or as little as 38% of S-II. Undoubtedly, this variability reflects difficulties in obtaining complete maps and accurate measures of proportions of body parts represented in S-II.

The physiologically defined S-II was coextensive with the myeloarchitectonically defined S-II region described above. Therefore, label could be assigned to S-II reliably on the basis of myeloarchitectonic criteria. In addition, because the general arrangement of body parts in S-II was consistent across cases, transported label found in different locations in S-II could be related to the representations of body parts with some accuracy.

The parietal ventral area, PV. A complete representation of the contralateral body surface was found within the architectonically distinct PV region. Recordings were obtained from over 100 penetrations in PV in five grey squirrels, and general physiological characteristics were determined. The receptive fields were on the contralateral body surface, although some receptive fields along the midline extended slightly onto the ipsilateral body surface. Receptive field sizes were generally similar to those found for neurons in S-II. However, several differences were detected. For example, receptive fields on the forepaw frequently were restricted to single digits or just the distal portions of all four digits for sites in PV (Figs. 6, 7), while such restricted fields were not found for sites in S-II. Unlike S-I and S-II neurons, neurons in PV periodically were activated by light stimulation of both the glabrous and hairy surfaces of the skin. The strongest responses were frequently obtained when the skin was lightly scratched rather than tapped, especially for the forepaw and hindpaw. Such enhanced responses to moving stimuli were unique to neurons in PV. Finally, the posterior portion of PV responded to low-threshold auditory stimulation such as clicks and tapping sounds. Again, this was a unique feature of PV.

Overall, PV formed an inverted representation of the body, with the digits of the forelimb and hindlimb directed medially, the trunk located ventrally, and the face congruent with the face representation of S-I at the upper lip, nose, and teeth representations. The representation of the

Fig. 2. Lightfield photomicrographs of sections cut in a plane parallel to the cortical surface illustrating subdivisions of the somatosensory cortex. In A, the heavily myelinated primary somatosensory area, S-I, is surrounded by less-well-myelinated motor cortex rostrally and by PM, S-II, and PV caudally. The lightly myelinated oval in the center of S-I is the unresponsive zone that serves as a reliable landmark. In more superficial sections, such as in A, S-II and PV are less well myelinated than S-I, and borders between the three fields are easily identified. The rostral border of S-II with S-I is not readily apparent in the deeper layers of the cortex shown in B. However, the caudal and lateral borders of S-II can be distinguished from surrounding regions of the cortex in these sections. PM = parietal medial area. For other abbreviations see Figure 1. In both A and B, rostral is right and medial is up.

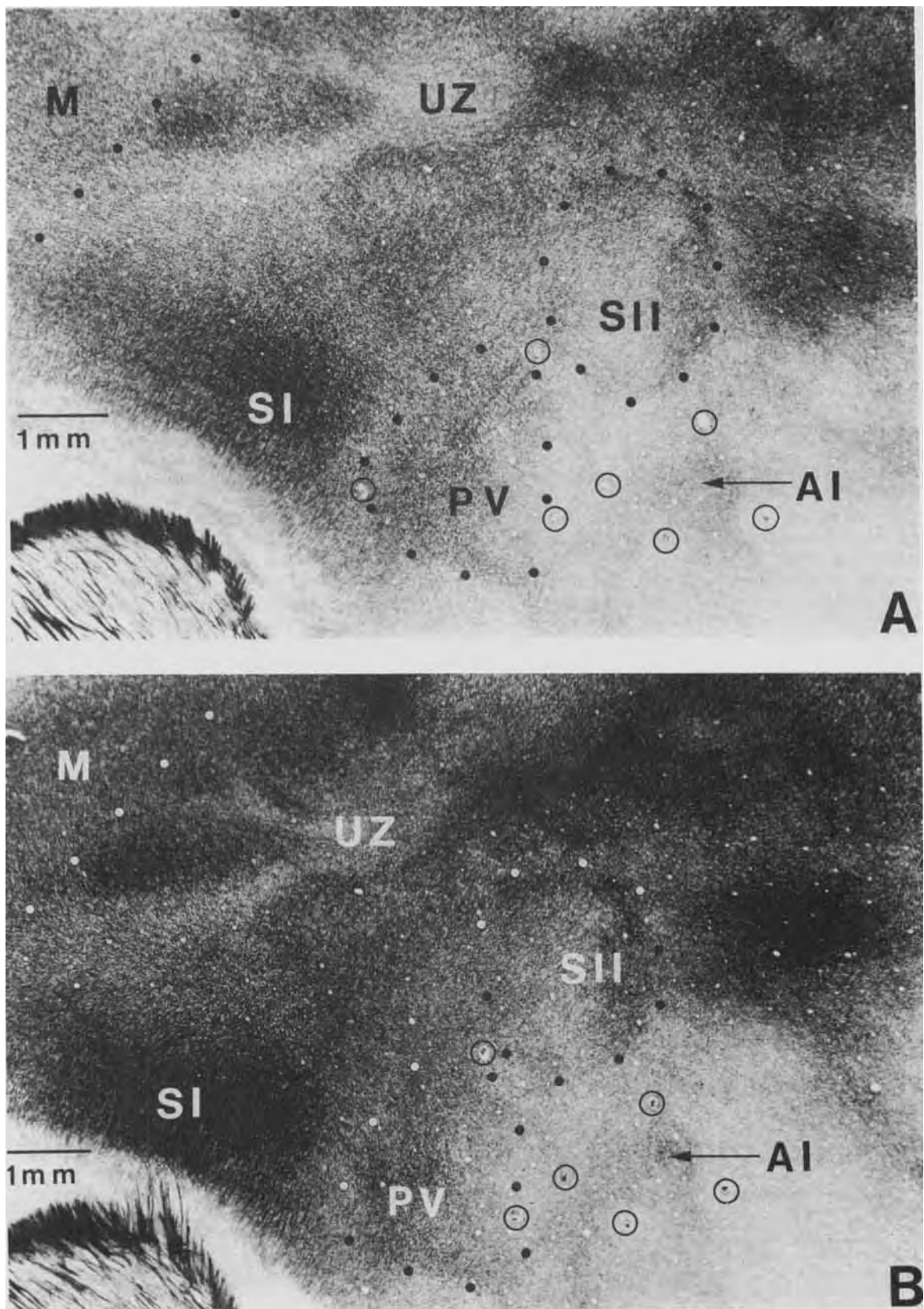


Fig. 3. Lightfield photomicrographs of sections cut in a plane parallel to the cortical surface illustrating the change in density of myelination in PV as one progresses from (A) middle to (B) deeper cortical layers. In these figures, the rostral border of PV is not as easily identified as in more

superficial cortical layers depicted in Figure 2. However, the caudal and lateral boundaries of PV are distinguishable. Microlesions (open circles) around PV and A-I allow physiologically determined subdivisions to be related to myeloarchitecture. For abbreviations see Figure 1.

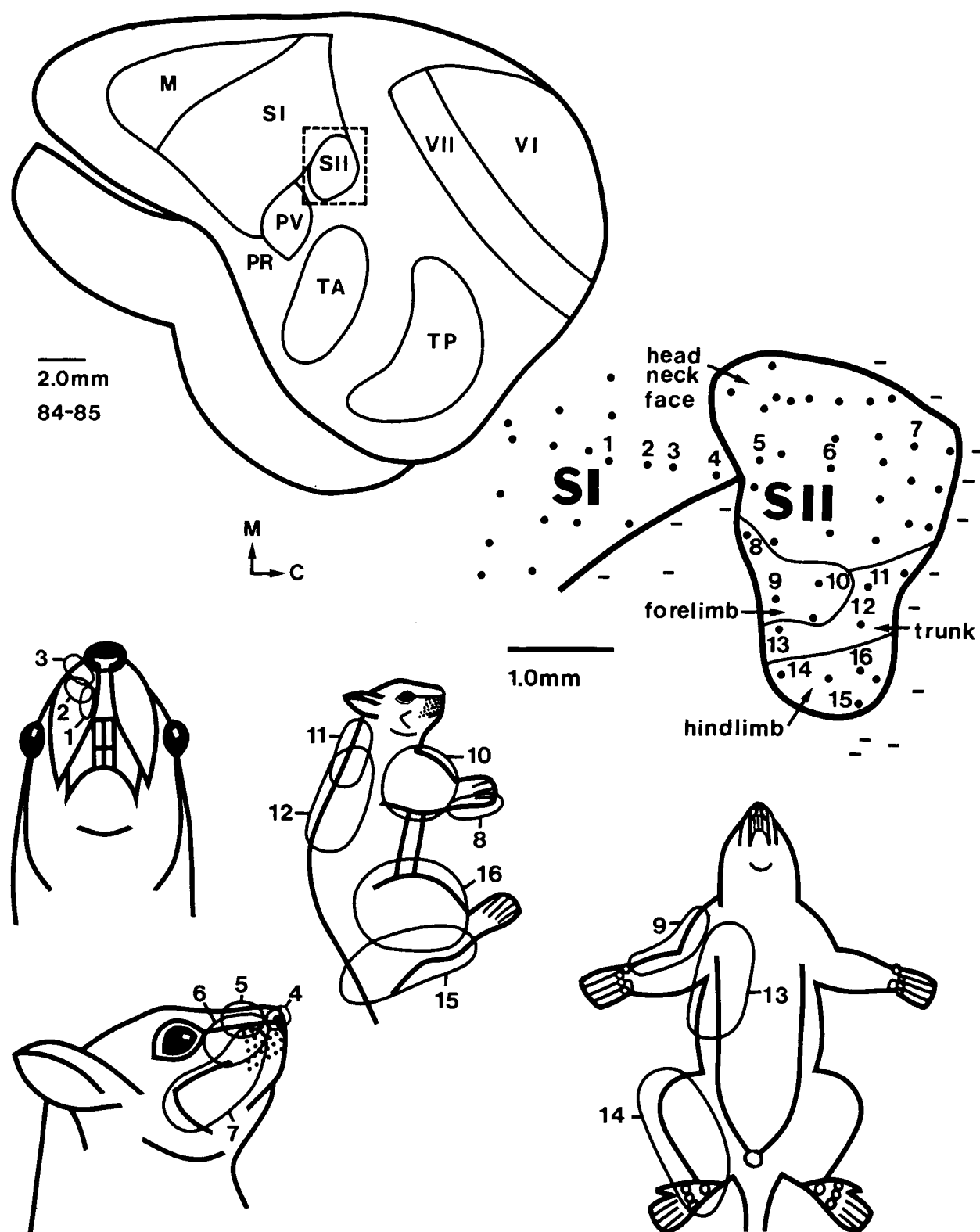


Fig. 4. Receptive fields for recording sites in S-I and S-II. Upper left: cortical areas on flattened cortex as revealed in myelin-stained sections. Solid lines mark architectonic subdivisions of the cortex. Dashed lines indicate the location of the recorded region of the cortex shown at greater magnification. Upper right: In this magnified view, dots indicate penetrations where neurons responded to light cutaneous stimulation. Hyphens indicate penetrations where neurons were unresponsive to cutaneous stim-

ulation. Below: Receptive fields for numbered electrode penetrations in S-I and S-II. Penetrations 1-7 progress across S-I/S-II border. Note the increase in receptive field size as well as the reversal in receptive field progression as the S-I/S-II border is crossed. Lines within S-II separate electrode penetrations with receptive fields on the head, neck, and face, on the forelimb, on the trunk, or on the hindlimb. PR = parietal rhinal area.

