

Topographic Organization of Corticospinal Projections from the Frontal Lobe: Motor Areas on the Medial Surface of the Hemisphere

San-Qiang He,¹ Richard P. Dum,^{2,3} and Peter L. Strick^{1,2,3}

Departments of ¹Physiology and ²Neurosurgery, SUNY Health Science Center at Syracuse, and ³Research Service, Veterans Affairs Medical Center, Syracuse, New York 13210

We examined the topographic organization of corticospinal neurons in the four premotor areas on the medial wall of the hemisphere of macaques. These motor areas include the supplementary motor area (SMA) and three areas buried within the cingulate sulcus: the caudal cingulate motor area on the dorsal bank (CMA_d), the caudal cingulate motor area on the ventral bank (CMA_v), and the rostral cingulate motor area (CMA_r). In one set of animals, we injected one fluorescent tracer into lower cervical segments of the spinal cord and another fluorescent tracer into lower lumbosacral segments to define the topographic organization of arm and leg representation within each premotor area. Similarly, in another set of animals, we injected different tracers into upper cervical and lower cervical segments to provide an indication of the topographic organization of proximal and distal arm representation within the arm representation of each premotor area.

We found that all four of the premotor areas on the medial wall project to cervical and lumbosacral segments of the spinal cord. Three of these areas (SMA, CMA_d, and CMA_v) are like the primary motor cortex in having distinct arm and leg representations. The arm representation in each of the four motor areas on the medial wall contains separate regions that project densely to upper or to lower cervical segments. This observation suggests that each motor area contains distinct proximal and distal representations of the arm. Surprisingly, the size of the distal representation is comparable to or larger than the size of the proximal representation in each motor area. Thus, contrary to some previous hypotheses, the anatomical substrate exists for the premotor areas on the medial wall to be involved in the control of distal, as well as proximal arm movements. Our results provide a new map for guiding the exploration of the motor functions of the medial wall of the hemisphere. Furthermore, the observations of the present study support our suggestion that each of the premotor areas may be an important source of descending commands for the generation and control of movement.

[Key words: cingulate, frontal lobe, monkey, motor control, premotor cortex, pyramidal tract, supplementary motor area]

This is the second article in a series of reports about the topographic organization of the corticospinal system in macaques (He et al., 1993). In this article, we describe the topographic organization of corticospinal neurons in the four premotor areas on the medial wall of the hemisphere (Dum and Strick, 1991b). These premotor areas are the supplementary motor area (SMA) on the superior frontal gyrus and three motor areas which are buried in the cingulate sulcus: the caudal cingulate motor area on the dorsal bank (CMA_d), the caudal cingulate motor area on the ventral bank (CMA_v), and the rostral cingulate motor area (CMA_r).

Using electrical stimulation of the cortical surface, Penfield and Welch (1951) and Woolsey et al. (1952) demonstrated the existence of a motor area on the medial wall of the hemisphere which was termed the supplementary motor area (SMA). Both groups agreed that the SMA occupied the medial part of the superior frontal gyrus and the dorsal bank of the cingulate sulcus. However, they disagreed on the spatial arrangement of body parts within the SMA. Penfield and Welch (1951) claimed that the leg representation in the SMA was ventral to the arm representation, whereas Woolsey et al. (1952) believed that the leg representation was located caudal to the arm representation. Thus, from its very discovery, there has been considerable controversy about the somatotopic organization of the SMA.

It is now clear that the region termed the SMA in earlier studies contains more than a single motor area (Dum and Strick, 1991b; Luppino et al., 1991; Matelli et al., 1991; Matsuzaka et al., 1992). Furthermore, considerable evidence suggests that additional motor areas lie buried in the cingulate sulcus (Muakassa and Strick, 1979; Godschalk et al., 1984; Strick, 1985; Hutchins et al., 1988; Dum and Strick, 1989, 1991a,b, 1993; Holsapple and Strick, 1989, 1991; Luppino et al., 1991; Matelli et al., 1991; Shima et al., 1991; Morecraft and Van Hoesen, 1992, 1993; Lu et al., 1994). However, the number of motor areas on the medial wall, as well as the extent and topographic organization of each area, remains the subject of controversy (e.g., Dum and Strick, 1991b; Luppino et al., 1991; Morecraft and Van Hoesen, 1992).

In the present study, we examined questions about the number, extent, and topographic organization of motor areas on the medial wall by injecting distinct tracers into different segmental levels of the spinal cord. This approach was used in two sets of

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Correspondence should be addressed to Dr. Peter L. Strick, Research Service (151), Veterans Affairs Medical Center, Syracuse, NY 13210.

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mental levels of the same animal. In one set of experiments ($n = 2$; animals H1 and H2), we injected one of the fluorescent tracers into lower lumbosacral segments (L6–S1). Then, a week later, we injected the other fluorescent tracer into lower cervical segments (C7–T1) (Fig. 1A). In a second set of experiments ($n = 5$; animals H3–H7), we injected one of the fluorescent tracers into lower cervical segments (C7–T1) and then, injected the other fluorescent tracer into upper cervical segments (C2–C4) (Fig. 1B). After the appropriate survival time (15–30 d, He et al., 1993; their Table 1), each animal was deeply anesthetized and perfused transcardially with 0.1 M phosphate buffer (pH 7.4), followed by 4% (weight/volume) paraformaldehyde in phosphate buffer and 4% paraformaldehyde in phosphate buffer with 10% (volume/volume) glycerol.

Histological procedures

Blocks of spinal cord containing the injection sites and a large brain block that included the frontal lobe were frozen and sectioned in the coronal plane at a thickness of 50 μm . Every tenth section of spinal cord and cortex was processed for cytoarchitectonic analysis (Gower procedure in Mesulam, 1982). The remaining sections were immediately mounted onto gelatin-coated slides, air dried, and stored uncovered in the dark at 4°C (Huisman et al., 1983).

Analytical procedures

We examined sections of spinal cord and cortex using fluorescent illumination (Leitz filter D, 355–425 nm excitation wavelength). Injection sites, section outlines and labeled neurons were plotted using a computer-based charting system (MD2, Minnesota Datametrics). This system uses optical encoders to measure x-y movements of the microscope stage and stores the coordinates of charted structures.

At least every tenth section of spinal cord was examined to determine the spread of tracer. As in other studies (Huisman et al., 1983; Kuypers and Huisman, 1984; Condé, 1987), three concentric zones of fluorescent labeling could be defined in the spinal cord at the site of FB and DY injections (e.g., He et al., 1993, their Figs. 1, 2). Zone I was defined as the central region surrounding the needle track that contained an almost solid mass of fluorescent material. Zone II was defined as the adjacent region that contained large numbers of intensely fluorescent neurons and glia amid a bright background of fluorescence. Zone II gradually changed into zone III which contained some background tissue fluorescence and weakly fluorescent neurons and glia. Prior studies have found that the effective area of uptake and transport of FB and DY is confined to zones I and II (e.g., Bentivoglio et al., 1980; Kuypers and Huisman, 1984; Condé, 1987). Therefore, only these two zones were included within our "injection sites" (see Fig. 3 in He et al., 1993).

We charted the location of each labeled neuron found on at least every fourth section through the frontal lobe. Three different types of maps were generated from these charts to display the topographic distribution of corticospinal neurons on the medial wall.

Flattened maps. The plots of individual sections were aligned on the junction of the medial wall of the hemisphere with the lateral surface and this point of alignment (midline) was kept fixed. Then, the medial wall of the hemisphere was divided into four segments: the medial aspect of the superior frontal gyrus (SGm), the dorsal bank of the cingulate sulcus (CgSd), the ventral bank of the cingulate sulcus (CgSv), and the cingulate gyrus (CgG). Layer V from these segments was unfolded and reflected upward from the midline (Fig. 2) (see Dum and Strick, 1991b). An adjacent portion of the lateral surface of the hemisphere was flattened and displayed downward from the midline in order to show the parts of the SMA and the hindlimb representation in area 4 that extend from the medial wall onto the lateral surface. This method for displaying the medial wall is similar to that first employed by Woolsey et al. (1952).

Density maps. Layer V of each section in the flattened maps was divided into 200 μm bins. The number of neurons labeled with a particular tracer was then counted in each bin and assigned a color code. Four color levels were used with the white, yellow and red colors reserved for bins with a density in the upper 15–20% of the total sample.

These bins contained approximately 35–50% of the total labeled neurons and were termed "high density" bins.

The relative amount of cortex that was allotted to proximal (upper cervical) or distal (lower cervical) representation was assessed by counting the number of high density bins that projected to a given cervical level. The percentage of high density bins projecting to each level was calculated and then the results from H3 and H7 were averaged. We chose this method because direct measurements of area can be influenced by the spatial distribution of bins.

Overlap maps. Each 200 μm bin of a flattened map was given a color code depending on the type(s) of labeled neurons present in that bin. Bins containing only FB labeled neurons were coded blue, bins containing only DY labeled neurons were coded yellow and bins with FB neurons and DY neurons were coded red. Red bins were termed "overlap bins." The extent of overlap between cortical regions containing neurons labeled with FB and regions with neurons labeled with DY was quantitatively analyzed by calculating the percentage of overlap bins in each motor area. Bins containing only a single neuron were not included in overlap maps comparing the origin of lower cervical and lower lumbosacral projections. The overlap maps comparing the origin of lower and upper cervical projections examined overlap of the "high density" bins only.

We created two summary diagrams of our observations, one indicating the location of arm and leg representation in the premotor areas and the other indicating the location of proximal and distal arm representation. To construct each diagram, the results from all animals with tracer injections into the appropriate segmental levels were overlaid onto a standard map of the medial wall. Some size adjustment of individual data sets was necessary to achieve the best fit. The maps of proximal and distal arm representation were restricted to the regions containing high density bins. Then, we enclosed areas that consistently contained labeled neurons after tracer injections into a given segmental level.

Definition of cortical areas

The location and cytoarchitectonic designations of the four premotor areas on the medial wall are illustrated in Figure 2B. We identified the border between the SMA and the primary motor cortex based on the change in density of large layer V neurons (see He et al., 1993, for details). This border was located approximately 9–10 mm caudal to the level of the genu of the arcuate sulcus. Rostral to the SMA lies a portion of area 6 which has been termed the Pre SMA (Matsuzaka et al., 1992). This cortical area does not have substantial projections to the primary motor cortex or to the spinal cord (Dum and Strick, 1991b). The borders of the remaining cingulate motor areas were defined by previously established criteria (Dum and Strick, 1991b; for review, see Dum and Strick, 1993).

Results

Location and extent of injection sites

We will present results from four representative animals in which fluorescent tracers were injected into the gray matter at different segmental levels of the spinal cord. In animals H1 and H2, one fluorescent tracer was injected into lower cervical segments (C7–T1) and another tracer was injected into lower lumbosacral segments (L6–S1) of the same animal (Fig. 1A). In animals H3 and H7, one fluorescent tracer was injected into upper cervical segments (C2–C4) and a second one was injected into lower cervical segments (Fig. 1B).

The location and extent of injection sites in these animals were described and displayed in a prior paper (He et al., 1993, their Figs. 1–3, Table 1). Briefly, the injection sites were largely confined to the gray matter of the injected segmental levels of the spinal cord. No animal exhibited significant damage or

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Figure 3. Maps of corticospinal neurons projecting to lower cervical and lower lumbosacral segments. *Top*, Animal H1. *Bottom*, Animal H2. Every fourth coronal section was plotted to create these maps. *Yellow dots*, neurons that project to lower lumbosacral segments (L6–S1); *blue dots*, neurons that project to lower cervical segments (C7–T1). See Figure 2 for abbreviations.

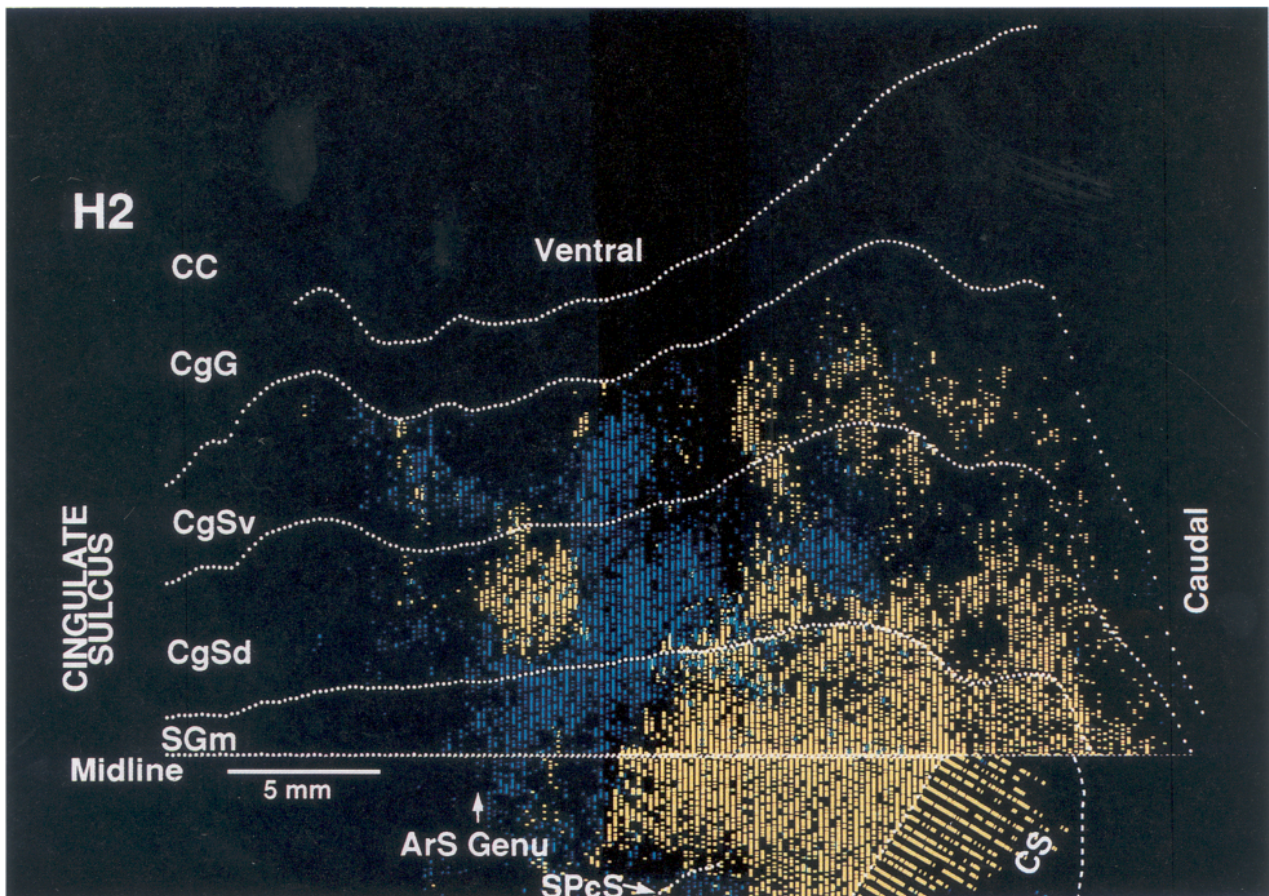
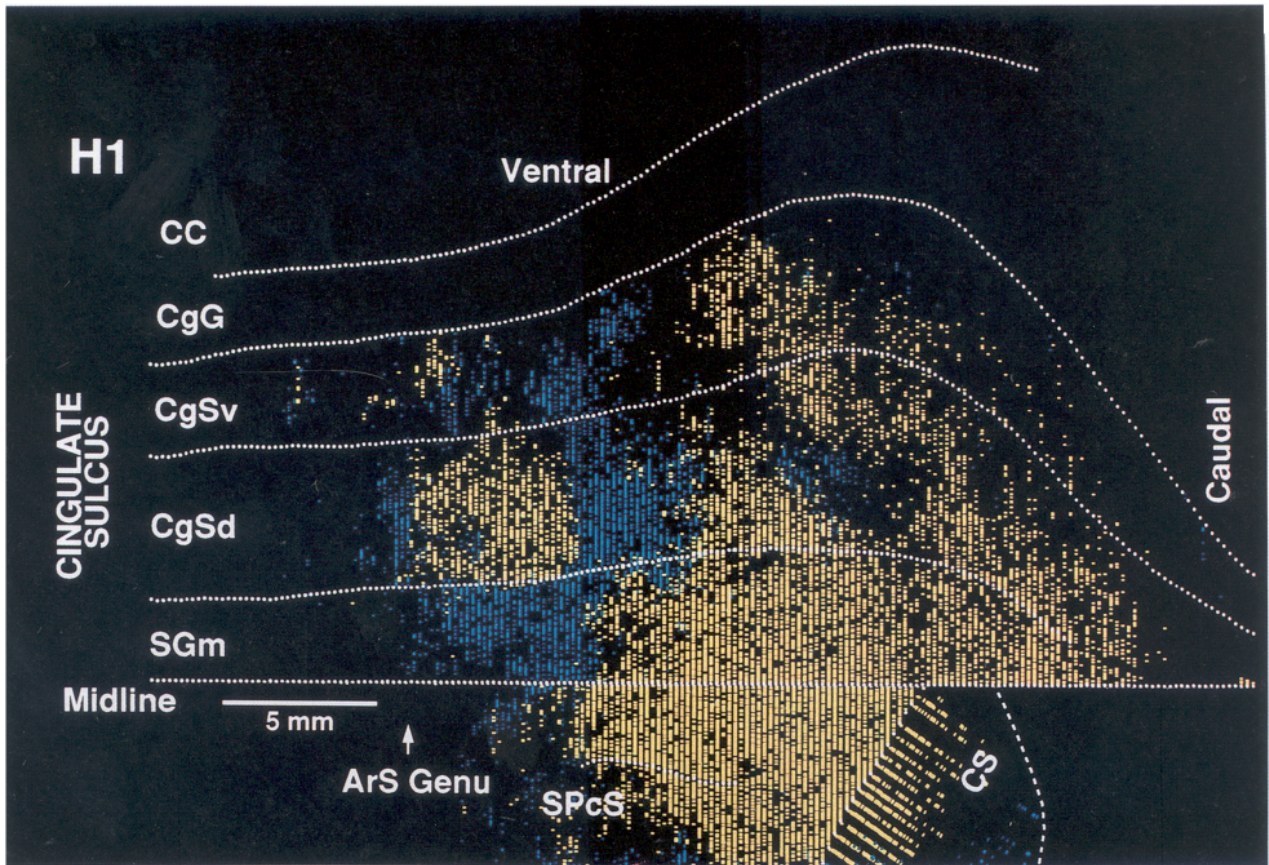


Table 1. Number of corticospinal neurons projecting to lower cervical (C7–T1) and lower lumbosacral segments (L6–S1) in the premotor areas and the primary motor cortex

Motor areas	Animal									
	H1					H2				
	C7–T1 (%)	L6–S1 (%)	DL (%)	Total (%)	%	C7–T1 (%)	L6–S1 (%)	DL (%)	Total (%)	%
MI	4610 (46)	5375 (54)	4 (<1)	9989 (100)	52.0	5619 (46)	6550 (54)	6 (<1)	12,175 (100)	53.0
PMd	1306 (48)	1398 (52)	10 (<1)	2714 (100)	14.1	1998 (63)	1163 (37)	11 (<1)	3172 (100)	13.8
PMv	122 (98)	1 (<1)	2 (2)	125 (100)	0.6	49 (100)	0 (0)	0 (0)	49 (100)	0.2
SMA	1362 (50)	1381 (50)	19 (<1)	2762 (100)	14.2	1560 (51)	1476 (49)	22 (<1)	3058 (100)	13.3
CMA _d	1099 (51)	1059 (49)	2 (<1)	2160 (100)	11.2	1788 (69)	805 (31)	4 (<1)	2597 (100)	11.3
CMA _v	351 (33)	699 (67)	0 (0)	1050 (100)	5.5	799 (58)	574 (42)	2 (<1)	1375 (100)	6.0
CMA _r	365 (80)	93 (20)	1 (<1)	459 (100)	2.4	442 (82)	98 (18)	2 (<1)	542 (100)	2.4
Total	9215 (48)	10,006 (52)	38 (<1)	19,259 (100)	100.0	12,255 (53)	10,666 (47)	47 (<1)	22,968 (100)	100.0

Neuron counts are based on the data from every fourth section and are not corrected. DL, double-labeled neurons. Neuron counts for individual injection sites do not include double-labeled neurons.

spread of tracer into the dorsolateral funiculus where most of the corticospinal axons descend.

All four animals had tracer injections into lower cervical segments. Injection sites at this location were most extensive in animals H2 and H3 and involved almost all of the gray matter from the caudal half of C7 through the T1 segment. In the other two animals (H1 and H7), the dorsal horn and intermediate zone of the lower cervical segments were well filled, but their ventral horns were only intermittently involved. The extent of the injection sites within the lower lumbosacral segments was nearly complete in H1 and included most of the gray matter of L6, L7, and rostral S1. In H2, tracer filled the gray matter of the lower lumbosacral segments except for the lateral parts of caudal L7 and rostral S1. Tracer injections into upper cervical segments almost completely filled the gray matter in H3. In H7, tracer largely filled the gray matter in C2 and C3, but was primarily located in the lateral parts of C4. In summary, each injection site in every animal contained multiple regions where tracer completely filled the gray matter. This fact, along with the consistent topographic patterns we observed (see below and He et al., 1993), supports the adequacy of our injection sites.

Corticospinal neurons on the medial wall of the hemisphere

The results from animals with tracer injections into lower cervical and lower lumbosacral segments (H1, H2) define the topographic organization of arm and leg representation within each premotor area. On the other hand, the results from animals with tracer injections into upper cervical and lower cervical segments (H3, H7) may indicate the topographic organization of proximal and distal musculature within each of the arm representations (for discussion, see He et al., 1993). Therefore, we will present the results from the two types of experiments in separate sections. In each section, we will describe the topographic organization of corticospinal neurons found in individual

premotor areas. These descriptions will not include the corticospinal neurons found in regions of the medial wall that lie caudal to the central sulcus (Fig. 3). This region of cortex contains several somatosensory areas (e.g., Woolsey, 1958; Murray and Coulter, 1981b) and will be described in a future report.

Few, “double labeled” neurons were found in the premotor areas after tracer injections into lower cervical and lower lumbosacral segments (only 0.2% of the total sample of labeled neurons in H1 and H2) (Table 1). Likewise, few, “double labeled” neurons were found in the premotor areas after tracer injections into upper cervical and lower cervical segments (only 3–6% of the total sample in H3 and H7) (Table 2). Consequently, “double labeled” neurons are not displayed on our maps.

We observed some variability in the absolute numbers of neurons that were labeled by tracer injections into lower cervical segments (H1, 9215; H2, 12,255; H3, 6264; H7, 7731). Similarly, the percentage of neurons that were labeled following tracer injections upper and lower cervical segments also differed (Table 2). The completeness of the injection sites probably contributed to this variability (He et al., 1993, their Fig. 3). However, it is important to note, that the number of axons in the medullary pyramids of macaques was reported to vary by a factor of two (Russell and DeMeyer, 1961).

Corticospinal projections to lower cervical and lower lumbosacral segments

Approximately 48% of the corticospinal neurons in the frontal lobe that projected to lower cervical or lower lumbosacral segments were located outside the primary motor cortex and in the premotor areas (Figs. 2B, 3–6; Table 1) (Dum and Strick, 1991b). The majority of these corticospinal neurons (~70%) were located in the premotor areas on the medial wall of the hemisphere. The largest percentage in the premotor areas on the medial wall was found in the SMA (~14% of the total number

Table 2. Number of corticospinal neurons projecting to upper cervical (C2–C4) and lower cervical segments (C7–T1) in the premotor areas and the primary motor cortex

Motor areas	Animal									
	H3					H7				
	C2–C4 (%)	C7–T1 (%)	DL (%)	Total (%)	%	C2–C4 (%)	C7–T1 (%)	DL (%)	Total (%)	%
MI	3048 (57)	2100 (39)	208 (4)	5356 (100)	30.0	1743 (34)	3171 (62)	200 (4)	5114 (100)	43.3
PMd	2397 (66)	1044 (29)	189 (5)	3630 (100)	20.2	973 (39)	1475 (59)	48 (2)	2496 (100)	21.1
PMv	776 (92)	56 (7)	9 (1)	841 (100)	4.7	358 (78)	92 (20)	9 (2)	459 (100)	3.9
SMA	1849 (62)	902 (30)	235 (8)	2986 (100)	16.6	372 (25)	1100 (73)	29 (2)	1501 (100)	12.7
CMA _d	529 (35)	742 (50)	219 (15)	1490 (100)	8.3	162 (17)	759 (81)	16 (2)	937 (100)	7.9
CMA _v	900 (51)	752 (42)	125 (7)	1777 (100)	9.9	122 (19)	527 (80)	8 (1)	657 (100)	5.6
CMA _r	1108 (59)	668 (36)	100 (5)	1876 (100)	10.5	33 (5)	607 (95)	1 (<1)	641 (100)	5.4
Total	10,607 (59)	6264 (35)	1085 (6)	17,956 (100)	100.0	3763 (32)	7731 (65)	311 (3)	11,805 100	100.0

Neuron counts are based on the data from every fourth section and are not corrected. DL, double-labeled neurons. Neuron counts for individual injection sites do not include double-labeled neurons.

of corticospinal neurons in the frontal lobe). Nearly as many corticospinal neurons (~11%) were found in the CMA_d, whereas smaller percentages of corticospinal neurons were located in the CMA_v (6%) and CMA_r (2.4%). In general, the numbers of corticospinal neurons in the motor areas on the medial wall that projected to lower cervical segments was similar to the number projecting to lower lumbosacral segments. The only exception was the CMA_r where a greater proportion of corticospinal neurons projected to lower cervical segments.

Arm and leg representation in the premotor areas on the medial wall

SMA. Large numbers of labeled neurons were found in the SMA following tracer injections into lower cervical and lower lumbosacral segments of the spinal cord (Figs. 3–6, Table 1). Corticospinal neurons that projected to lower cervical segments were located in a region of the SMA that began just rostral to the level of the arcuate genu. This region of labeled corticospinal neurons continued caudally along the superior frontal gyrus for 7–8 mm. Some corticospinal neurons were found in SMA regions that extend ventrally onto the dorsal bank of the cingulate sulcus and dorsally onto the lateral surface of the hemisphere (compare Fig. 2*B* with Figs. 3–6). Corticospinal neurons that innervated lower cervical segments were generally located in regions that correspond to the arm area of the SMA as defined by anatomical or physiological criteria (e.g., Penfield and Welch, 1951; Woolsey et al., 1952; Brinkman and Porter, 1979; Muakkassa and Strick, 1979; Macpherson et al., 1982; Hummelsheim et al., 1986; Mitz and Wise, 1987; Hutchins et al., 1988; Dum and Strick, 1991a,b; Luppino et al., 1991; Matsuzaka et al., 1992).

Corticospinal neurons that projected to lower lumbosacral segments were located in a region of the SMA that began immediately caudal to the arm representation of the SMA and continued caudally up to the leg representation of the primary motor

cortex (Figs. 3–6). In fact, there was no obvious change in the density of corticospinal neurons at the border between the SMA and primary motor cortex (Figs. 5, 6) even though the density of large neurons in layer V changed at this border. The observation that the density of corticospinal neurons in the SMA was comparable to that in the primary motor cortex further emphasizes the importance of SMA projections to the spinal cord (Dum and Strick, 1991b).

Only 8–10% of the bins containing corticospinal neurons after tracer injections into lower cervical and lower lumbosacral segments were overlap bins (Table 3). These bins were primarily located within the region of the SMA that projected to lower lumbosacral segments (Fig. 7). Despite the presence of these bins, neurons projecting to lower cervical segments originated from regions of the SMA that were largely separate from those projecting to lower lumbosacral segments (Figs. 3–7). These observations provide additional evidence that the SMA contains distinct arm and leg representations and that the arm representation is located rostral to the leg representation (Figs. 7, 8).