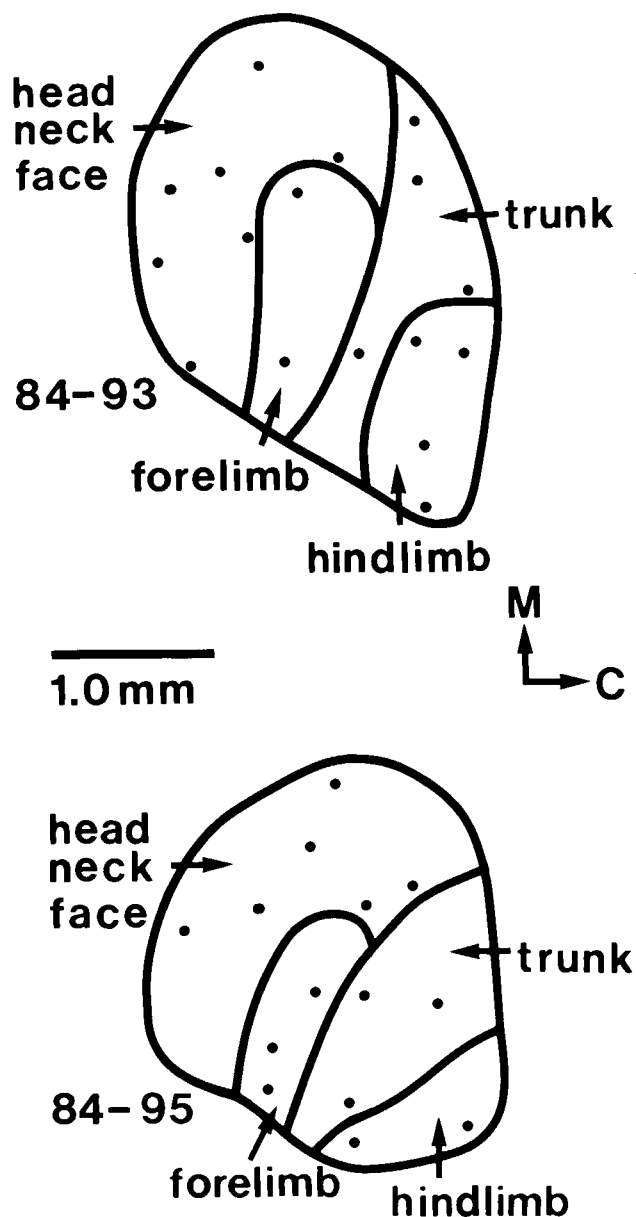


Fig. 5. The somatotopic organization of S-II as determined in two other mapping experiments. In each case, the architectonic border of S-II corresponds to the outer boundary of the field. Dots mark electrode penetrations. Electrode penetrations with neurons having receptive fields on the same general body region are indicated. Compare with Figure 4 and note the consistency in basic organization. Also see Nelson et al. ('79) for three additional maps. Because limbs "point" ventrally or rostroventrally, the orientation of the "homuncular" representation in S-II has been characterized as "erect" (see text).

forelimb extended mediolaterally in PV, so that mediolateral progressions of recording sites in the forelimb region produced receptive field sequences that moved from distal to proximal on the body (Fig. 6, penetrations 13-17; Fig. 7, penetrations 11-14). Selected progressions of recording sites from the rostral to the caudal in PV related to the receptive field sequences from the head to the hindlimb (Fig. 6, penetrations 4-8; Fig. 7, penetrations 6-10). Although similar

parts of the face were represented in both PV and S-I along the common border, with cells on either side of S-I/PV border responding to stimulation of the nose, upper lip, and teeth, the physiological boundary between the two fields was clearly discernable due to the dramatic increase in receptive field size with progressions of recording sites from S-I to PV. In most instances, there was also a clear reversal in the receptive field sequence with recording progressions across S-I/PV border (Fig. 6, penetrations 1-3, and Fig 7, penetrations a-g).

PV was found to be about 8-9 mm² in surface area (Fig. 8). About one half of PV appeared to be devoted to the face (45%, case 84-115; 55%, case 85-20). The upper face, vibrissae, and top of the head were represented most medially in PV. These representations were bounded mediocaudally by cortex that was unresponsive to somatosensory or auditory stimulation and were bordered rostrally by the representation of the nose in S-I. The cortex devoted to the nose in PV was immediately lateral to the head and upper face representations. Rostrally, the nose representation was adjacent to the nose representation in S-I, and caudally, it was adjacent to the forepaw representation in PV (Fig. 8). The upper lip representation was found immediately ventral to the nose representation in PV, where it was contiguous with the upper lip representation of S-I. Further caudally, recording sites were found in PV for which receptive fields on the upper lip expanded to include part or all of the lower lip. The cortex caudal to the representation of the lips was devoted to the chin. This cortex was bounded laterally by trunk and caudally by forelimb representations. The teeth were represented in the most ventral portion of the face sector of PV. In most instances, PV was bounded ventrally by cortex unresponsive to tactile or auditory stimulation.

The representation of the forelimb in PV was immediately caudal to the representation of the face. The forelimb occupied less than one third of PV (29%, case 84-115; 25%, case 85-20), and was represented from distal to proximal in a mediolateral sequence so that the digits pointed medially in the representation and the wrist and forearm were found more laterally (Figs. 6, 7). As illustrated in Figure 8, the hand and wrist formed most of the forelimb representation. The arm representation, just ventral to the hand and wrist representations, occupied a smaller portion of the cortex. Receptive field sizes in the forelimb varied. For example, receptive fields for the digits were typically small, containing one digit or all five digit tips only, whereas receptive field sizes for the wrist were somewhat larger, and those for the lower and upper arm were larger still. A receptive field for neurons in the arm representation sometimes included part of the upper trunk, the entire arm, and part of the hand (Fig. 6, penetration 17).

The trunk was represented in the most ventral tenth of PV (12% in case 84-115; 8% in case 85-20). The trunk adjoined the face representation at the chin and the forelimb representation at the upper arm. For rostrocaudal rows of microelectrode penetrations, the corresponding receptive fields progressed from the upper trunk to the lower trunk (Figs. 6, 7). Because the trunk representation occupied a small amount of the cortex, few penetrations were placed in this part of PV. The receptive field sizes for neurons in the trunk representation were the largest observed in PV. These receptive fields often encompassed an entire upper or lower ventral trunk region and included parts of the limbs (Figs. 6, 7). The trunk representation was bounded ventrally by a region weakly responsive to moderately in-

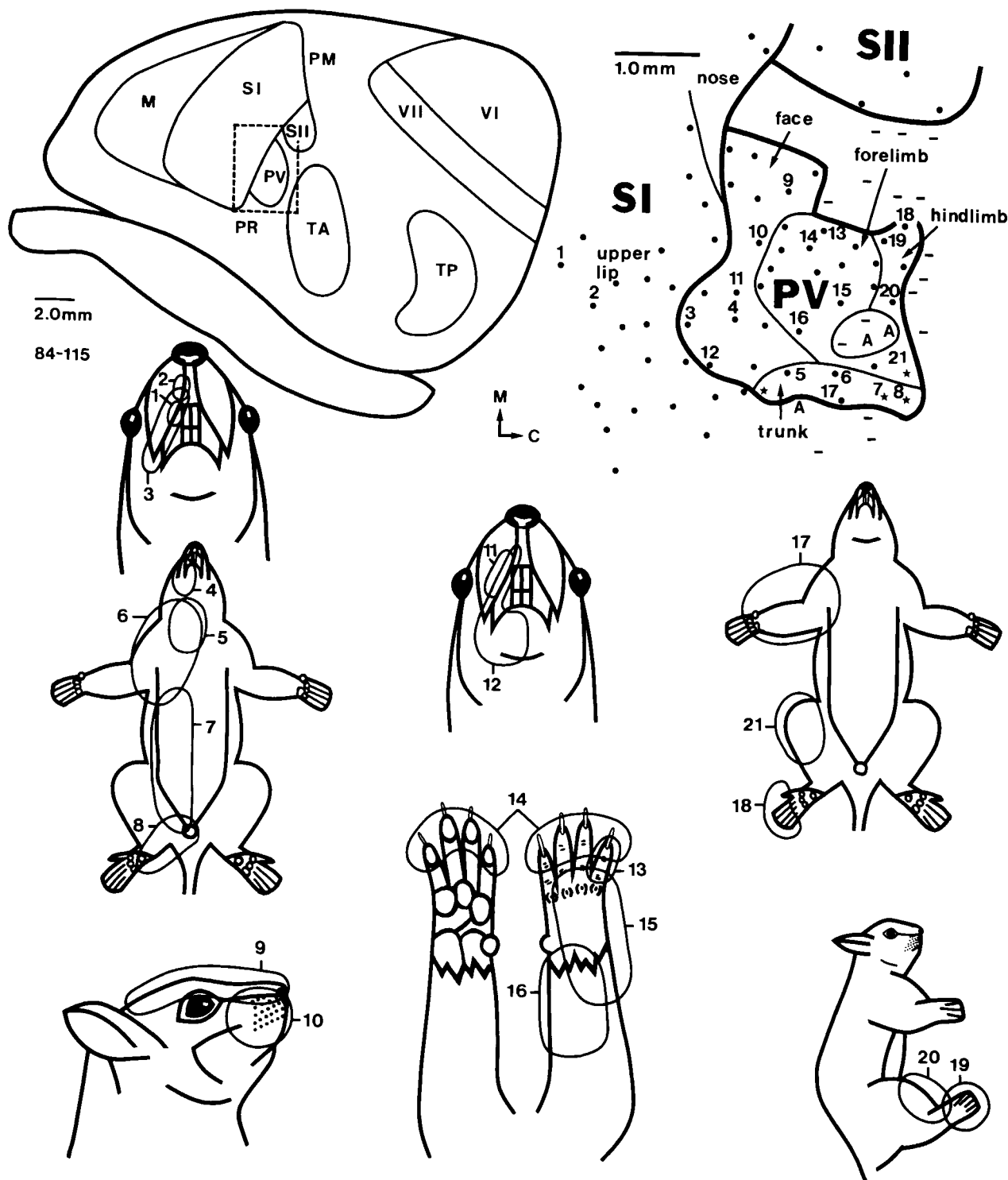


Fig. 6. The somatotopic organization of the parietal ventral area, PV. Upper left: a section from the flattened brain with architectonic borders. The dashed box marks the region of the cortex enlarged on the upper right. Within the enlarged view, dots mark electrode penetrations where neurons responded to light cutaneous stimulation. Stars indicate penetration where neurons responded to both light cutaneous and auditory stimulation, while the letter A denotes a penetration where only auditory responses were detected. Hyphens mark penetrations where neurons were unresponsive to cutaneous or auditory stimulation. Receptive fields on the squirrel bodies below are numbered to correspond to numbered penetrations on the brain

on the upper right. Receptive field 14 was on both dorsal (hairy) and ventral (glabrous) aspects of the forepaw. Note that the receptive fields for neurons in PV are larger than those for neurons in the S-I. Also, distal limbs are represented dorsally and proximal limbs ventrally in PV, so the orientation of the "homuncular" representation can be characterized as "inverted" (see text). In this and other figures, receptive fields extending past the outlines of the body surface indicate that the receptive field continues onto skin not seen in the view drawn (e.g., 6, 9, 10) or includes discontinuous skin surfaces (e.g., 14). Abbreviations as in previous figures.