CMA_d. The CMA_d lies ventral to the SMA and is located on the dorsal bank of the cingulate sulcus (Fig. 2*B*). This cortical area has a cytoarchitecture which is distinct from the SMA and lies in a subfield of area 6 (area 6c) (Dum and Strick, 1991b). Substantial numbers of corticospinal neurons were found in the CMA_d after tracer injections into either lower cervical or lower lumbosacral segments of the spinal cord. In fact, the number of corticospinal neurons found in the CMA_d was comparable to that found in the SMA (Table 1).

The regions of the CMA_d that projected to lower cervical segments were quite separate from those that projected to lower lumbosacral segments (Figs. 3–7). Indeed, only 9–10% of the bins in the CMA_d were overlap bins (Table 3). Corticospinal projections to lower cervical segments originated from two spatially separate regions in the CMA_d (Figs. 3; 4, sections 302, 459; 5–7). This

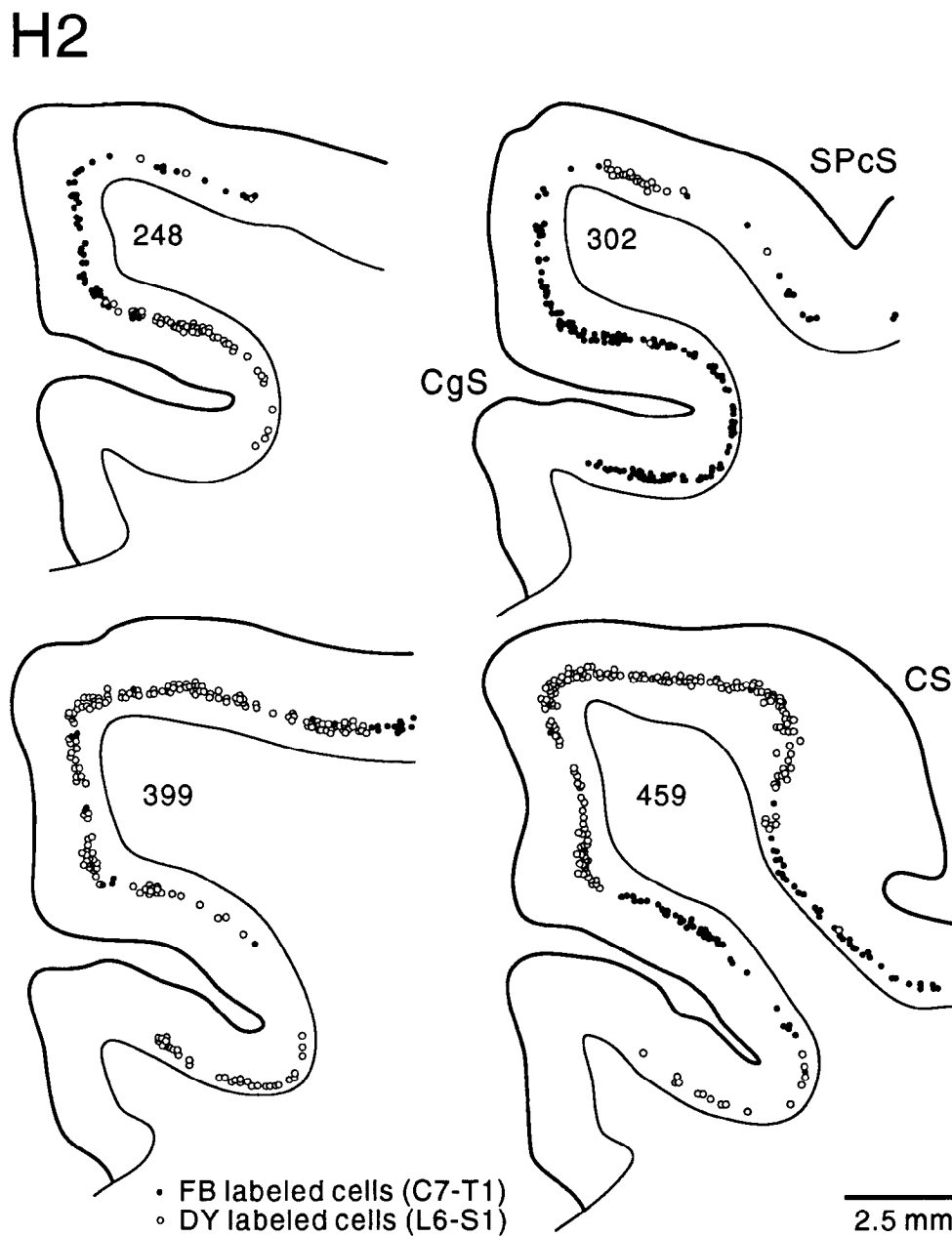


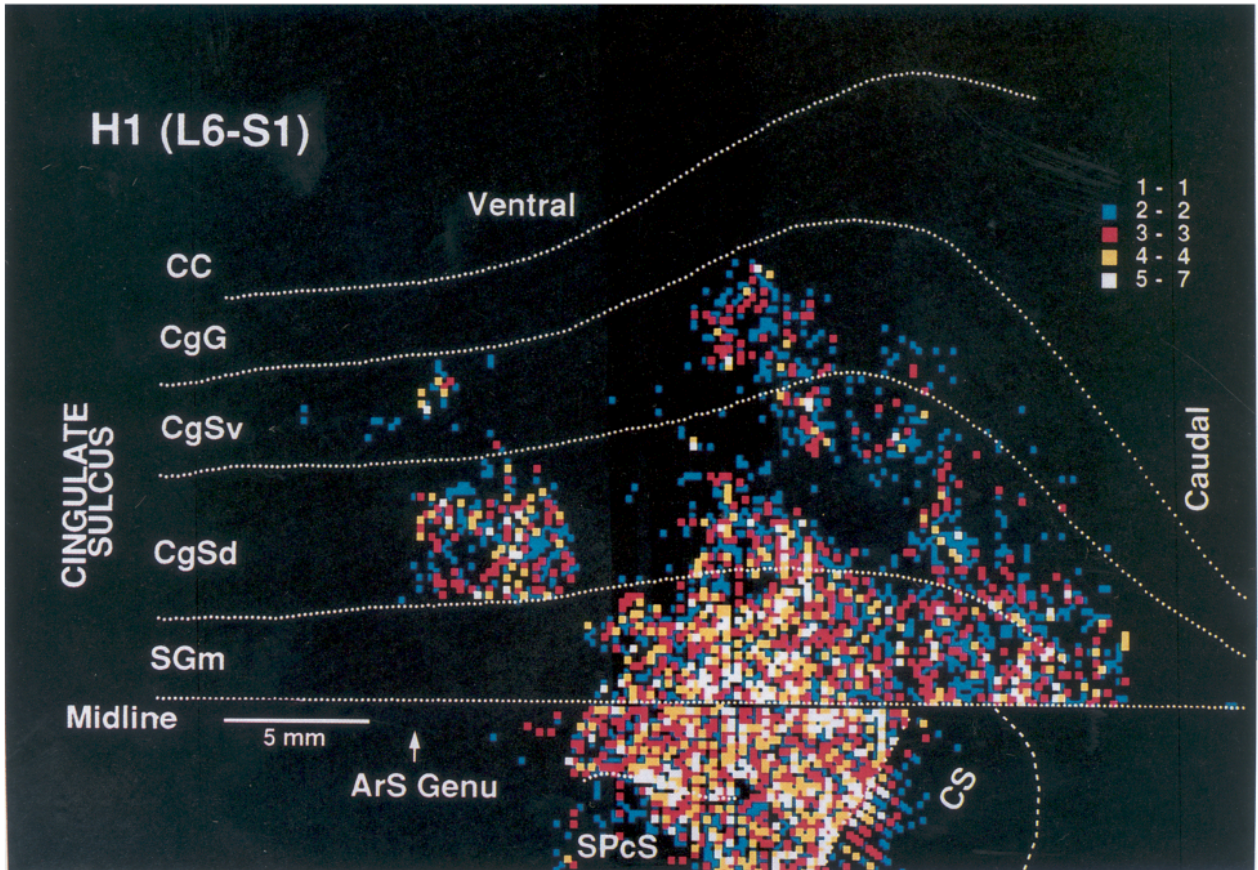
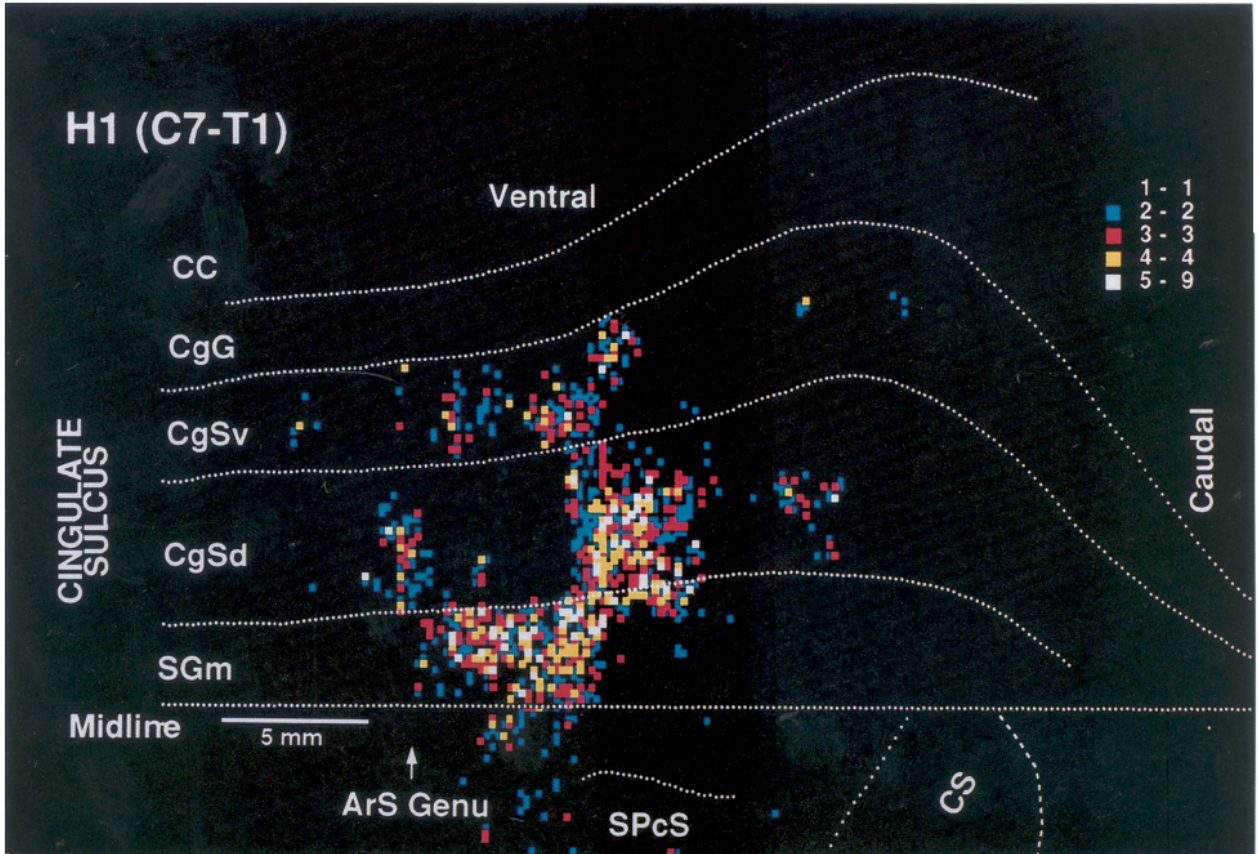
Figure 4. Coronal sections from animal H2. *Solid dots*, Neurons projecting to lower cervical segments. *Open circles*, Neurons projecting to lower lumbosacral segments. The location of each section is indicated by the numbered arrows in Figure 8.

result has been apparent in every animal in which a localized injection of tracer filled the lower cervical segments ($n = 7$) (Hutchins et al., 1988; Dum and Strick, 1989, 1991b). Corticospinal projections to lower lumbosacral segments also originated from two spatially separate regions within the CMAAd (Figs. 3; 4, sections 248, 399; 5–7). Each group of neurons projecting to lumbosacral segments was located just rostral to a group projecting to cervical segments. Thus, these observations indicate that the CMAAd contains two somatotopically organized groups of corticospinal neurons—a large group in the rostral two-thirds of the CMAAd and a smaller group in its caudal third (Figs. 7, 8). Fur-

thermore, the pattern of arm and leg representation in the body maps in the CMAAd is reversed relative to that in the SMA.

It is noteworthy that the large leg representation at the rostral end of the CMAAd was located just ventral to the arm representation in the SMA (Figs. 7, 8). This arrangement may explain the controversy about the pattern of body representation within the SMA in which one group placed the leg representation ventral to the SMA arm representation (Penfield and Welch, 1951), rather than caudal to it (Woolsey et al., 1952). The presence of a dense projection to lower lumbosacral segments within the rostral portion of the CMAAd makes it easy to understand why

Figure 5. Density of corticospinal neurons projecting to lower cervical and lower lumbosacral segments in animal H1. *Top*, Lower cervical segments. *Bottom*, Lower lumbosacral segments. See Materials and Methods for the procedures used for the density analysis. The key at the upper right indicates the color coding for the number of labeled neurons in each bin. *White*, *yellow*, and *red* bins represent approximately the upper 20% of the total sample of bins. Bins containing only one cell are not displayed in this and the other density maps. See Figure 2 for abbreviations.



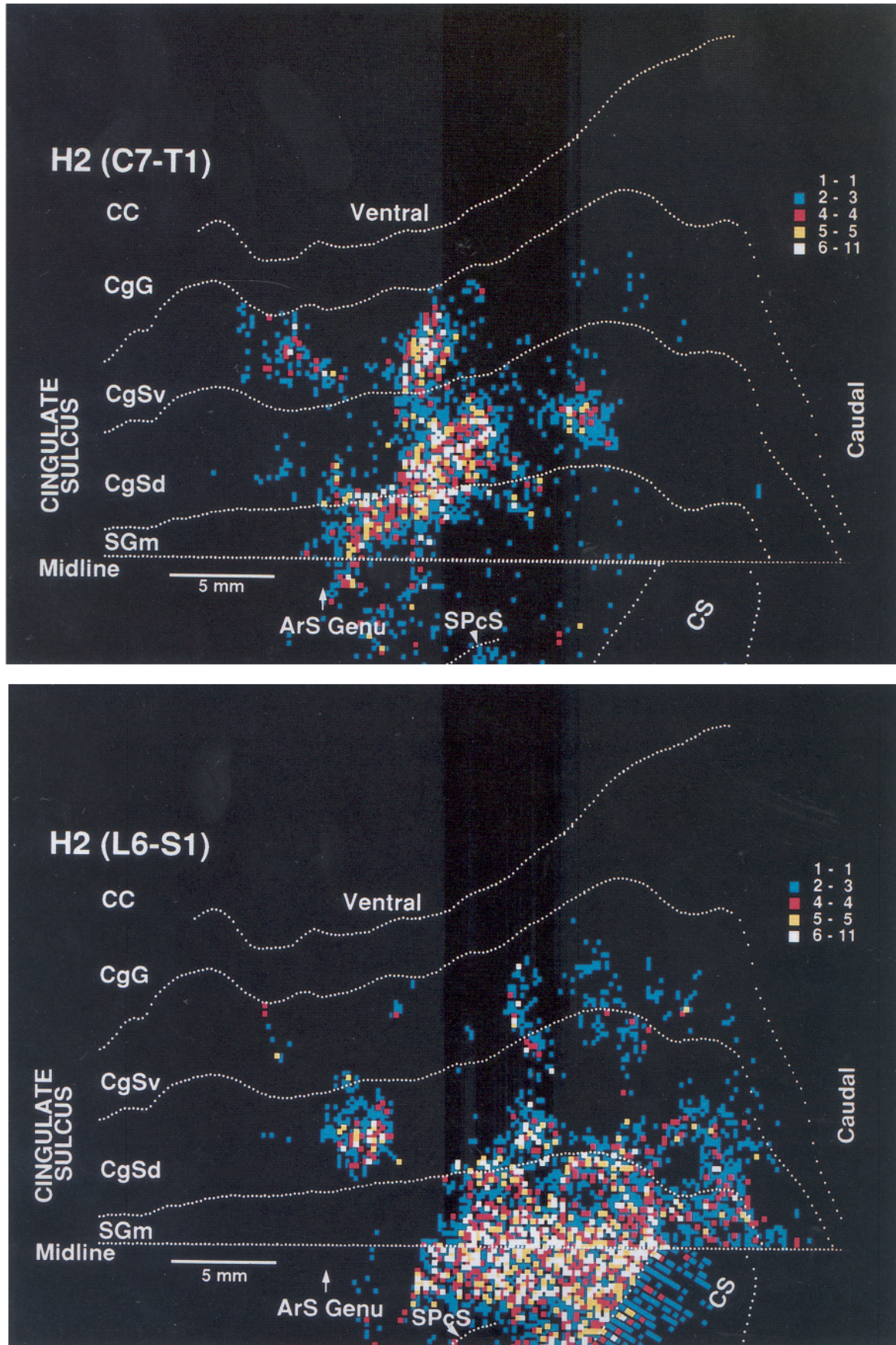


Figure 6. Density of corticospinal neurons projecting to lower cervical and lower lumbosacral segments in animal H2. *Top*, Lower cervical segments. *Bottom*, Lower lumbosacral segments. See Figures 2 and 5 for conventions and abbreviations.

Table 3. Overlap of the regions containing corticospinal neurons projecting to lower cervical (C7-T1) and lower lumbosacral segments (L6-S1) in the premotor areas and the primary motor cortex

Motor areas	Animal							
	H1				H2			
	C7-T1 bins (%)	L6-S1 bins (%)	Overlap bins (%)	Total (%)	C7-T1 bins (%)	L6-S1 bins (%)	Overlap bins (%)	Total (%)
MI	1735 (45)	2087 (54)	53 (1)	3875 (100)	2050 (48)	2165 (50)	91 (2)	4306 (100)
PMd	493 (43)	555 (49)	90 (8)	1138 (100)	796 (59)	508 (38)	48 (3)	1352 (100)
PMv	77 (99)	1 (1)	0 (0)	78 (100)	31 (100)	0 (0)	0 (0)	31 (100)
SMA	529 (46)	533 (46)	95 (8)	1157 (100)	532 (52)	389 (38)	102 (10)	1023 (100)
CMA _d	432 (43)	486 (48)	96 (9)	1014 (100)	579 (63)	249 (27)	96 (10)	924 (100)
CMA _v	185 (31)	407 (68)	9 (1)	601 (100)	291 (46)	314 (50)	26 (4)	631 (100)
CMA _r	186 (78)	19 (8)	34 (14)	239 (100)	240 (80)	37 (12)	23 (8)	300 (100)

Every bin containing at least one neuron was counted. Bin counts for individual injection sites do not include overlap bins. Overlap bins contain at least one neuron projecting to lower cervical and at least one neuron projecting to lower lumbosacral segments.

Penfield and Welch (1951) apparently associated the leg representation of the CMA_d with the arm representation in the SMA.

CMA_v. The CMA_v is located largely on the ventral bank of the cingulate sulcus, and lies in a subfield of area 23 (area 23c) (Fig. 2B; Dum and Strick, 1991b). This cortical field is ventral to the CMA_d. Five to six percent of the corticospinal neurons labeled after tracer injections into lower cervical or lower lumbosacral segments were located in the CMA_v (Table 1).

The regions of the CMA_v that projected to lower cervical segments were almost entirely separate from those that projected to lower lumbosacral segments (Figs. 3–7). Only 1–4% of the bins in the CMA_v were overlap bins (Table 3). In fact, the regions of the CMA_v that projected to the two segmental levels were separated by a region which was devoid of labeled neurons. Corticospinal neurons that projected to lower cervical segments were situated in the ventral bank of the cingulate sulcus beginning at levels 2–3 mm caudal to the arcuate genu and extending further caudally for 3–4 mm (Figs. 3–6). Corticospinal neurons that projected to lower lumbosacral segments were located more caudally. They began on the ventral bank of the cingulate sulcus and extended onto the dorsal bank of the sulcus in the caudal part of the CMA_v. Thus, the CMA_v contains distinct arm and leg representations with the arm representation rostral to the leg (Figs. 7, 8). As noted above, additional clusters of labeled neurons that projected to cervical or lumbosacral segments lay just caudal to the central sulcus and the main group of corticospinal neurons in the CMA_v. These neurons were located in regions of the medial wall related to somatosensory function and, will not be described further in this report.

CMA_r. The CMA_r is located in the banks of the cingulate sulcus within a subfield of area 24 (24c) (Fig. 2B; Hutchins et al., 1988; Dum and Strick, 1991b). This cortical field is found both rostral and caudal to the genu of the arcuate sulcus. The CMA_r contained 2–3% of the neurons labeled after tracer injections into lower cervical or lower lumbosacral segments (Table 1).

Although tracer injections into both cervical and lumbosacral segments labeled neurons in the CMA_r, many more neurons were labeled after the tracer injections into lower cervical segments (Table 1; see also Table 2). The ratio of CMA_r neurons that projected to lower cervical versus lumbosacral segments was 4:1 (Table 1). In contrast, when all the cortical areas in the frontal lobe were considered together, this ratio was 1:1. In this respect, the CMA_r is unique among the medial wall motor areas in having a corticospinal projection that is more focused upon cervical segments.

In H1, neurons projecting to lumbosacral segments tended to be concentrated more rostral and more ventral than those that projected to lower cervical segments (Figs. 3, top; 5). This arrangement was not as apparent for H2, although the peak density of lumbosacral projections from the CMA_r in H2 was located rostrally on the ventral bank of the cingulate sulcus (Figs. 3, bottom; 6). Compared with other medial wall motor areas, the CMA_r had more overlap bins (8–14%, Table 3). Because of this and the fact that few neurons in the CMA_r projected to lumbosacral segments, it is difficult to determine whether the CMA_r is somatotopically organized (Figs. 7, 8).

Proximal and distal arm representation in the premotor areas on the medial wall

After tracer injections into cervical segments of the spinal cord, the percentage of corticospinal neurons in the premotor areas on the medial wall (32–45%) was comparable to that in the arm area of the primary motor cortex (30–43%) (Table 2). When all of the premotor areas were considered, the majority (57–70%) of the neurons projecting to cervical segments were located in the arm representations of the premotor areas. These findings confirm our prior observations that the total number of corticospinal neurons in the arm representations of the premotor areas equaled or exceeded the total number of corticospinal neu-

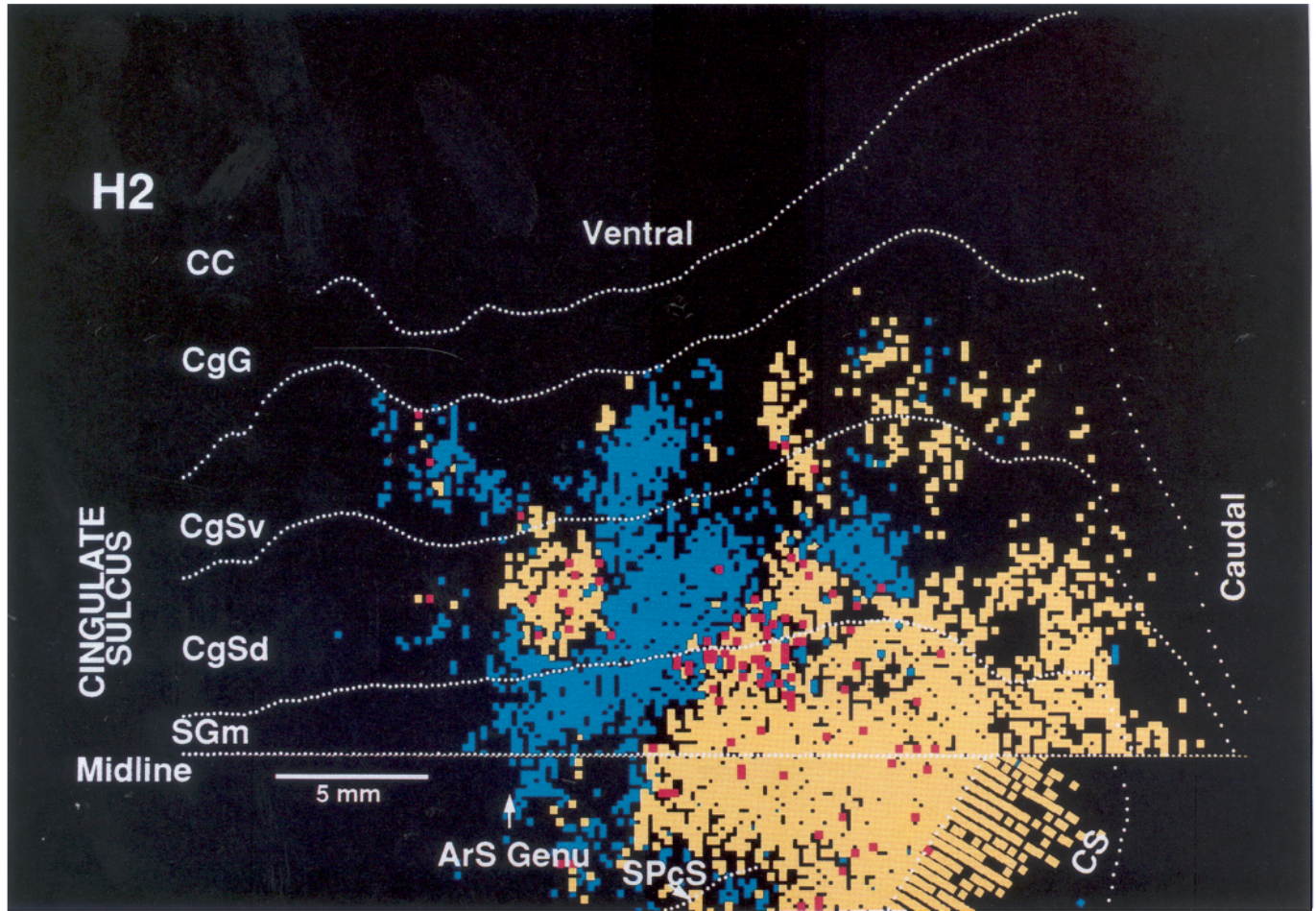


Figure 7. Overlap map of corticospinal neurons projecting to lower cervical and lower lumbar segments. Layer V of each section was divided into bins 200 μm wide (see Materials and Methods for details). *Blue* bins contain only neurons that project to cervical segments; *yellow* bins contain only neurons that project to lumbosacral segments; *red* bins contain two or more neurons projecting to cervical segments and two or more neurons projecting to lumbosacral segments (“overlap” bins). Note that few overlap bins are present in any of the cortical motor areas. See Figure 2 for conventions and abbreviations.

rons in the arm representation of the primary motor cortex (Dum and Strick, 1991b).

Within the “arm” representation of each premotor area on the medial wall of the hemisphere, the regions that contained corticospinal neurons projecting to upper cervical segments overlapped considerably with those projecting to lower cervical segments (Figs. 9–11). For example, in H3, we found that between 17 and 19% of the bins in each premotor area on the medial wall contained neurons projecting to upper cervical segments and neurons projecting to lower cervical segments (Table 4). Although this amount of intermingling may seem large, it is considerably less than what we observed in the arm area of the primary motor cortex (28%) (Table 4; He et al., 1993).

Despite the presence of intermingling, we found that the regions that projected *most densely* to lower cervical segments were largely separate from those that projected *most densely* to upper cervical segments in each of the premotor areas (Figs. 12, 13). We examined this issue by generating “overlap” maps which displayed only ‘high density’ bins (Fig. 13). In these maps, bins with a high density of neurons projecting to lower cervical segments were colored blue, those with a high density of neurons projecting to upper cervical segments were yellow and those with a high density of both types of neurons were red

(see Materials and Methods for further details). Less than 4% of the bins in these maps were red (i.e., “high density” overlap bins) (Fig. 14).