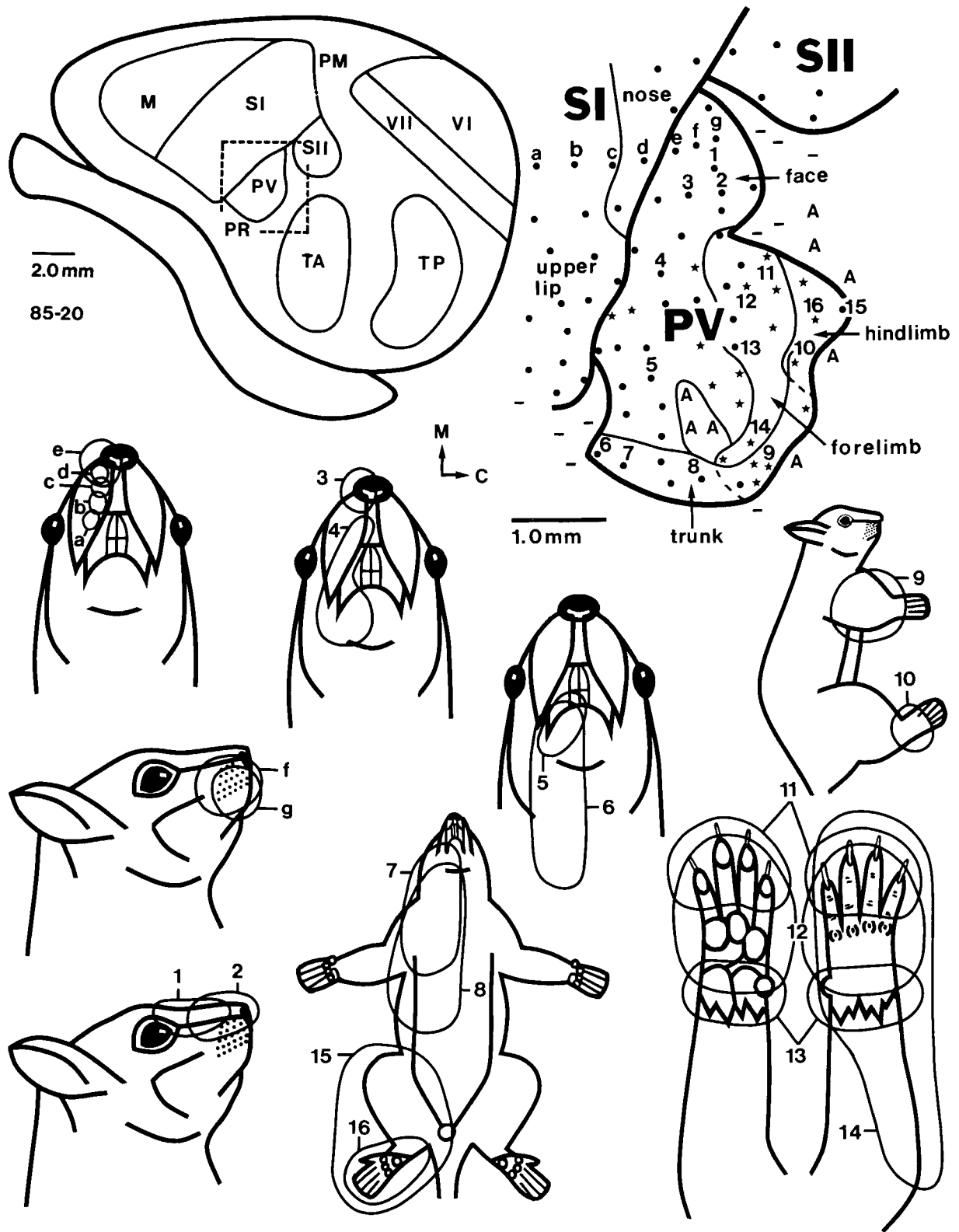


Fig. 7. The organization of the parietal ventral area, PV, in another case. Compare with Figure 6. Note the increase in receptive field sizes and the caudalward reversal of the receptive field progressions as recording sites progressed from S-I to PV (see receptive fields for sites a-g). Conventions as in Figure 6.

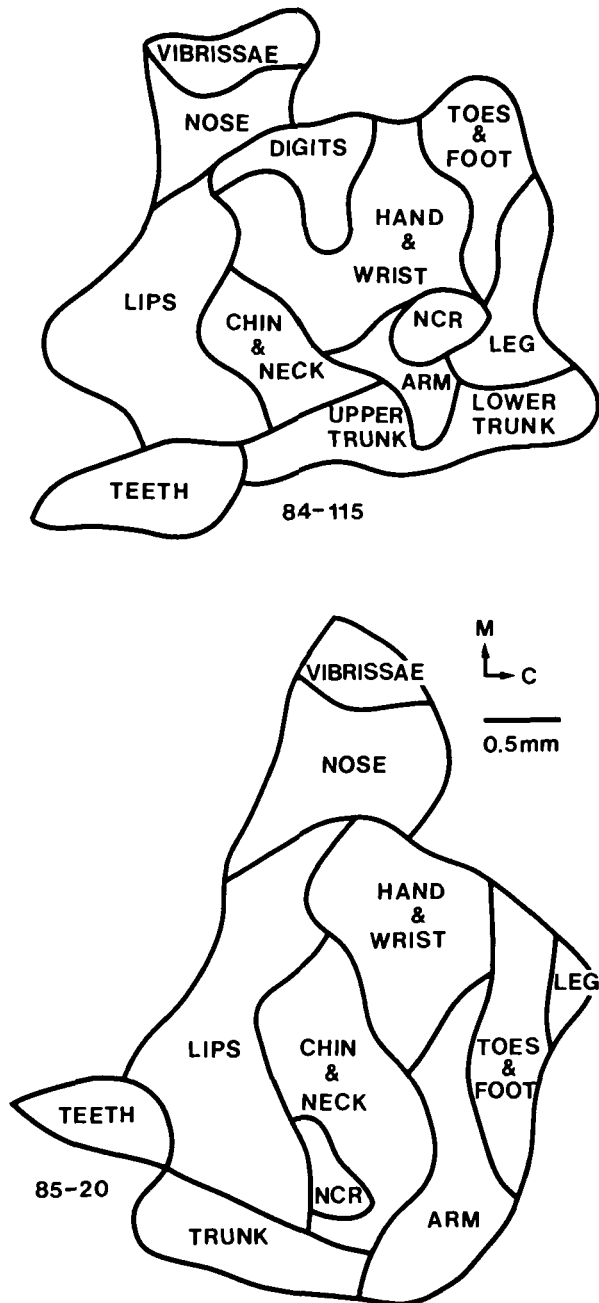


Fig. 8. Details of the somatotopic organizations of PV in the experiments illustrated in Figures 6 and 7. Lines in PV segregate groups of electrode penetrations whose neurons have receptive fields on the same designated body part. In each map, a region of three or four penetrations was found where neurons had no cutaneous response (NCR). Although the two maps differ in detail, the overall organization is that of an inverted "homunculus" with the digits and toes directed medially and the trunk located ventrally.

tense auditory stimulation and dorsally by the hindlimb representation.

The representation of the hindlimb, slightly over one tenth of the total area of PV (14%, case 84-115; 11%, case 85-20), was immediately caudal to the representation of the forelimb and adjoined the lower trunk/genital representa-

tion laterally. Like the representation of the digits of the forepaw, those of the hindpaw were directed medially. The distal hindlimb was represented medially, and the proximal hindlimb was represented laterally. The hindlimb representation was bounded caudally by the cortex that was responsive to low-threshold auditory stimulation (Fig. 9).

Auditory responses in PV. In addition to the neuronal responses to somatic stimuli in PV, responses to auditory stimuli were observed in certain parts of PV as well (see starred penetrations in Figs. 6, 7, 9). Neurons in PV responded to clicks and sounds produced by tapping objects together. However, these neurons were not highly activated by pure tones, and best frequencies were not determined. The extent of the cortex responsive to both somatosensory and auditory stimulation varied from case to case. For instance, case 85-20 (Fig. 6) had 19 electrode penetrations in which both auditory and somatosensory responses were recorded. In this case, the entire hindlimb representation, half of the trunk and forelimb representations, and part of the face representation were responsive to both somatosensory and auditory stimulation. Case 84-115 (Fig. 6), on the other hand, had only three somatosensory/auditory penetrations, one in the hindlimb and two in the trunk.

While responses to auditory and somatosensory stimuli were recorded in the same penetrations, the best responses to either somatosensory or auditory stimuli were obtained from different cortical depths. The best somatosensory responses were from depths of 500–700 μm , while the best auditory responses were from 900–1,200 μm from the pial surface. Recordings were obtained from neuron groups that were activated by both auditory and somatosensory stimuli, but it was not certain that individual neurons responded to both stimuli.

Cortex lateral and caudal to PV was responsive to auditory but not to somatosensory stimuli (Fig. 9). The region that was responsive to auditory stimuli included A-I and the parietal rhinal area (PR). A-I is easily identified by a characteristic tonotopic organization and neurons selective for best frequencies (Merzenich et al., '76; Luethke et al., '85), as well as by dense myelination (Fig. 3B). The PR (parietal rhinal) region includes the rostral auditory area (Merzenich et al., '76), which represents frequencies in a reverse pattern from that in A-I, and adjoining auditory cortex. We found that neurons in the PR region rapidly habituated to repeated auditory stimuli.

Cortical connections of S-I

Injections of WGA-HRP were placed in different parts of the primary somatosensory cortex in four grey squirrels. In two cases a single injection was placed just lateral to the unresponsive zone (UZ) in the representation of the upper lip and part of the lower lip (not shown). In another case, a single injection was placed in the upper lip/nose representation (Fig. 11). The dense injection core (about 1.0 mm wide) also included the lateral margin of UZ and some of the representation of the vibrissae. In the final case, three small injections were placed in a mediolateral row in part of S-I just medial to UZ. This cortex was devoted to the shoulder and forearm representations (Fig. 12A). In all cases the injection was completely confined to S-I.

All four cases demonstrated a local pattern of intrinsic connections within S-I. The intrinsic pattern was most extensive in case 84-50 where the injection core included the lateral margin of UZ (Fig. 10A). In this case, labeled cells

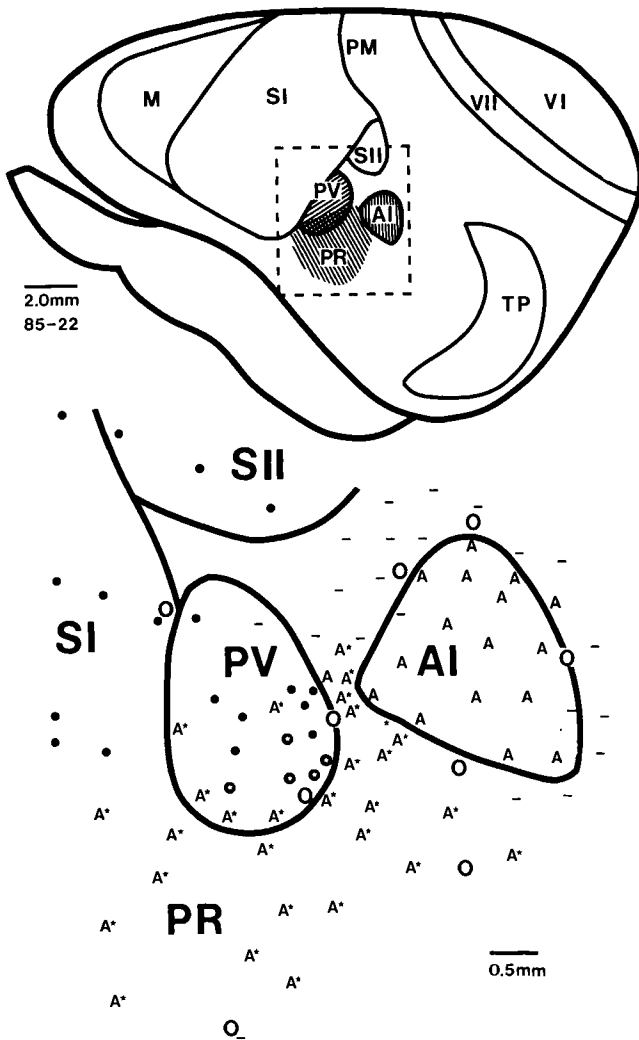


Fig. 9. The physiological response properties of neurons in PV and surrounding regions of the cortex. Above: architectonic subdivisions of cortex on a section parallel to the surface of the flattened cortex. Somatic and auditory areas of interest are located, and the region of auditory and somatosensory overlap is crosshatched. Below: an enlarged view of the region enclosed by a dashed box above. Solid lines indicate architectonic borders. A's mark electrode penetrations in primary auditory cortex where neurons responded consistently to repeated clicks and tones. A*'s mark sites outside of A-I where responses to repeated auditory stimuli habituated. Dots mark somatosensory sites, while circles filled with stars indicate penetrations where neurons were activated by both auditory and light tactile stimuli. Hyphens are sites that were unresponsive to somatosensory or auditory stimuli, while O's are sites marked by electrolytic lesions. Note the good correspondence between physiological and architectonic borders (within 200 μ m). Other conventions as in previous figures.

and terminals surrounded the injection core and filled UZ. In addition, a rostral extension of intrinsic label was located along the lateral margin of the hand representation in lightly myelinated cortex extending from UZ. Other smaller foci of intrinsic label were in the medial cortex devoted to the forearm and forepaw representations. Both diffuse label suggesting anterograde transport and labeled cells indicating retrograde transport were found lateral to the injection site in the cortex devoted to the lips. The two cases with the

injection in the representation of the upper and lower lips (not shown) also had a zone of intrinsic label around the dense injection core. Some of this adjoining label extended laterally toward the representation of the oral cavity, rostrally into the cortex representing the lower lip, and medially into UZ. A rostral locus of label was in the less myelinated cortex along the lateral margin of the representation of the forepaw. The case with injections medial to UZ (Fig. 12) had intrinsic connections around the injection sites, several small foci of label rostral to the injection sites in parts of S-I devoted to the arm, trunk, and leg, and a focus extending rostrally along the lateral margin of the forepaw representation. In this case, very little intrinsic label was found in UZ. Taken together, these four cases indicate that intrinsic connections are likely to be distributed in a fairly uniform manner along the margins of the injection sites, in several separate small foci in the cortex devoted to related body parts (other parts of the face for face injections, other parts of the body for body injections), and somewhat densely in UZ and the less myelinated cortical strips that extend from UZ (Fig. 1). However, it is important to note that the lateral injections in the representation of the face, but not the medial injections in the representation of the forelimb, resulted in label in UZ. Thus, it appears that some body parts in S-I are interconnected with UZ while others may only relate to the smaller, lightly myelinated zones, jutting out from UZ.