The spatial separation within each premotor area of regions which projected to different cervical levels was clearly evident in the “overlap” maps (Fig. 13). We have previously presented evidence that this type of data indicates the topographic organization of proximal and distal representation within each arm area (He et al., 1993). Therefore, the following section will describe the differential location of regions with dense projections to upper or lower cervical segments.

SMA. Corticospinal neurons that projected to lower cervical segments were found approximately 2–9 mm caudal to the genu of the arcuate sulcus (Figs. 9, top; 10, 12, bottom). Rostrally within this region, corticospinal neurons were found throughout the full width of the medial part of the superior frontal gyrus, whereas caudally neurons were most concentrated at the juncture of the superior frontal gyrus with the dorsal bank of the cingulate sulcus. In general, the part of the SMA that most densely innervates lower cervical segments corresponds to a caudal and ventral region within the arm representation (Fig. 13). This is particularly clear in H2 and H3 (Figs. 6, 12, 13).

A small number of high density bins with neurons projecting

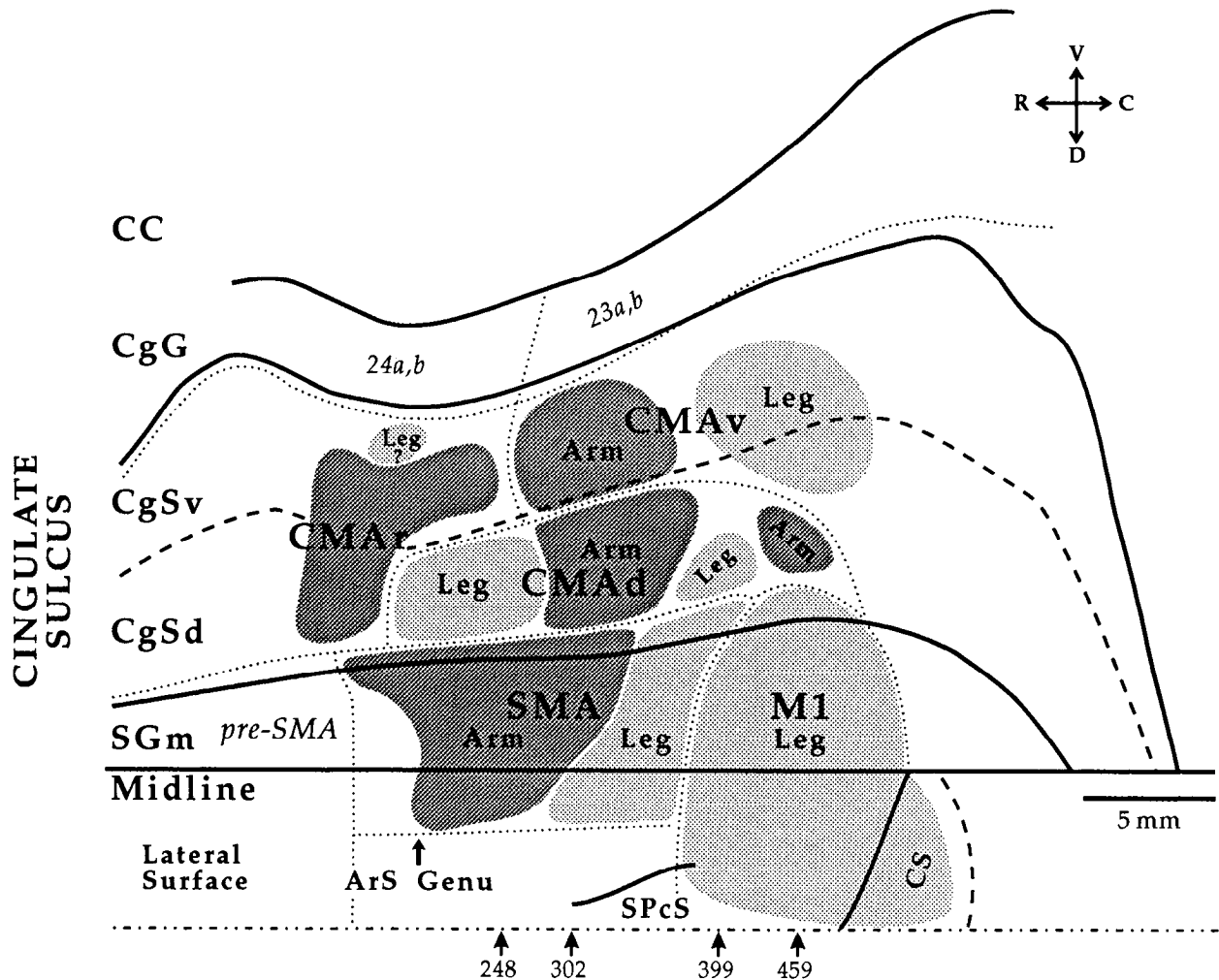


Figure 8. Summary of “arm” and “leg” representation in each motor area on the medial wall of the hemisphere. In this map, the arm representations are based on the location of neurons that project to upper and lower cervical segments (animals H1, H2, H3, and H7). The leg representations are based on the location of neurons that project to lower lumbosacral segments (animals H1 and H2). *Arrows and numbers* indicate the locations of the sections shown in Figure 4. See Figure 2 for conventions and abbreviations.

to lower cervical segments was found in the part of the SMA that extends onto the lateral surface of the hemisphere (e.g., see H1, Fig. 5, top; H2, Fig. 6, top). These neurons were located at or caudal to the level of the genu of the arcuate sulcus. This small cluster of labeled neurons appears to be separate from the main focus of SMA projections to lower cervical segments (Fig. 15).

Most neurons that projected to upper cervical segments were found approximately 0–5 mm caudal to the genu of the arcuate sulcus (Figs. 9, bottom; 10, 12, top). The majority of the high density bins that contained neurons projecting to upper cervical segments were located on the medial wall of the hemisphere, but some of them extended onto the adjacent lateral surface. We found negligible overlap (4%) of the high density bins projecting to upper cervical segments with those projecting to lower cervical segments (Figs. 13, 14). However, the high density bins projecting to the two cervical levels were interdigitated in the center of the SMA arm representation. This suggests that the pattern of arm representation in this portion of the SMA may be complex. On the other hand, the region of the SMA that most densely innervated upper cervical segments tended to be rostral and somewhat dorsal to the region that most densely innervated

lower cervical segments (Figs. 13, 15). Thus, separate regions within the SMA provide dense projections to each cervical level. This observation implies that the SMA contains distinct proximal and distal regions within its arm representation (Fig. 15).

When the results from H3 and H7 were averaged, the number of high density bins with neurons projecting to lower cervical segments was nearly equal to the number with neurons projecting to upper cervical segments (Fig. 14). This observation suggests that the amount of the SMA allotted to the representation of the distal arm is comparable to that allotted to the representation of the proximal arm. In this respect, the arm area of the SMA is quite similar to the arm area of the primary motor cortex where comparable amounts of cortex were allotted to the representation of proximal and distal musculature (Fig. 14; He et al., 1993).

CMAc. High density bins with neurons projecting to lower cervical segments formed two groups within the arm representation of the CMAc (Figs. 12, 13; see also Figs. 5, 6). The largest group was located on the dorsal bank of the cingulate sulcus at levels 5–10 mm caudal to the genu of the arcuate sulcus. The second, smaller group was located more caudally, approximately 12–14 mm from the genu of the arcuate sulcus.

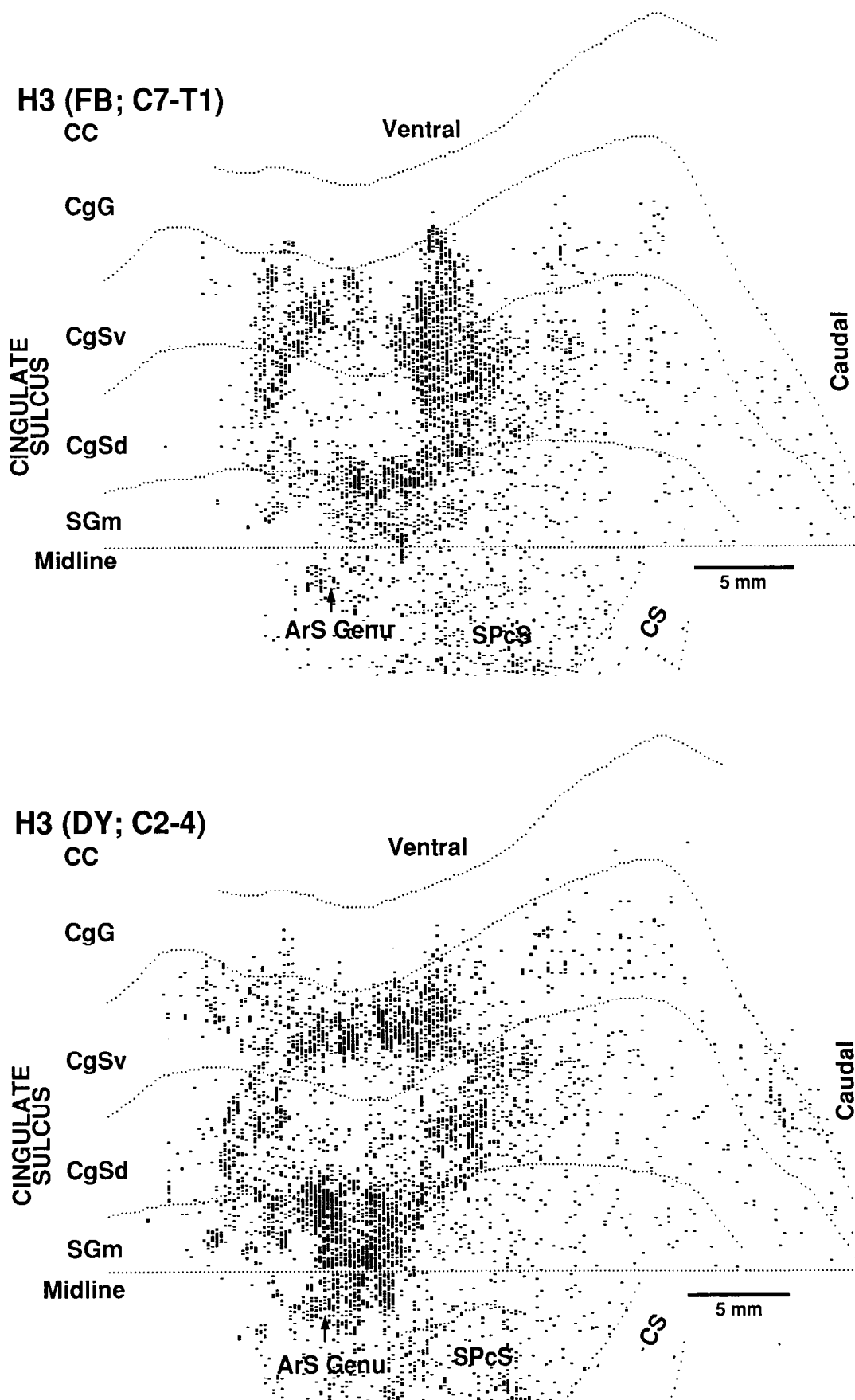


Figure 9. Maps of corticospinal neurons projecting to different cervical segments in animal H3. *Top*, Neurons labeled by tracer injections into lower cervical segments (C7–T1). *Bottom*, Neurons labeled by tracer injections into upper cervical segments (C2–4). Each labeled neuron is indicated by a solid dot. See Figure 2 for conventions and abbreviations.

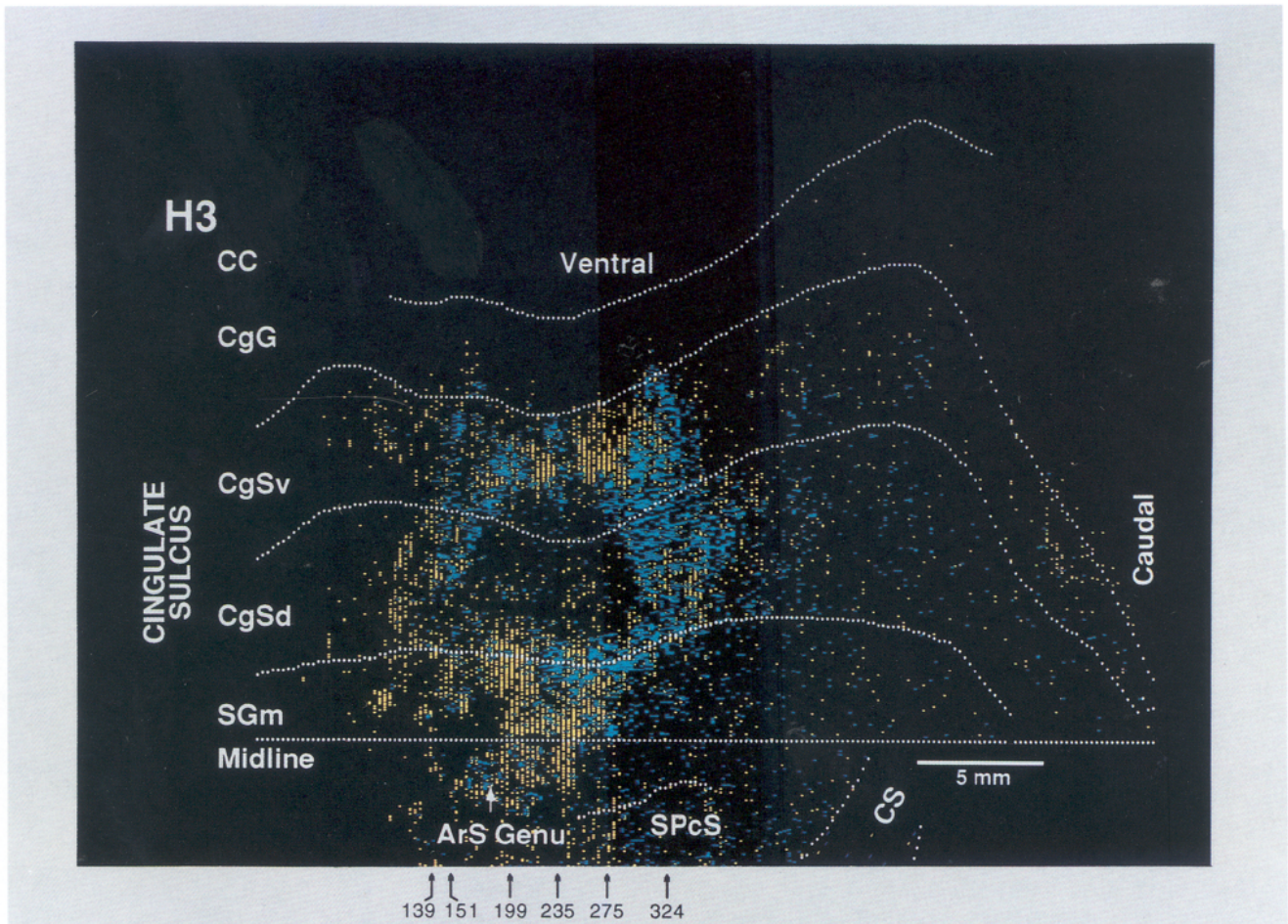


Figure 10. Combined map of corticospinal neurons projecting to upper and lower cervical segments in animal H3. *Yellow dots*, neurons projecting to upper cervical segments (C2–C4). *Blue dots*, neurons projecting to lower cervical segments (C7–T1). *Arrows and numbers* indicate levels of sections shown in Figure 11. See Figure 2 for conventions and abbreviations.

High density bins with neurons projecting to upper cervical segments were only present rostrally within the arm representation of the CMA_d. Within this region of the CMA_d, the corticospinal projections to different cervical levels were topographically organized. High density bins projecting to lower cervical segments were found throughout the dorsal bank of the cingulate sulcus, whereas those projecting to upper cervical segments were most concentrated near the juncture of the dorsal bank with the medial wall (Figs. 12, 13). Although some high density bins projecting to lower cervical segments were found among those projecting to upper cervical segments, the number of overlap bins was negligible (2%). Consequently, the CMA_d appears to be as topographically organized as the SMA (Fig. 15).

In the CMA_d, the number of high density bins with neurons projecting to lower cervical segments was approximately four times greater than the number projecting to upper cervical segments (Fig. 14). This result and the absence of high density bins with neurons projecting to upper cervical segments in the caudal part of the CMA_d suggest that the representation of the distal arm is emphasized in the CMA_d (Figs. 13, 15). In this respect, the arm representation of the CMA_d is quite different from the arm representations of both the SMA and primary motor cortex.

CMA_v. High density bins with neurons projecting to lower cervical segments were found on the ventral bank of the cingulate sulcus, 5–9 mm caudal to the genu of the arcuate sulcus

(Figs. 12, 13; see also Figs. 5, 6). Many of these bins were located in the depths of the cingulate sulcus. Caudally, these bins extended from the depth of the sulcus to the juncture of the ventral bank with the cingulate gyrus. High density bins with neurons projecting to upper cervical segments tended to be located more rostrally and were found 4–7 mm caudal to the genu of the arcuate sulcus. Very few overlap bins were found in the arm representation of the CMA_v (1%). When the results from H3 and H7 were averaged, the number of high density bins in the CMA_v with neurons projecting to lower cervical segments was approximately 2 times the number projecting to upper cervical segments (Fig. 14). Thus, the arm representations of the CMA_v and CMA_d are similar in that both are topographically organized and both have large representations of distal musculature (Fig. 15).

CMA_r. Within the arm representation of the CMA_r, both banks of the cingulate sulcus contained high density bins with neurons projecting to either upper or lower cervical segments (Figs. 12, 13). In general, the majority of the high density bins were located on the ventral bank. The high density bins on the dorsal bank tended to be rostral to the level of the arcuate genu, whereas those on the ventral bank could extend for 1–3 mm on either side of the genu. In some instances, a gap or low density region separated the high density bins on the ventral bank from those on the dorsal bank (e.g., H1, Fig. 5, top; H2, Fig. 6, top), but this was not always the case (e.g., H3, Fig. 12).

H3

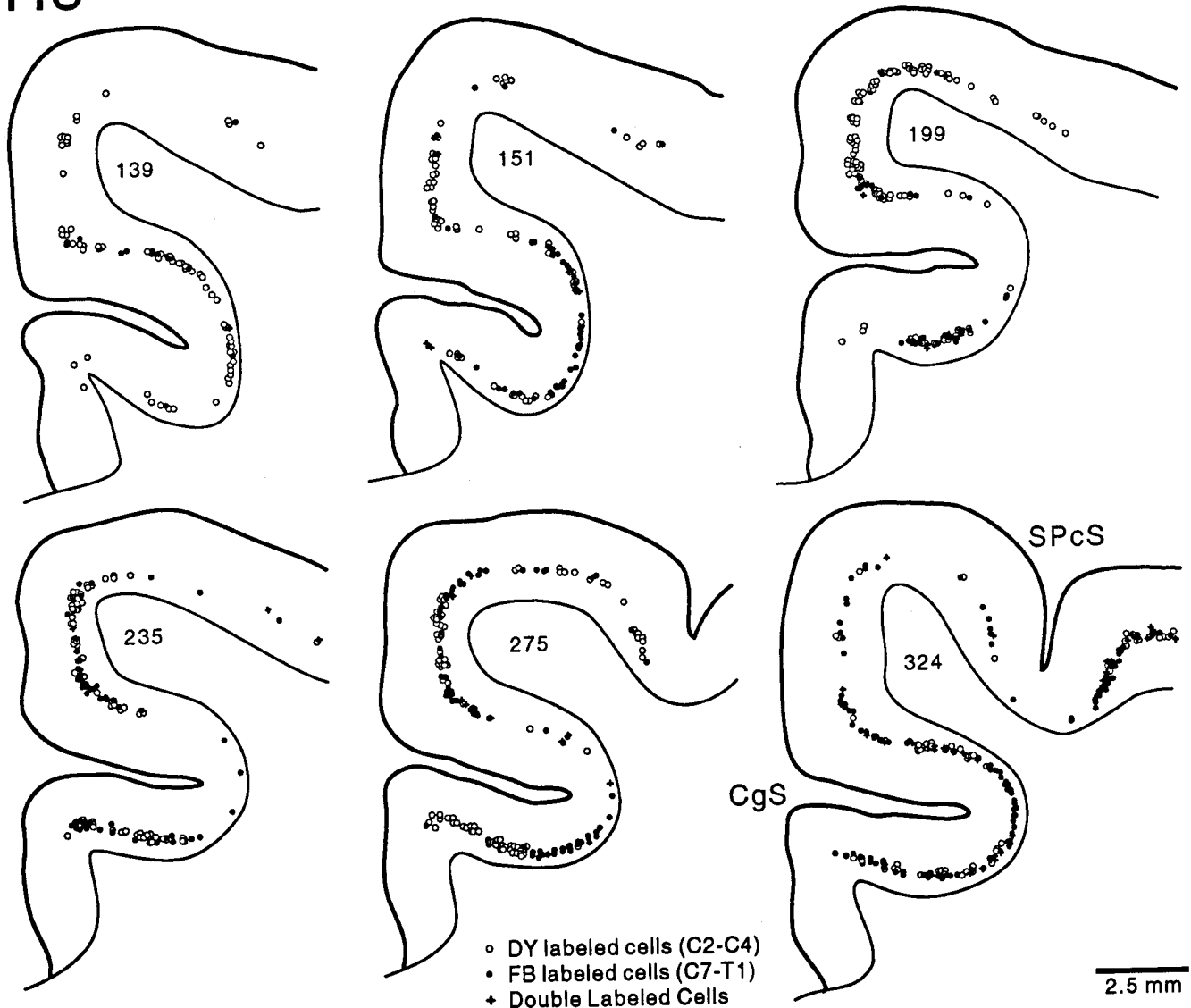


Figure 11. Coronal sections from animal H3. *Solid dots*, Neurons projecting to lower cervical segments. *Open circles*, Neurons projecting to lower lumbosacral segments. *Plus signs*, “Double labeled” neurons. The location of each section is indicated by the numbered arrows in Figure 10. See Figure 2 for conventions and abbreviations.

Although the location and number of high density bins innervating different segmental levels varied somewhat among animals, high density bins with neurons projecting to upper cervical segments tended to be split into two groups (Figs. 12, 13). On the dorsal bank of the sulcus, these bins were located rostral to those projecting to lower cervical segments. Conversely, on the ventral bank, the high density bins projecting to upper cervical segments were usually caudal to those projecting to lower cervical segments. Although the number of overlap bins in the CMAR was small (4%), the high density bins projecting to different cervical segments exhibited some intermingling on the ventral bank (Fig. 13). Thus, the map of arm representation in the CMAR is quite complex (Fig. 15). Even so, the number of high density bins in the CMAR with neurons projecting to lower cervical segments was approximately three times the number projecting to upper cervical segments (Fig. 14). This result sug-

gests that a substantial representation of the distal musculature exists in the arm area of the CMAR.

Discussion

There are three major findings of the present study. *First*, we found that all four of the premotor areas on the medial wall of the hemisphere project to cervical and lumbosacral segments of the spinal cord. Three of these premotor areas (SMA, CMAd, and CMAv) are like the primary motor cortex in having distinct arm and leg representations (Fig. 8; for comparison with the primary motor cortex, see He et al., 1993, their Fig. 17). *Second*, we found that each premotor area projects to both upper and lower cervical segments. In fact, the two cervical levels receive their densest input from largely separate regions within each premotor area. This observation suggests that each premotor area contains distinct representations of both distal and proximal

Table 4. Overlap of the regions containing corticospinal neurons projecting to upper cervical (C2–C4) and lower cervical segments (C7–T1) in the premotor areas and the primary motor cortex.

Motor areas	Animal							
	H3				H7			
	C2–C4 bins (%)	C7–T1 bins (%)	Overlap bins (%)	Total (%)	C2–C4 bins (%)	C7–T1 bins (%)	Overlap bins (%)	Total (%)
MI	995 (39)	850 (33)	731 (28)	2576 (100)	536 (22)	1163 (49)	689 (29)	2388 (100)
PMd	968 (53)	620 (34)	231 (13)	1819 (100)	420 (31)	795 (58)	150 (11)	1365 (100)
PMv	351 (87)	31 (8)	23 (5)	405 (100)	160 (72)	37 (17)	26 (11)	223 (100)
SMA	611 (46)	460 (35)	246 (19)	1317 (100)	242 (27)	510 (56)	152 (17)	904 (100)
CMAd	325 (35)	423 (46)	174 (19)	922 (100)	128 (26)	310 (63)	56 (11)	494 (100)
CMAv	348 (44)	307 (39)	138 (17)	793 (100)	75 (19)	286 (72)	33 (9)	394 (100)
CMAr	492 (51)	307 (31)	173 (18)	972 (100)	31 (7)	382 (90)	11 (3)	424 (100)

Every bin containing at least one neuron was counted. Bin counts for individual injection sites do not include overlap bins. Overlap bins contain at least one neuron projecting to upper cervical and at least one neuron projecting to lower cervical segments.

arm musculature (Fig. 15). *Third*, we found that the size of the distal representation in each premotor area on the medial wall is comparable to or larger than the size of its proximal representation (Figs. 14, 15). Thus, the anatomical substrate exists for the premotor areas on the medial wall to make substantial contributions to the control of distal, as well as, proximal arm movements.

Methodological considerations

Our conclusions about body representation in the premotor areas are based on tracer injections into different segmental levels. We have thoroughly discussed the limitations of this approach in a prior publication (He et al., 1993) and therefore, will only briefly review the logic behind our experimental strategy here. We have argued that the cortical regions containing a high density of neurons labeled after tracer injections into a given segmental level will, in most instances, be concerned with the body part *most* represented at that level. For example, the interneurons and motoneurons *most* heavily represented in lower cervical segments are those involved in the control of distal musculature, whereas the interneurons and motoneurons *most* heavily represented in upper cervical segments are those involved in the control of more proximal musculature (Kuypers, 1981; see also He et al., 1993). As a consequence, it is likely that regions containing a high density of neurons labeled by tracer injections into lower cervical segments will be concerned with the control of distal forelimb movements. Similarly, the regions with a high density of neurons labeled by tracer injections into upper cervical segments will be concerned with the control of proximal forelimb movements. Despite the absence of a strict somatotopic organization at the segmental level, this approach is capable of defining the macro-organization of body representation in each of the cortical motor areas.