Cases with S-I injections also demonstrated reciprocal patterns of ipsilateral and contralateral cortical connections with other fields. The ipsilateral connections were with S-II, PV, PM, PR, and motor cortex (Figs. 10, 12). In addition, the locations of the foci of label varied within these fields in a manner suggesting that most connections are somatotopically matched. In cases 84-50 (Figs. 10, 11) and 84-99 (not shown) injections in lateral S-I devoted to the face labeled parts of PV and S-II that adjoin S-I and that also represent the face. Other label was in the lateral motor cortex where electrical stimulation evokes face movements (unpublished experiments). Within the parietal medial strip of the cortex (PM) immediately caudal to S-I, reciprocal connections were lateral, just medial to S-II, suggesting that the face is represented in lateral PM. The injections in medial S-I, where the forelimb is represented, produced label in caudolateral parts of S-II and caudomedial parts of PV known to represent the limbs. In addition, anterograde and retrograde label was found in the medial part of the motor cortex where limb and trunk movements are evoked and in a more medial part of PM. Thus, the connection patterns of S-I with M, S-II, and PV, where the somatotopic patterns of representations are known, were at least roughly homotopic. In contrast, foci in PR did not vary much according to the placement of the injection in S-I, and no somatotopic pattern was evident.

Of the ipsilateral targets of S-I, the connections to PV appeared to be slightly more dense than those of S-II, PR, and motor cortex, while connections to PM were less dense. Foci of connections were distributed over large portions of motor cortex, and they varied in density. Foci in PV and S-II were smaller, but they occupied proportionately equivalent amounts of these representations.

Callosal connections were with parts of S-I representing body parts equivalent to that of the injection site (Figs. 10B, and 12B). Thus, the lateral cortex representing one side of the face projected to the cortex representing the other side of the face in the opposite S-I, and the medial cortex repre-

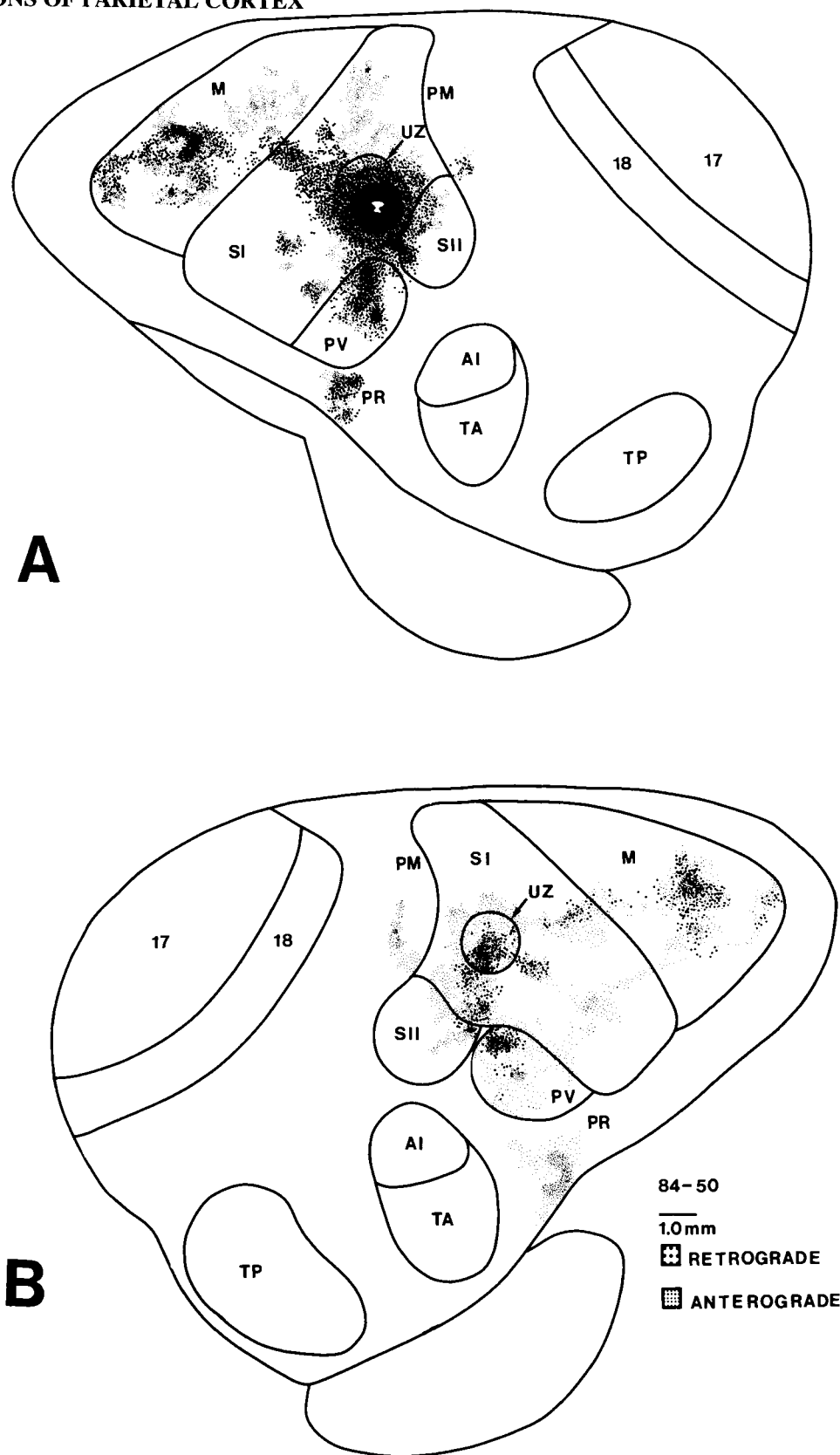


Fig. 10. Cortical connections of S-I. An injection of WGA-HRP (black circle) was placed in the representation of the upper lip. The injection core extended slightly into the UZ. Drawings include label from several sections imposed on single brain sections from the injected (A) and contralateral (B)

hemispheres. Retrogradely labeled cell bodies and presumptive anterograde label are indicated by coarse and fine dots, respectively. Other abbreviations are as in previous figures.

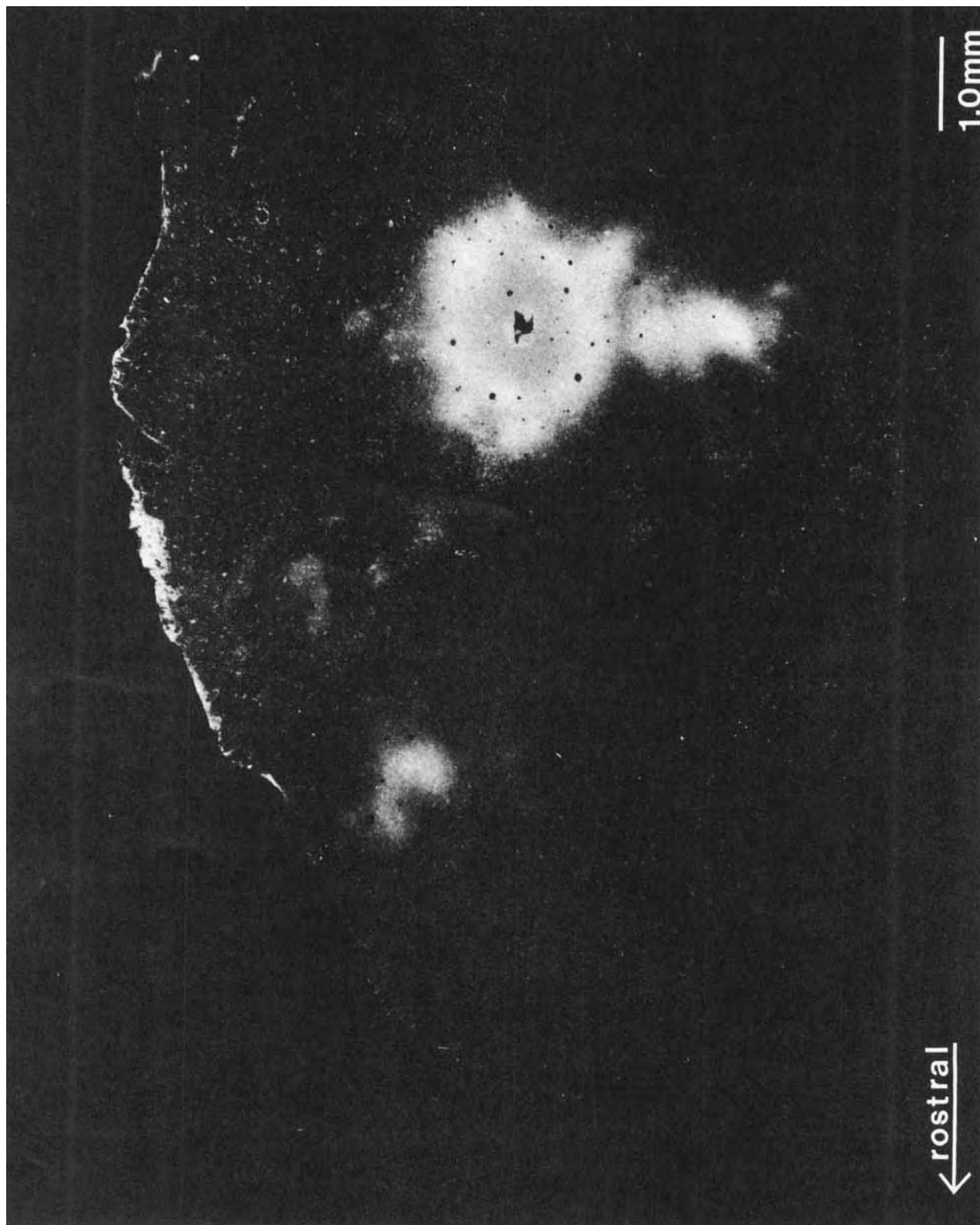


Figure 11

senting the forelimb projected to the medial cortex devoted to the other forelimb. The three medial injections produced only two light foci in the contralateral S-I (Fig. 12B). This is in agreement with previous evidence that callosal connections of the forelimb in S-I are light and unevenly distributed (Gould and Kaas, '81). The injection that involved the lateral margin of UZ produced dense label in the contralateral UZ as well as in PV, PR, S-II, and PM, and motor cortex. The more extensive pattern of callosal connections involving areas in addition to S-I was not seen in the other three cases where the injection did not include part of UZ. Thus, UZ may be a specialized part of S-I with more extensive callosal connections.

Cortical connections of S-II

Two grey squirrels were used to determine the cortical connections of the second somatosensory area, S-II. One injection was placed in the shoulder/neck representation of S-II (not shown), while the other was centered on the forelimb and included parts of the face and trunk representations in S-II (Fig. 13A). Although both injections were restricted to S-II, the injections filled much of the area so that the full extent of local connections within S-II was not determined. However, the spread of intrinsic label immediately around the injection site was apparent in each of the two cases.

In addition to the intrinsic connections, the results revealed reciprocal connections of S-II with other somatosensory areas. Despite the proportionately large injection sites, there was evidence from these cases that connections are somatotopic. In both cases, dense anterograde label was found in more superficial sections, suggesting feedback from S-II to S-I. Reciprocal connections were observed in both cases with representations in S-I that corresponded to those injected in S-II. For example, the single injection in Figure 13A was concentrated in the forelimb, trunk, and face representations in S-II, and the labeled regions in S-I related to the same body parts. The most medial patch of labeled cell bodies and terminals in S-I (Fig. 13A) corresponded to the trunk representation. Cortex in S-I devoted to the forelimb, lateral to the cortex devoted to the trunk, also contained a rather dense collection of labeled cells and terminals. Finally, the cortex in S-I representing face regions adjacent to the face representations in S-II was labeled both anterogradely and retrogradely. In the case where the injection was centered on the shoulder and neck portion of S-II, label was found in the shoulder and neck portions of S-I.