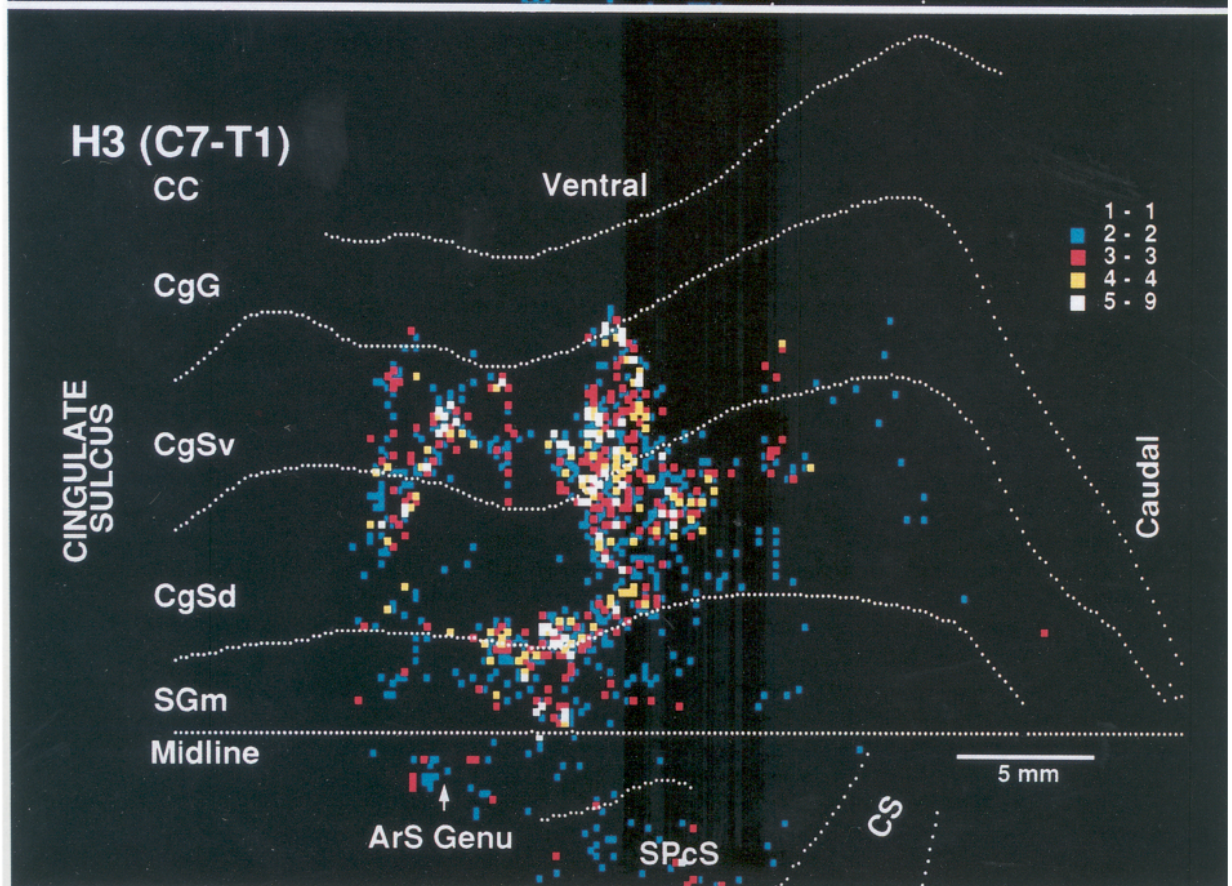
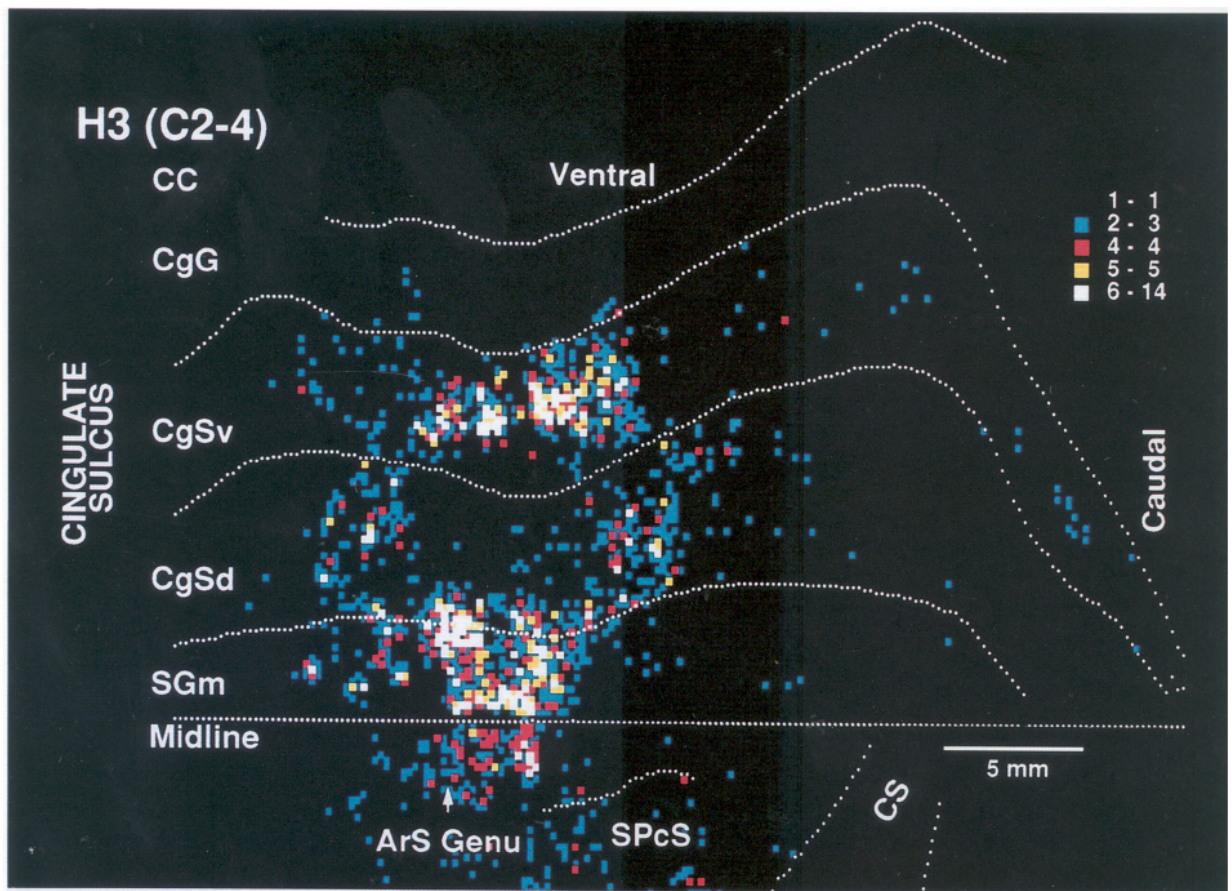
Our discussion of body maps in the premotor areas is limited to the representation of the arm and leg because our injection

sites were placed in cervical and lumbosacral segments of spinal cord. Thus, our observations do not provide any evidence about the location of face representation in the premotor areas. On the other hand, the results of anatomical and physiological mapping suggest that the SMA and CMAr each contain a representation of the face along with representations of the arm and leg (Brinkman and Porter, 1979; Muakkassa and Strick, 1979; Godschalk et al., 1984; Strick, 1985; Mitz and Wise, 1987; Luppino et al., 1991; Matsuzaka et al., 1992; Morecraft and Van Hoesen, 1992). The face representation in both of these cortical areas is located rostral to the representation of other body parts. In contrast, there is no evidence for a face representation in the CMAd and CMAv. Although this issue should be explored further, some of the premotor areas may lack a complete map of the body.

Revision of the map of arm representation in the SMA

Our map of the SMA (Figs. 8, 15) represents a significant revision of that originally proposed by Woolsey and coworkers (1952). Woolsey's SMA included both the mesial aspect of the superior frontal gyrus and the dorsal bank of the cingulate sulcus. The results of recent studies indicate that this region contains at least four functional areas: the pre-SMA, the SMA, the CMAd, and the CMAr (pre-SMA: Rizzolatti et al., 1990; Luppino et al., 1991; Matsuzaka et al., 1992; CMAd and CMAr: Hutchins et al., 1988; Dum and Strick, 1991a,b; Shima et al., 1991). The definition of the SMA is generally restricted to the part of area 6 on the mesial aspect of the superior frontal gyrus which has *dense* projections to the primary motor cortex and to the spinal cord (for references and review, see Dum and Strick, 1991b).

The results of the present study suggest that the arrangement of body parts within the SMA differs substantially from that described by Woolsey et al. (1952). The most striking differences are found in the arm area of the SMA. In Woolsey's map, the distal forelimb was represented dorsally in the SMA at levels



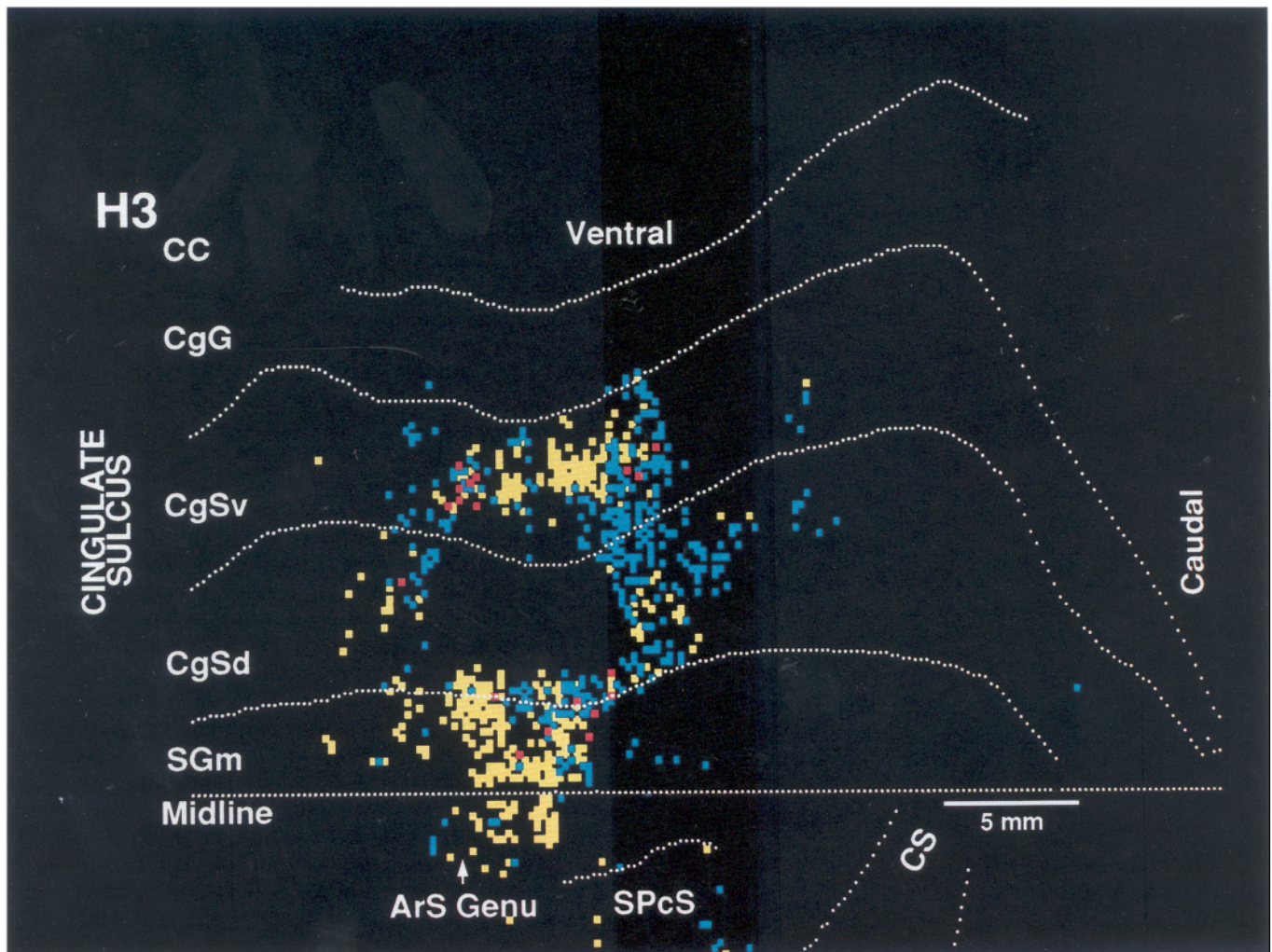


Figure 13. Overlap map of corticospinal neurons projecting to upper cervical and lower cervical segments. Only "high density" bins are displayed (i.e., the white, yellow, and red bins in Fig. 12). *Blue bins* contain only neurons that project to lower cervical segments; *yellow bins* contain only neurons that project to upper cervical segments; *red bins* contain a high density of neurons projecting to lower cervical segments and a high density of neurons projecting to upper cervical segments ("overlap" bins). Note that although there is some intermingling of blue and yellow bins, few red ("overlap") bins are found in any premotor area. See Figure 2 for conventions and abbreviations.

largely rostral to the genu of the arcuate sulcus; the proximal forelimb was represented more caudally and ventrally (Fig. 2A). In contrast, we found that the entire representation of the arm is located largely caudal to the genu of the arcuate sulcus (Figs. 8, 15; see also Dum and Strick, 1991a,b). Furthermore, our results indicate that the representation of the arm is oriented opposite to that in Woolsey's map. We found that the distal forelimb is mainly represented ventral and caudal to more proximal body parts (Figs. 13, 15). We also found a small isolated representation of the distal forelimb in the most dorsal portion of the SMA which extends onto the lateral surface of the hemisphere. This is where the thumb is represented in Woolsey's map. Perhaps the orientation of the arm in Woolsey's map was strongly influenced by this small component of the distal forelimb representation.

Our view regarding the pattern of arm representation in the SMA is supported by the observations of Macpherson et al. (1982) who found that intracortical stimulation evoked movements of the distal forelimb at sites which were located ventrally within the SMA proper. Although other studies using intracortical stimulation have questioned whether proximal and distal arm movements are topographically represented within the SMA (e.g., Mitz and Wise, 1987; Luppino et al., 1991), the illustrations from those studies confirm that movements of the distal forelimb were generally evoked from sites within the ventral half of the SMA (Mitz and Wise, 1987, their Fig. 7; Luppino et al., 1991, their Figs. 9, 10). Conversely, proximal movements were evoked throughout the SMA, but clearly predominated in its dorsal half. The differential location of distal and proximal movements was particularly evident in case Mk-5r of Luppino

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Figure 12. Density of corticospinal neurons projecting to upper and lower cervical segments in animal H3. *Top*, Upper cervical segments (C2–C4). *Bottom*, Lower cervical segments (C7–T1). The key at the upper right indicates the color coding for the number of labeled neurons in each bin. See Figures 2 and 5 for conventions and abbreviations.