Connections with PV also appeared to be somatotopically matched. In Figure 13A, the rostromedial patch of label in PV corresponds to the upper face representation, the patch of label caudal to this corresponds to the hand representation, and the most lateral focus of label is in the expected

location of the trunk representation. The interconnections of S-II and PM were in agreement with the hypothesis that the face is represented laterally and the body medially in PM. Thus, the most medial part of PM was not labeled, while intermediate and lateral levels were labeled after the face, forelimb, and trunk injections in S-II (Fig. 13A). Finally, in both cases of S-II injections, label was found in the band of cortex encircling S-II caudolaterally. In case 84-95, some additional label was located rostral to S-I on the medial wall just medial to motor cortex. Label was also found in PR. In both cases, the most dense ipsilateral connections of S-II were with S-I. However, these connections were only slightly more dense than those with PV, PR, or PM.

In both cases with an S-II injection, dense label was observed in the portion of S-II of the contralateral hemisphere that closely matched the dense injection core in location. Thus, the representation of a particular body part in S-II in one hemisphere appears to be reciprocally connected to the representation of the same body part in the contralateral hemisphere (Fig. 13B). The callosal connections in the S-II formed several clumps or patches. The only other contralateral connections observed were with the area of the cortex encircling S-II, and these were seen in only one (not shown) of the two cases. Like the ipsilateral cortical connections with this S-II bordering region, labeled cell bodies and terminals formed small patches.

Cortical connections of PV

Injections of WGA-HRP were confined to PV in three cases. These cases demonstrated local intrinsic connections and reciprocal ipsilateral connections with S-II, S-I, PM, motor cortex, PR, the cortex just dorsal to the rhinal fissure, and possibly subdivisions of the auditory cortex. Callosal connections were with PV and adjoining regions of the cortex. As for S-II, the injections were large relative to the size of PV, but there was some evidence that most connections were somatotopically matched.

Considering both distribution and density, the major interconnections of PV were with S-I (Figs. 14A, 15A, 16A). The anterograde label was most apparent in superficial sections, suggesting a "feedback" pathway (see Maunsell and Van Essen, '83). After a large injection that included portions of the face, forelimb, and hindlimb representation in PV, label was scattered over similar representations in S-I (Figs. 14A, 15A). The label in S-I partly included UZ. Other locations of label were in a broad band just medial to UZ where the forelimb is represented, and more medially where the foot and hindlimb are represented. The gap in the label in medial S-I may correspond to the trunk representation, which was probably outside the dense injection core in PV. Additional foci of label were in caudolateral S-I that is devoted to the upper lip and face, while rostromedial S-I, devoted to the lower lip and jaw, was relatively free of label. A more restricted injection in PV, centered in the portion representing the forelimb, resulted in label largely confined to the portion of S-I representing the forelimb and the medial part of UZ (Fig. 16A). A third case with an injection in the forelimb portion of PV produced similar results.

Other major connections were between PV and the motor cortex, M. The two cases with injections in the forelimb region of PV resulted in concentrations of labeled cells and terminals in the medial portion of M where the forelimb is represented, while the large injection in PV produced

Fig. 11. A darkfield photomicrograph of an injection site in S-I and transported label in a section from the flattened cortex reacted for HRP, case 84-50 (see Fig. 10). The dark center of the bright circle is the damage resulting from the injection pipette. The central gray circle is the dense label of the injection, while the white fringe around the gray indicates local transport of the label. Patches of white immediately medial and rostral to the injection site consist of labeled cell bodies and axons in other parts of S-I. The large puff of white label immediately ventral to the injection site is in PV. The dense white patch of label in the rostral pole of the cortex is in the motor cortex. Compare with Figure 10.

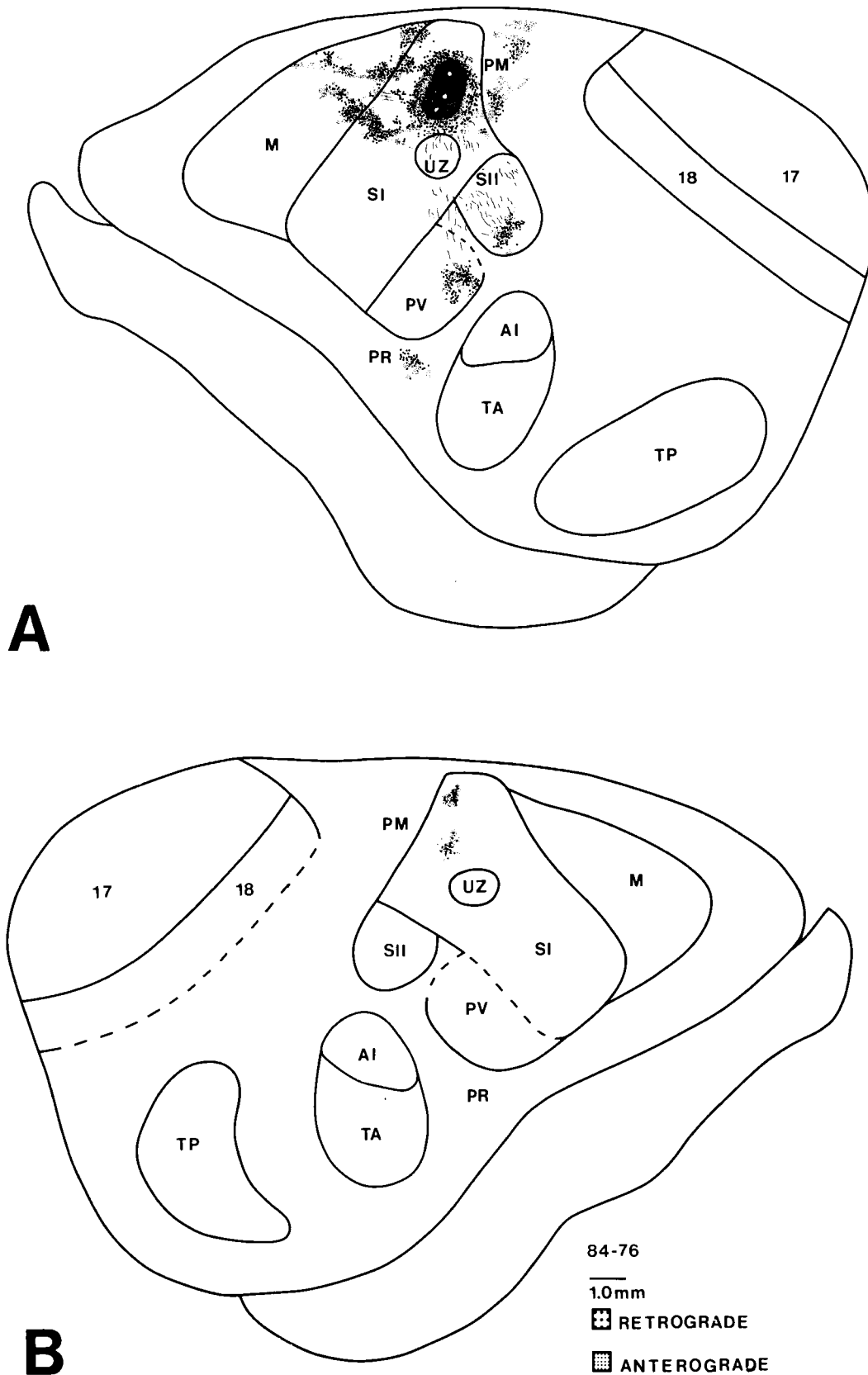


Fig. 12. Ipsilateral (above) and contralateral (below) cortical connections of S-I. Three restricted injections of WGA-HRP were placed in the forelimb representation in the S-I. Solid lines indicate architectonic borders while dashed lines mark uncertain borders estimated by position. Short, irregular

lines are labeled axons. Compare with Figure 10 and note the sparseness of callosal connections when UZ is not involved in the injection site. Other conventions as in Figure 10.

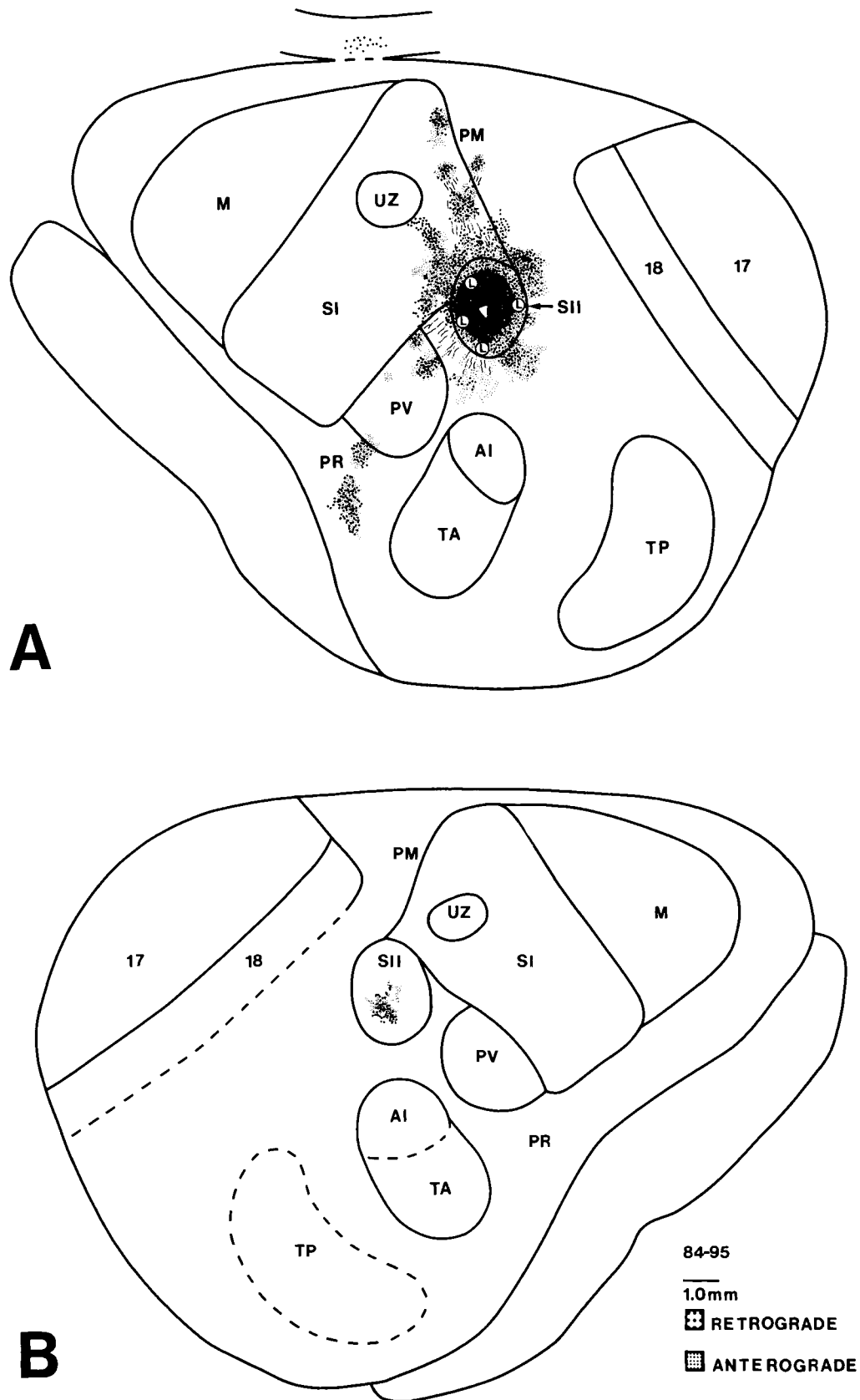


Fig. 13. Ipsilateral (above) and contralateral (below) cortical connections of S-II. An injection of WGA-HRP into the forelimb and face representation. Open circles with L's mark lesions placed just within the physiological limits of S-II. Solid lines indicate architectonic boundaries. Conventions as in previous figures. See Figure 5 for the somatotopic map of S-II for this case.

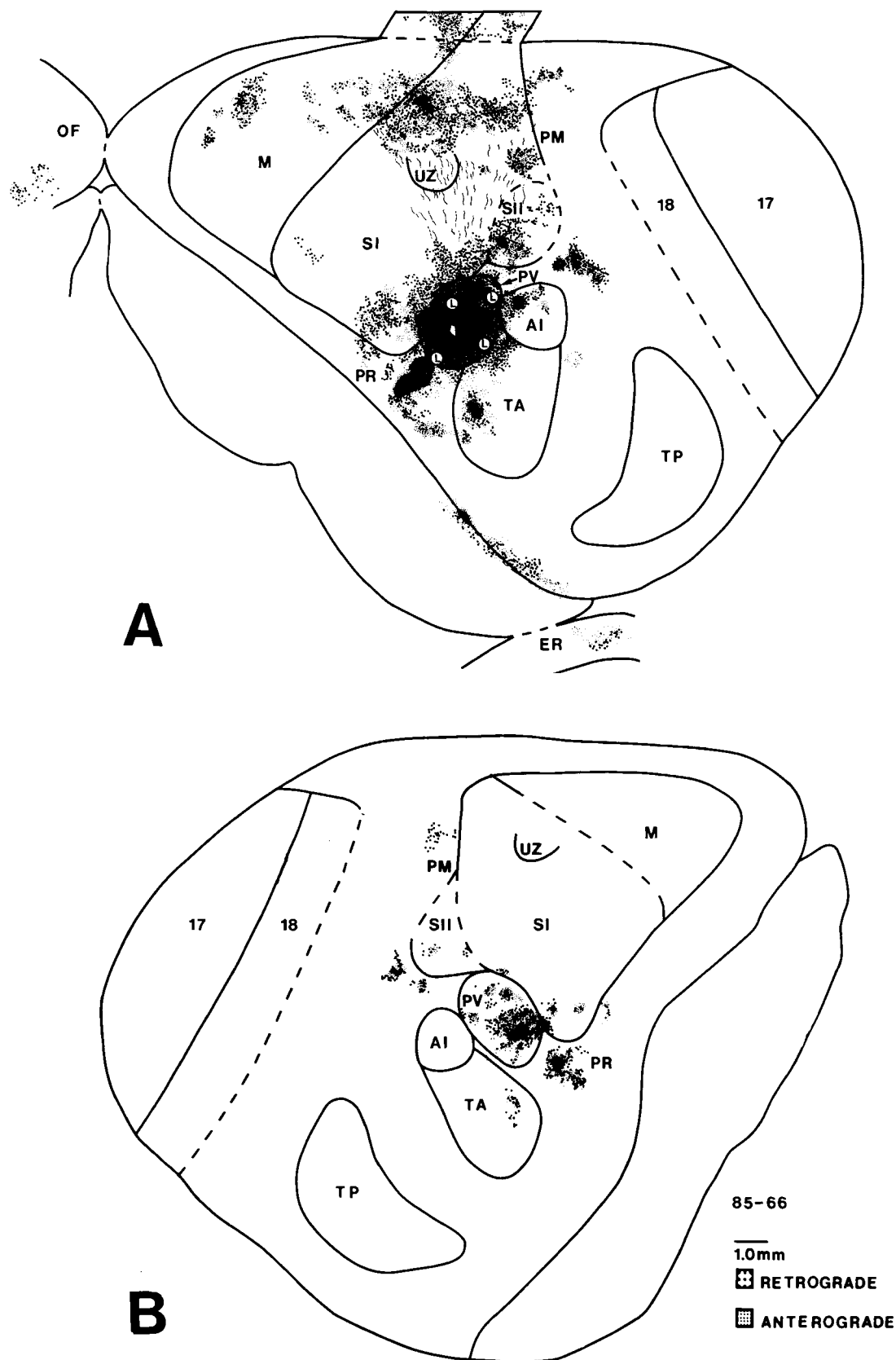


Fig. 14. Ipsilateral (above) and contralateral (below) connections of PV. An injection was placed in the representation of the face and forelimb. Microlesions (circles with L's) were used to mark the physiological borders of PV; ER = entorhinal cortex; OF = the orbitofrontal cortex. Other conventions as in previous figures.

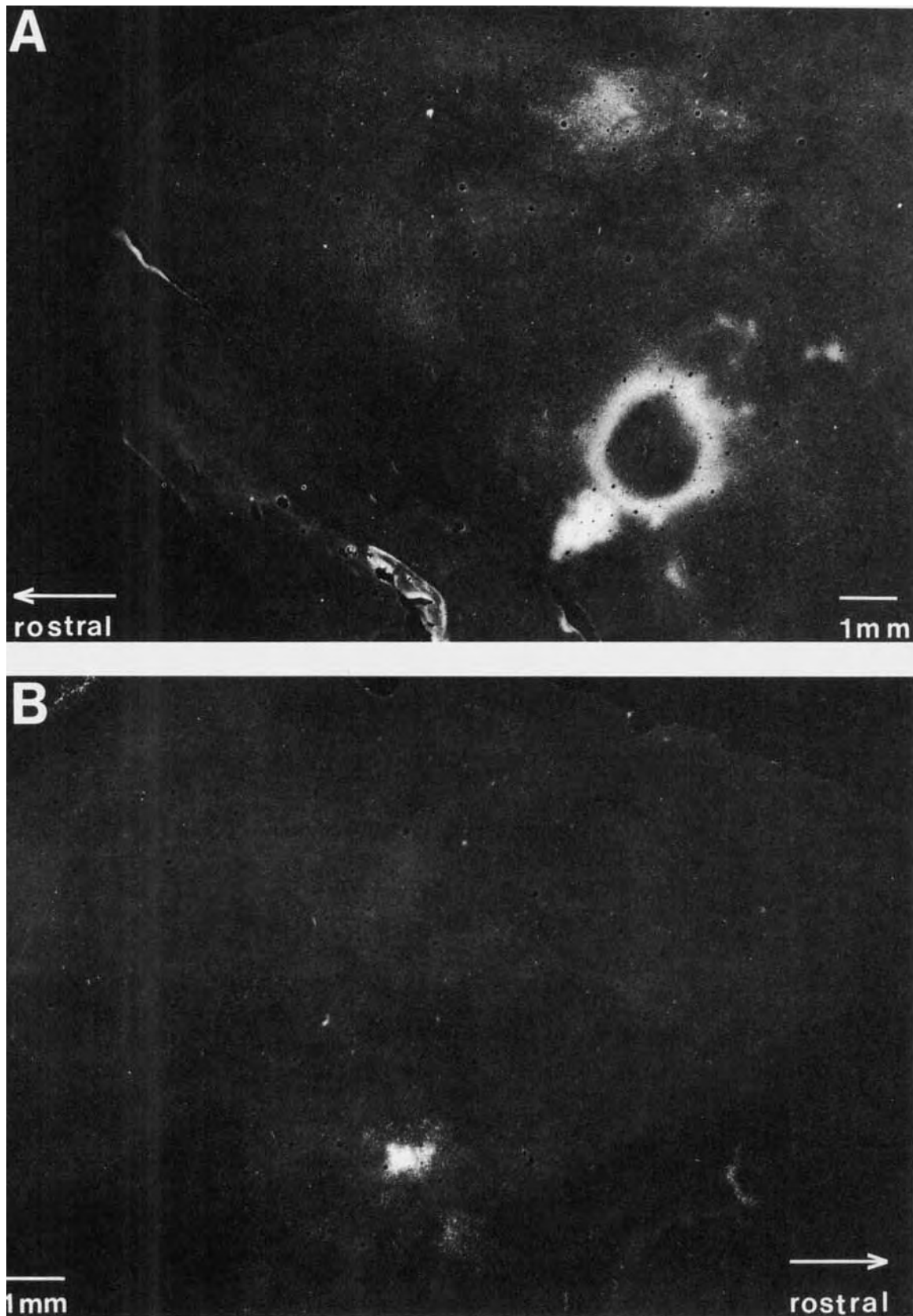


Fig. 15. Darkfield photomicrographs of brain sections reacted for HRP after WGA-HRP injection in PV (case 85-66, compare with Fig. 14). A. The right cerebral hemisphere with the injection site (dark core with white halo). Note the dense white label ventral to the injection site in PR. B. The left cerebral hemisphere. The dense label is in PV while less dense label is in the PR. Abbreviations as in previous figures.

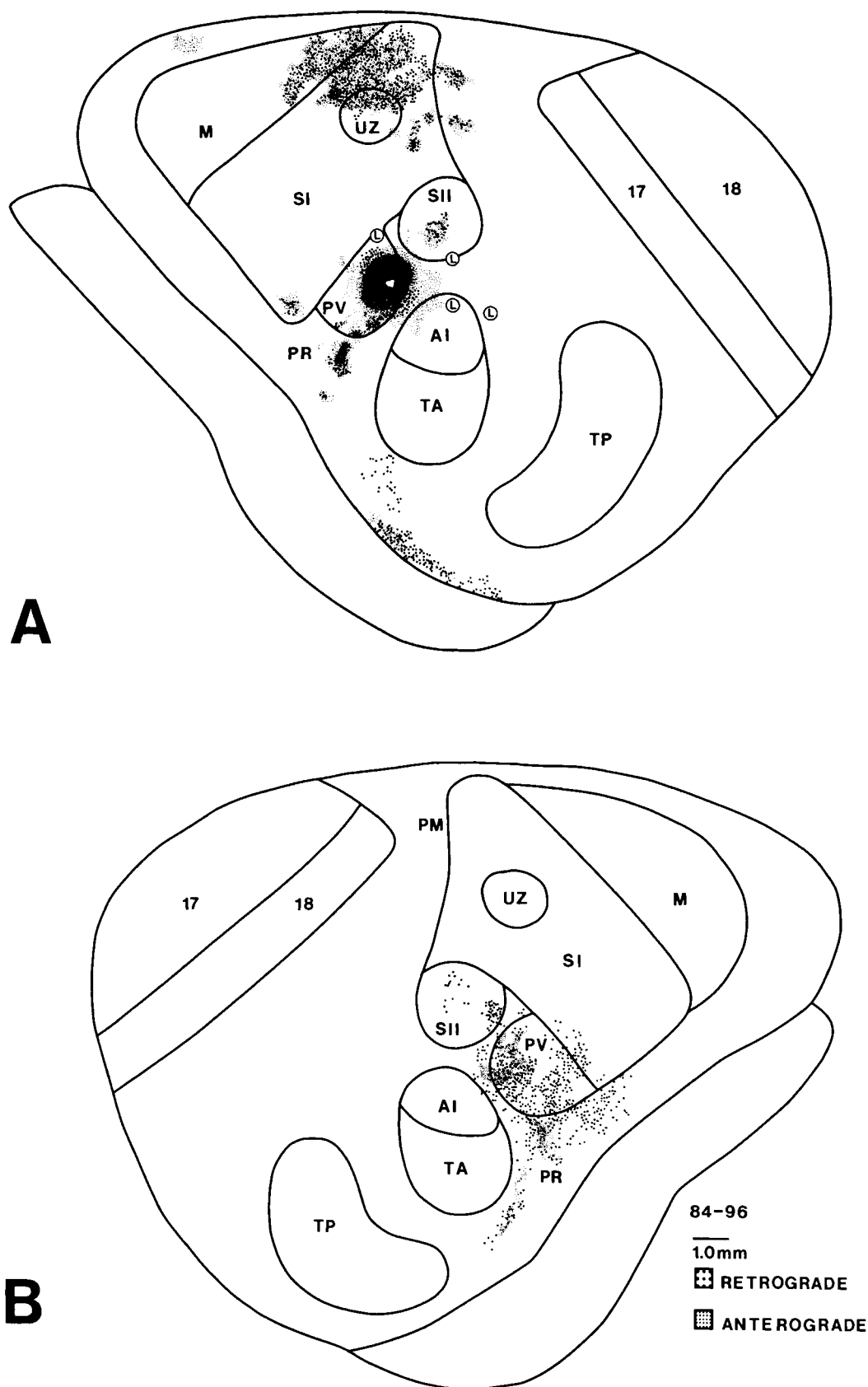


Fig. 16. Ipsilateral (above) and contralateral (below) connections of PV. An injection was placed in the forelimb representation. Conventions as in previous figures.

clumps of label scattered over more of M. Similarly, the more restricted forelimb injections in PV resulted in more restricted label in S-II in a centered location (Fig. 16A) that closely matches the expected location of the forelimb representation (Fig. 5). The restricted PV injections produced label in middle mediolateral levels of PM, consistent with the proposed somatotopic organization of PM. Surprisingly, the large injection in PV resulted in relatively little label in PM. However, a dense focus of label just caudal to S-II raises the possibility that PM extends laterally to the caudal margin of S-II, where parts of the head may be represented in PM.

Very dense concentrations of label were found just lateral to PV in part of PR. There was no evidence of a topographic pattern, and the concentration of label in only part of PR suggests that the field is functionally heterogeneous. The two restricted PV injections produced zones of superficial anterograde label that extended caudally to include rostral A-I. The larger PV injection resulted in both labeled cells and fine, scattered label in A-I. In addition, label was apparent in several locations in TA (Fig. 16A).

In two of the three cases of PV injections (Figs. 14A, 16A), label was also found in a band along the rhinal fissure. The orbitofrontal cortex (OF) and the entorhinal cortex (ER) were sparsely labeled in one case (Fig. 14A), and sparse scattered label was inconsistently observed in several other locations across the three cases.

The callosal connections of PV (Figs. 14B, 15B, 16B) were more extensive than those observed for S-I or S-II. Label was scattered over much of the contralateral PV, but there was a clear suggestion that it was most concentrated in the part of the contralateral PV that matched the injection site. Dense callosal connections were also noted in the portion of PR that roughly matched the portion with the dense ipsilateral connections. Two of the three cases had sparse scattered label in S-II (Figs. 14B, 16B). In case 85-66 with the large injection, callosal label was also apparent in PM and the cortex caudal to S-II (Fig. 14B).

In addition to these results, the present study provided information on the subcortical connections of the somatosensory cortex. These results will be described in a subsequent paper (Krubitzer and Kaas, in preparation).

DISCUSSION

In the present study, electrophysiological and anatomical procedures were combined in the same animals to reveal subdivisions, somatotopic patterns, and processing sequences in somatosensory cortex of squirrels. The most important discovery was of a previously unknown somatosensory cortical representation that we termed by location the parietal ventral area (PV). Thus, squirrels, and perhaps other rodents and other mammals, have at least three systematic representations of the body surface in the parietal cortex: the primary somatosensory cortex (S-I), secondary somatosensory cortex (S-II), and PV. Furthermore, similarities in the S-II and PV in relative size, responsiveness to somatosensory stimuli, connections, and position along the caudal border of S-I suggest that if both fields exist in other mammals, they could have been confused in individual experiments. An unusual feature of PV is that it also contains neurons that respond to auditory stimuli. Finally, connections of S-I, S-II, and PV identify two other regions of parietal cortex with dense somatosensory inputs: the parietal medial area (PM), which is medial to S-II, and the parietal rhinal area (PR), which is ventral to PV. Thus, at least five interconnected cortical fields in squirrels may be

predominantly somatosensory in function. These results and conclusions are discussed further below.

The organization and connections of S-I

Although the microelectrode mapping results on the organization of S-I in squirrels were quite limited in the present study, results were consistent with the previously reported organization (Sur et al., '78). As in S-I of other mammals (Kaas, '83), S-I in the squirrel is "standing on its head" so that a large lateral sector of the cortex represents the head, the more medial cortex is devoted to the forelimb, while the trunk and hindlimb are represented most medially.

A striking feature of S-I in squirrels is the occurrence of a 1-mm oval of the cortex centered in S-I that is unresponsive to light cutaneous stimuli in the typical anesthetized preparation (Sur et al., '78). While most of S-I has a well-developed layer IV that is tightly packed with granule cells, UZ zone has a less distinct layer IV. A contribution of the present study was to show how distinctive the unresponsive zone, UZ, is in surface-view brain sections stained for myelin. These sections not only clearly demonstrate UZ as a lightly myelinated oval surrounded by a densely myelinated S-I, but also show two lightly stained bandlike rostral extensions of UZ, the most medial of which reaches the motor cortex and separates the forelimb from the face representation. In rats, a similarly located dysgranular "unresponsive zone" separates forelimb and face representations and has rostralward extensions to the motor cortex (C. Welker, '76; Akers and Killackey, '78; Chapin and Lin, '84; Welker et al., '84). Much earlier, Krieg ('46) illustrated an oval of architectonically distinct cortex within S-I region of rats (distinguished as "2a" within a large "area 2") that may have been UZ. Given that squirrels and rats are on quite different branches of rodent evolution, separating perhaps 60 million years ago (e.g., Eisenberg, '81), it is likely that this UZ was present in the common ancestor, and we expect that UZ zones and bands exist in many other rodents as well. S-I of rodents appears to be homologous with area 3b of primates (Kaas, '83), but it is not certain whether UZ should be considered part of S-I, or part or all of another field within and perhaps around S-I (see Akers and Killackey, '78).

Cortical connections of S-I in squirrels are summarized in Figure 17. There are widespread intrinsic connections within S-I including major connections from granular S-I to UZ. UZ, in turn, projects strongly to UZ of the other hemisphere, the motor cortex, as well as to other areas. Similar connections of the dysgranular UZ zone within S-I have been previously described by Gould ('81) for squirrels and Akers and Killackey ('78) for rats. Akers and Killackey ('78) further postulated that the dysgranular UZ within S-I was part of a more extensive system including the dysgranular bands seen extending from UZ and dysgranular fringes of cortex along the rostral and caudal borders of granular S-I. Although the lightly myelinated UZ in squirrels has two lightly myelinated rostralward extensions that probably correspond to the dysgranular bands in rats, architectonic, connectional, and microstimulation (unpublished) data suggest that the moderately myelinated cortex bordering S-I rostrally in squirrels is the motor cortex, and the cortex immediately caudal to S-I contains several somatosensory areas (PV, S-II, PM) that are unlike UZ.

The dense callosal connections of UZ in squirrels also have been noted in a description of the total pattern of callosal projections (Gould and Kaas, '81). In addition, a

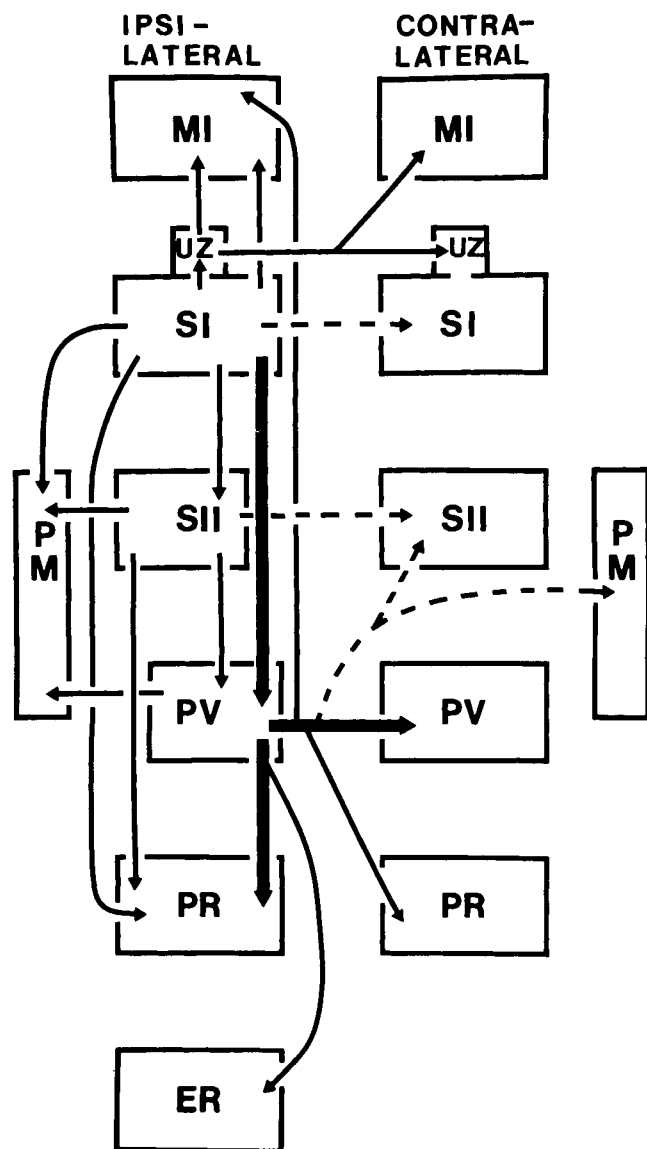


Fig. 17. Major processing sequences in the somatosensory cortex of squirrels. Arrows indicate the probable "feedforward" projections. Thick arrows mark major projections and dashed lines indicate sparse projections. See text for details. MI, the primary motor cortex; SI, the first somatosensory area; UZ, the "unresponsive zone" of S-I; S-II, the second somatosensory area; PM, the parietal medial area; PV, the parietal ventral area; PR, the parietal rhinal cortex; ER, the entorhinal cortex.

band of cortex between UZ and the motor cortex, corresponding to the medial band of light myelination in the present study, was shown to have dense callosal connections. Granular S-I of squirrels also projects callosally, and the study of Gould and Kaas ('81) shows that these connections are extremely variable in density according to the body region in the representation.

In the same hemisphere, granular S-I of squirrels projects rostrally to the motor cortex and caudally to PM, S-II, PV, and PR. The most dense connections are with PV and the least dense are with PM. Similarly, rostral connections of

S-I in rats (Akers and Killackey, '78) and mice (White and DeAmicis, '77; Porter and White, '83) are to the motor cortex. Caudal projections of S-I also have been described for rats (Akers and Killackey, '78) and mice (White and DeAmicis, '77), but there have been no architectonic or electrophysiological identifications of projection zones. Some caudalward projections have been attributed to S-II, largely on the basis of position, and some to a caudal "dysgranular" fringe. Present results suggest that the most medial of these projections are to PM, while other projections could be to any or all of S-II, PV, and PR.

The organization and connections of S-II

The somatotopic features and architectonic characteristics of S-II in squirrels have been previously described by Nelson et al. ('79). We remapped the field in comparable detail in three squirrels (Figs. 4,5), and the combined reports now show head, forelimb, trunk, and hindlimb regions of S-II for a total of six squirrels. In all cases, the head was represented along S-I border with the forelimb, trunk, and hindlimb following in a caudolateral cortical progression. The border of S-II with S-I was congruent so that similar parts of the head midline were represented along the common border. The S-II representation was found to be more somatotopic and less disrupted than S-I (Sur et al., '78), so that the nose and lips, forepaw, ventral trunk and hindpaw were all rostralateral, respectively, to the eye and cranium, forearm, dorsal trunk and thigh. When drawn relative to S-I on a lateral view of the brain, the body representation in S-II appears to be "standing on its feet" in a roughly normal position (Fig. 18). Such an orientation for S-II has been characterized as "erect" (Nelson et al., '79).

While S-II was first characterized as inverted in orientation (Woolsey, '52, '58; Lende and Woolsey, '56; T. Woolsey, '67; Pinto Hamuy et al., '56; Zeigler, '64), S-II subsequently has been described as erect in cats (Haight, '72; Burton et al., '82), raccoons (Herron '78), sheep (Johnson et al., '74), and some rodents (Campos and Welker, '76; Pimentel-Souza et al., '80) including squirrels (Nelson et al., '79). Present results support the conclusion that S-II in squirrels is erect, and also indicate that another somatosensory area, PV, is largely, but not completely, inverted in orientation. This raises the issue of whether or not S-II and PV have sometimes been confused. Early reports on the organization of S-II in rodents were based on recordings from large surface electrodes that reflected the activity of relatively large portions of the mapped fields, and it is not clear from the illustrated data if the somatotopic organization of the mapped fields had the erect orientation of PV or the inverted orientation of S-II. However, C. Welker and Sinha ('72) used microelectrodes to explore the somatosensory cortex in rats and described S-II as inverted. More recently, Pimentel-Souza ('80) also used microelectrodes to map S-II in another rodent (*aguoti*), and, in contrast, found S-II to be upright with an overall organization much like that of S-II in squirrels. Possibly the study of C. Welker and Sinha ('72) involved PV, rather than S-II, since the illustrated location of "S-II" in rats was in the relative position of the PV in squirrels. In addition, the orientation of S-II was described as inverted as in PV.

Other than the present report, there have been no studies of connections with lesions or injections confined to S-II in rodents. However, some information is available on S-II connections from injections of tracers into S-I or the motor cortex in mice and rats. Our studies show that S-II in

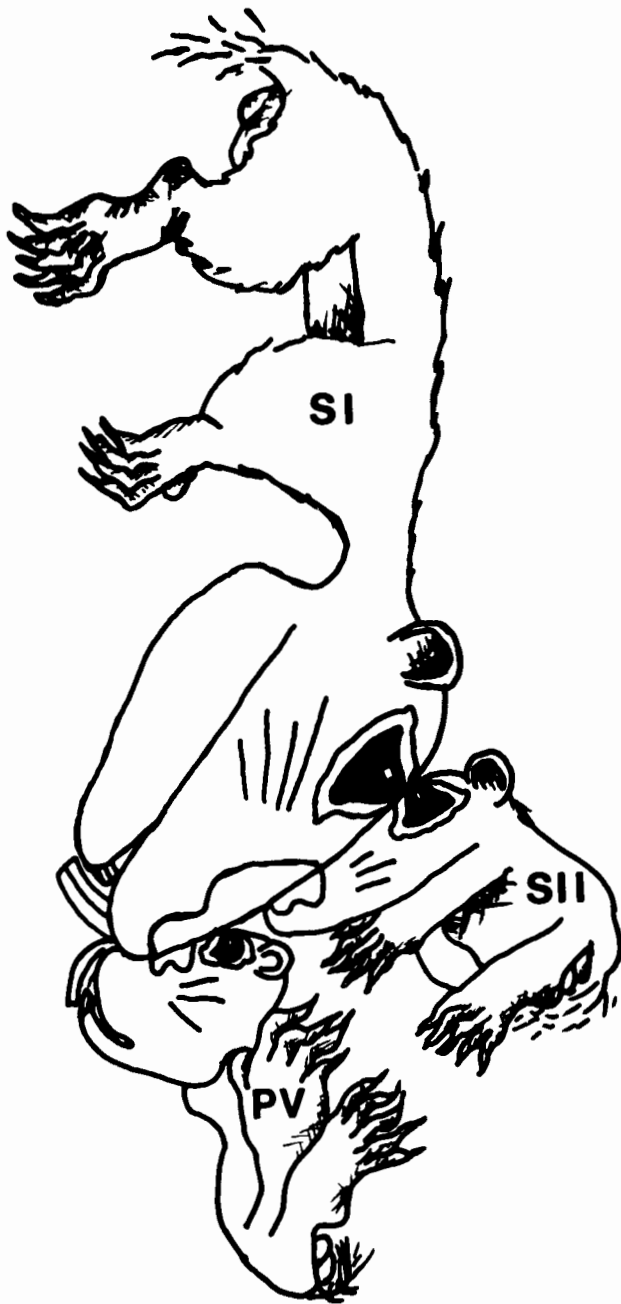


Fig. 18. A schematic portrayal of basic features of somatotopic organization of S-I, S-II, and PV in the traditional "homuncular" format. S-I is organized with the body in the cortex dorsal to the cortex devoted to the head, so that the general orientation is of an animal "standing on its head." In both S-II and PV the representations of the head adjoin S-I so that the face is rostral to the cranium. Thus, both representations of the head are in a roughly "erect" orientation. However, S-II and PV differ in that the limbs point ventrally in S-II and dorsally in PV. Thus, S-II can be characterized as "erect" in orientation, while the body in PV is "inverted." Rostral is right, dorsal is upper.

squirrels is interconnected ipsilaterally with S-I, PV, PM, and PR (Fig. 17). It was surprising that no obvious connections with the motor cortex were observed, since such connections have been described in mice (Porter and White, '83), rats (Donoghue and Parham, '83), cats (Jones and

Powell, '68; Kawamura and Otani, '70; Burton and Kopf, '84), and monkeys (Jones and Powell, '70; Pandya and Vig-nolo, '71; Jones et al., '78). However, the evidence for motor connections of S-II in monkeys can be questioned, since it is not certain that S-II, rather than a bordering field (see Robinson and Burton, '80b), is the source of the connections. This possible confusion seems less likely in cats, where S-II has been mapped in some detail and S-II can be located relative to fissure patterns (Haight, '72; Burton et al., '82). However, Burton and Kopf ('84) noted that the density of label in the motor cortex of cats after S-II injections was "much less" than that suggested by earlier studies (Jones and Powell, '68; Kawamura and Otani, '70). Finally, the reported connections between the motor cortex and "S-II" in mice (Porter and White, '83) are based on the presumptive location of S-II and could reflect connections of other fields. Thus, connections between S-II and the motor cortex may be sparse or absent in other mammals as well as squirrels.

Interconnections of S-I with S-II, as demonstrated in squirrels, appear to be a common feature of the mammalian cortex (see Burton and Kopf, '84, for review). Akers and Killackey ('78) report S-I connections with the presumed location of S-II in rats, but it seems quite possible that the described projections include other regions of cortex. In general, many of the connections of physiologically identified S-II in cats (e.g., Burton and Kopf, '84) appear to be quite similar to those of S-II in squirrels, suggesting that shared features will be found in a range of mammalian species. Thus, S-II in cats and squirrels projects to more medial cortex just caudal to S-I (PM in squirrels and "area 5" in cats) and to two areas just lateral to S-II (the areas PV and PR in squirrels and S-IV and insular cortex in cats).

Cases with injections that were centered in S-II of squirrels demonstrated major interconnections with central regions of S-II of the opposite hemisphere. Furthermore, these cases show that in squirrels the major source of callosal connections to S-II is from S-II, although some input is from PV. The input from PV appeared to involve parts of S-II devoted to distal limbs. Previously, callosal input to S-II in squirrels was shown to be uneven in density, but to include all major body parts in the representations, even the distal limbs (Gould and Kaas, '81), and present results are consistent with this conclusion. Investigators typically have concluded that parts of S-II devoted to the distal limbs in rodents and other mammals are "acallosal" (see Gould and Kaas, '81, for review), but this conclusion appears to be based on relatively insensitive procedures for revealing connections and on an assumption about the location of S-II and the body parts in S-II. Recently, there has been evidence that the portion of S-II in monkeys responding to stimulation of the hand has callosal connections (Manzoni et al., '84).

The organization and connections of PV

The parietal ventral area forms a second systematic representation of the body surface that adjoins the larger S-I representation along the caudal border of S-I devoted to the face. PV has not been previously described as an area distinct from S-II in rodents, although the lateral location and inverted organization described for S-II in rats by C. Welker and Sinha ('72) appears to more closely correspond to that of PV rather than S-II. The arrangement of body parts in PV does not form a simple homunculus as in S-II. The representation of the face and upper head in PV forms

a congruent (see Allman and Kaas, '75) or matched border with S-I, with more rostral skin on the head midline represented more medially in both S-I and PV. Thus, the representation of the head in PV is in the "erect" orientation (Fig. 18). In contrast, the trunk is represented laterally, the proximal limbs medial to the trunk, and the distal limbs most medially in PV. Thus, the body is in the "inverted" orientation.

In squirrels, PV is interconnected ipsilaterally with the motor cortex, S-I, S-II, PM, PR, and the entorhinal cortex (ER). Callosal connections are relatively widespread and include PV, S-II, and PR. Since PV is a newly defined area in squirrels, connections of PV have not been described as such in other rodents. However, some of the projections of S-I that have been attributed to S-II in rats (Akers and Killackey, '78) may have actually been to PV. In addition, projections to the motor cortex described as arising from S-II in mice (Porter and White, '83) and rats (Donoghue and Parham, '83) are more probably from PV, since in squirrels, PV, rather than S-II, is strongly connected with motor cortex.

PV possibly exists in other mammals as well. In the opossum, the ventral location and the responsiveness to auditory as well as somatic stimuli suggest that "S-II" (Pubols, '77) may correspond to PV. The fourth somatosensory area of cats is very similar to PV. In cats, S-IV has been described as a somatotopic representation of the body on the lateral border of the S-II (Clemo and Stein, '82, '83; Burton and Koph, '84). Like PV, S-IV appears to contain an inverted representation, and some neurons respond to auditory stimuli. In addition, both S-IV and PV project to more lateral cortex and to the cortex along the caudal border of S-I. However, S-IV does not appear to have connections with S-I and MI, as does PV. Thus, it is not certain if PV and S-IV are the same area with somewhat different patterns of connections, or if they are different areas in the same position relative to S-II. Further comparisons of subcortical connections of S-IV (Stein et al., '83) with those of PV may help answer this question. In monkeys, several body surface representations have been described in the S-II region (Robinson and Burton, '80b), and it is possible that one of these fields, perhaps the retroinsular area on the border of "S-II proper," is the homologue of PV. However, there is little information on the connections of the retroinsular area to test the validity of this hypothesis (see Friedman, '83).

At least part of PV in squirrels was bimodal, containing neurons responsive to somatic stimuli and neurons responsive to auditory stimuli. The somatosensory activation dominated, so that neurons throughout PV were easily activated by light touch, while neurons in only some penetrations were driven by auditory stimuli. In general, the best auditory responses were recorded at somewhat deeper recording depths than the best somatosensory responses, and the auditory responses were most often obtained in penetrations near auditory cortex in parts of PV representing the body rather than the head. While the significance of these observations on the distribution of auditory responses in PV is uncertain, responsiveness of the cortex in the general region of PV to both somatic and auditory stimuli has been reported for a number of mammals. The overlap of S-II with the auditory cortex described in studies using surface recordings in rodents (Lende and Woolsey, '56; Woolsey, '58; T. Woolsey, '67) could reflect the mixed responsiveness of PV, or volume conduction from separate but adjacent so-

matic and auditory fields. However, microelectrode recording studies in cats indicate that S-IV, the cortex caudal to S-IV (Clemo and Stein, '83), and the cortex caudal to S-II (Carreras and Anderson, '63) are activated by both somatic and auditory stimuli. In monkeys, retroinsular, granular insular, and adjacent portions of area 7b are responsive to auditory as well as somatosensory stimuli (Robinson and Burton, '80b).

Cortical processing of somatosensory information in rodents: A distributed system

The evidence indicates that squirrels have at least three systematic representations of the body surface and at least five interconnected somatosensory areas in the parietal region of the cortex. The cortical system in squirrels, although apparently somewhat simpler, is remarkably similar to that described for monkeys and cats where multiple somatosensory areas with complex interconnections have been described (see Merzenich and Kaas, '80, for review). Aside from S-I and S-II, which appear to exist in all eutherian mammals (see Kaas et al., '83), it is not certain which, if any, additional components of the cortical system in squirrels also exist in other mammals. Thus, there is uncertainty about the extent to which the similar systems in rodents, cats, and monkeys were already present in a common ancestor or evolved independently. Nevertheless, it appears that mammals with relatively simple brains, such as squirrels, and mammals with more complex brains, such as cats and monkeys, all process somatosensory information in a basically similar manner. In each of these mammals, a number of somatotopically organized cortical fields are so complexly interconnected that processing hierarchies can be only broadly defined. All three mammals also have more than one cortical field that receives sensory information over a rather direct route from the thalamus. These connections suggest that functions are distributed in the cortical system, and that sensory events activate neurons almost simultaneously in a number of cortical fields (see Merzenich and Kaas, '80). Yet, a semblance of a hierarchy is embedded in this distributed cortical system of squirrels (Fig. 17). Laminar patterns of connections, which have been classified into feedforward and feedback types (e.g., Maunsell and Van Essen, '83), have been useful in constructing hypothetical processing hierarchies. While our preparations were not ideal for an analysis of laminar patterns, both S-II and PV clearly provided widespread "feedback" to superficial layers of S-I. Thus, S-I may be considered the first level in a cortical hierarchy of processing, relaying information to UZ, PM, S-II, PV, and PR, although these fields may also receive more direct sensory information from the thalamus. Further steps in a hypothetical processing hierarchy are blurred by the manifold connections, but there may be reasons to consider some areas such as PR and PV as "higher" than S-II and PM on the basis of outputs to perirhinal and limbic structures. In monkeys, Mishkin and co-workers (e.g., Mishkin, '79; Turner et al., '80; Mishkin et al., '84; also see Pandya and Seltzer, '82) have argued that cortical fields with inputs into memory mechanisms in the limbic system form the final stages of cortical processing that relate to object identification. Thus, the somatosensory system of rodents, as well as cats and monkeys, appears to consist of a weakly hierarchical and distributed forebrain system with manifold parallel, divergent, and convergent processing channels. It is interesting

to note that fields both "early" (S-I and UZ) and "late" (PV) in the hierarchy relate strongly to motor cortex while an intermediate level (S-II) does not.

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