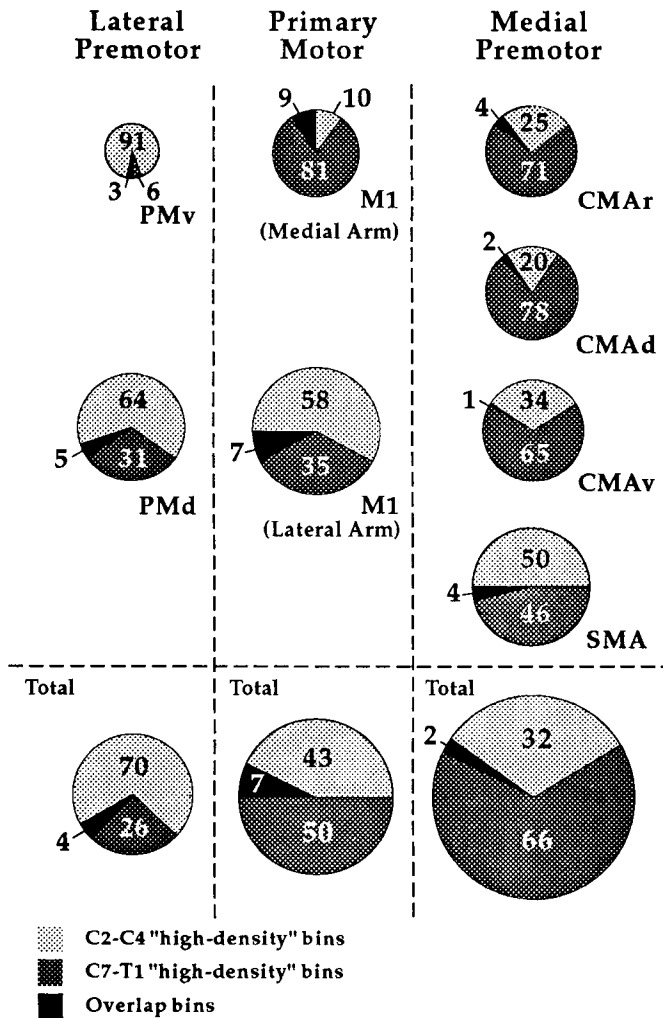


Figure 14. Distribution of 'high density' bins projecting to upper or lower cervical segments within each motor area of the frontal lobe. Numbers indicate the percentage of upper cervical, lower cervical and "overlap" bins in each motor area. Circles representing each cortical area are scaled according to the number of high density bins in each region (average of H3 and H7). Note that the premotor areas on the medial wall have a high percentage of bins that project densely to the lower cervical segments.

et al. (1991, their Fig. 10). Thus, the results of intracortical stimulation generally support our conclusion that the proximal and distal arm are most densely represented at different sites within the SMA.

Tokuno and Tanji (1993) did not find a "clearly segregated topography" in the arm region of the SMA or in the caudal cingulate motor areas. They injected two fluorescent tracers into different regions of the primary motor cortex—one tracer was injected into a region of proximal arm representation and another was injected into a region of distal arm representation. Direct comparisons between their study and ours are difficult because Tokuno and Tanji did not make an unfolded reconstruction of the medial wall and they did not define the regions of each premotor area that projected most densely to each injection site. Nevertheless, the differences between our conclusions and those of Tokuno and Tanji may be more apparent than real. Their basic finding was that projections from the premotor areas to the primary motor cortex were not as topographically organized as those from the parietal lobe. In contrast, our fundamental ob-

ervation is that the corticospinal projections from the SMA, as well as those from the CMAr and CMAv, are as topographically organized as the corticospinal projections from the primary motor cortex. Therefore, the disparity in our respective conclusions may simply result from a different frame of reference.

Extent of proximal and distal forelimb representation in the SMA

An enduring hypothesis about the function of the SMA is that it is involved in the control of body and limb posture. In particular, the output of the SMA has been thought to generate the base of proximal muscular support which is necessary for performing movements of distal limb segments (e.g., Travis, 1955; Denny-Brown, 1966; Wiesendanger et al., 1973; Humphrey, 1979; Wiesendanger, 1986; Tokuno and Tanji, 1993). This view of SMA function has been sustained by the results of mapping studies which suggested that the SMA contains only a small representation of the distal limb (e.g., Macpherson et al., 1982; Luppino et al., 1991). Our observations suggest that the function of the SMA is not limited to the control of proximal limb movements. We found that the size of the SMA region which projects most densely to lower cervical segments is comparable to the region which projects most densely to upper cervical segments. This result suggests that the amount of the SMA devoted to the distal forelimb is nearly equal to that devoted to the more proximal body parts. In fact, the relative size of the distal forelimb representation in the SMA appears to be quite similar to that in the primary motor cortex (Fig. 14). Thus, the anatomical substrate which would allow the SMA to be involved in the control of distal, as well as proximal limb movements, is present.

Similar arguments apply to proximal and distal representation in the cingulate motor areas. In particular, our results suggest that the size of the distal arm representation in the three cingulate motor areas is two to three times greater than that of their proximal representation (Fig. 14). Based on this size disparity, we propose that the three cingulate motor areas are particularly involved in the control of distal movement.

Body maps in the caudal cingulate motor areas

There is now general agreement that the cortex in a caudal portion of the cingulate sulcus is involved in skeletomotor function (e.g., Hutchins et al., 1988; Dum and Strick, 1991a,b; Luppino et al., 1991; Shima et al., 1991; Morecraft and Van Hoesen, 1992). However, the number of cortical areas contained in this region and the arrangement of body parts in these areas has been the subject of some controversy. For example, Morecraft and Van Hoesen (1992), using anatomical methods, found that the caudal portion of the cingulate sulcus contained a single map of the body in which the arm representation was rostral to the leg representation. Their map was located largely on the ventral bank of the cingulate sulcus in area 23c. In contrast, Luppino et al. (1991), using intracortical stimulation, described a single body map in the caudal portion of the cingulate sulcus in which the leg representation was rostral to the arm representation. Their leg representation was located largely on the dorsal bank of the cingulate sulcus and their arm representation was located largely on the ventral bank of the sulcus.

The use of a double labeling strategy has helped us to resolve the controversy about maps in the cingulate sulcus. The results of the present study support our view that the caudal portion of this sulcus contains two motor areas, the CMAr in area 6c and the CMAv in area 23c (Dum and Strick, 1991b, 1993). Each of

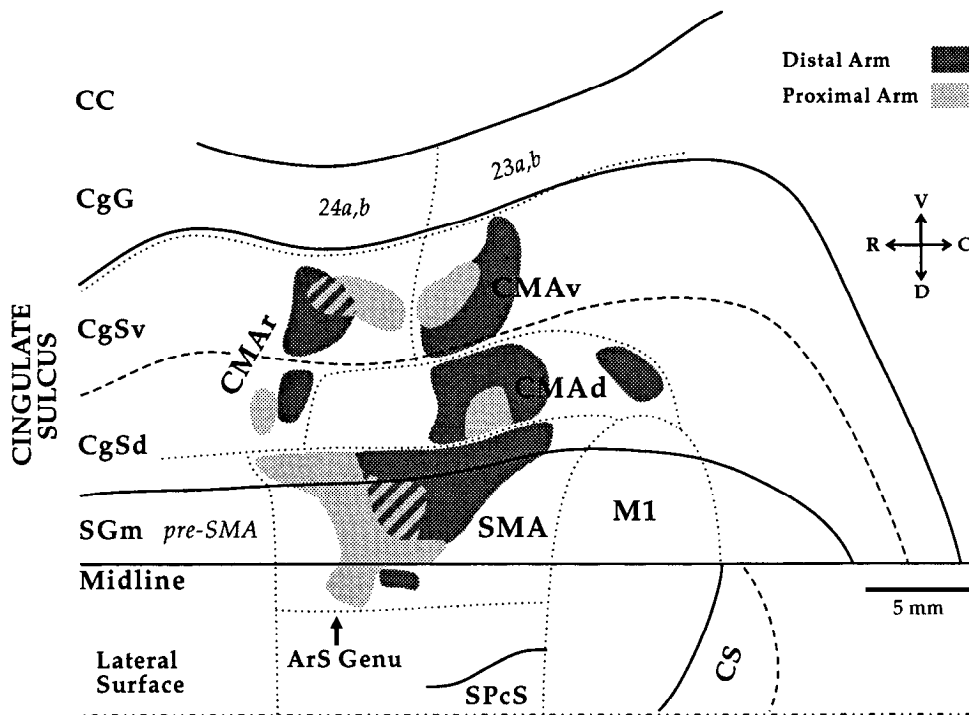


Figure 15. Summary of "proximal" and "distal" arm representation in each premotor area on the medial wall of the hemisphere. This map is based on the distribution of high density bins containing corticospinal neurons labeled following tracer injections into upper cervical (animals H3 and H7) and lower cervical segments (animals H1, H2, H3, and H7). The *mixed shading* indicates where high density bins projecting to different cervical levels were intermingled. See text for further description and discussion. See Figure 2 for conventions and abbreviations.

these motor areas has a separate arm and leg representation (Fig. 8). In the CMAv, the *leg representation is rostral* to the arm representation. In contrast, the *arm representation is rostral* to the leg representation in the CMAv. The present results also indicate that each of these motor areas has distinct regions that project to either upper or lower cervical segments. Thus, our evidence suggests that both motor areas contain separate representations of the distal and proximal arm (Fig. 15).

Prior studies support our view that the arm is represented on both banks of the cingulate sulcus. Other studies of the corticospinal system have shown that projections to cervical segments originate from both banks of the cingulate sulcus (Murray and Coulter, 1981a; Hutchins et al., 1988; Dum and Strick, 1991a,b; Galea and Darian-Smith, 1994). Both banks of the cingulate sulcus are interconnected with the arm area of the primary motor cortex (e.g., Muakkassa and Strick, 1979; Godschalk et al., 1984; Strick, 1985; Leichnetz, 1986; Dum and Strick, 1991a,b; Holsapple and Strick, 1991; Morecraft and Van Hoesen, 1992) and with the arm area of the SMA (Luppino et al., 1993). Furthermore, neurons related to active forelimb movements are found in caudal portions of both banks of the sulcus (Shima et al., 1991).

Differences in connectivity support the separation of the cingulate sulcus into the CMAv and CMAr (Dum and Strick, 1993). The CMAv is interconnected with regions of prefrontal cortex, whereas the CMAr is not (Bates and Goldman-Rakic, 1993; Morecraft and Van Hoesen, 1993; Lu et al., 1994). The CMAr, but not the CMAv, projects to the portion of the hand representation in the primary motor cortex which is buried in the anterior bank of the central sulcus (Holsapple and Strick, 1991). The two motor areas also differ in their connectivity with subdivisions of the ventrolateral thalamus (Holsapple and Strick, 1989). The major source of thalamic input to the CMAr originates from the nucleus ventralis lateralis pars oralis, a target of pallidal efferents. In contrast, the major source of thalamic input to the CMAv originates from caudal regions of the nucleus ven-

tralis lateralis pars caudalis, a target of cerebellar efferents. Based on these anatomical observations, we believe future studies will show that the CMAr and CMAv differ in their contributions to the generation and control of movement.

Why do some of the prior maps (Luppino et al., 1991, 1993; Morecraft and Van Hoesen, 1992) differ so strikingly from each other and from our maps? One explanation is that Morecraft and Van Hoesen considered almost all of the dorsal bank of the cingulate sulcus as part of the SMA (see Morecraft and Van Hoesen, 1992, their Fig. 3). Thus, they did not recognize the existence of the CMAr in area 6c on the dorsal bank. Similarly, Luppino et al. (1991, 1993) did not find an arm area on the dorsal bank. However, the procedures they used to explore the cingulate sulcus may have led to some distortions in their maps. For example, most of the penetrations by Luppino et al. (1991) were no more than 3 mm from the midline of the hemisphere. As a consequence, they did not explore a substantial portion of the cortex in the cingulate sulcus which extends 5–7 mm from the midline. Our data shows that a large portion of the corticospinal projection to lower cervical segments originates from this region of the sulcus (Fig. 15). In addition, Luppino et al. did not extensively explore the caudal portion of the ventral bank where our study and that of Morecraft and Van Hoesen (1992, 1993) place the hindlimb representation of the CMAv. Finally, Luppino et al. (1991) reconstructed their maps by projecting the responses evoked by intracortical stimulation onto the cortical surface. This method of reconstruction tends to underrepresent cortex in the fundus of a sulcus and overrepresent cortex near the entry into the sulcus. Thus, we believe that physiological studies which thoroughly explore both banks of the cingulate sulcus and use a topological method of reconstruction will confirm our proposal that each bank of the sulcus contains an arm and a leg representation.

Body map in the rostral cingulate motor area?

The CMAr is like the other premotor areas in projecting to both cervical and lumbosacral segments of the spinal cord. However,

we found that the portion of the CMAr that projects to lumbosacral segments is much smaller than the portion that innervates cervical segments. In addition, many of the corticospinal neurons in the CMAr that project to lumbosacral segments are intermingled with those that project to cervical segments. These observations suggest that although the CMAr has a representation of the arm and leg, the leg representation may be small and not entirely separate from the arm representation (Fig. 8).

Surprisingly, we found that a large percentage of the corticospinal neurons in the arm representation of the CMAr project to lower cervical segments. This result suggests that the CMAr, like the other motor areas on the medial wall, participates in some way in the generation and control of distal limb movements. This conclusion is supported by the results of Shima et al. (1991) who recorded neurons related to distal forelimb movements in a rostral portion of the cingulate sulcus that included the CMAr. It is important to note that the CMAr is unlike the other cingulate areas in having multiple groups of corticospinal neurons that project to a given cervical level. Thus, the map of arm representation in the CMAr appears to be quite complex.

Functional implications

As noted above, the medial wall of the hemisphere was thought to contain a single motor area, the SMA. As a consequence, studies of medial wall anatomy and physiology often attributed their results to this cortical area without regard to its precise location. The demonstration that the medial wall contains multiple motor areas requires that the connectivity and functions ascribed to the SMA be reevaluated. Some studies in macaques have reported that anatomical and physiological differences exist between rostral and caudal SMA (e.g., Brinkman and Porter, 1979; Tanji and Kurata, 1979; Wiesendanger and Wiesendanger, 1985a,b; Barbas and Pandya, 1987; Alexander and Crutcher, 1990; Bates and Goldman-Rakic, 1993). It is unclear whether these differences reflect variations within the SMA proper or the characteristics of the pre-SMA and SMA.

Similarly, in human studies, functional activations or lesions of the medial wall have usually been broadly assigned to the SMA, or if they are located quite rostrally, to the anterior cingulate cortex. However, the human medial wall is anatomically diverse as that of macaques (e.g., Braak, 1976, 1979, 1980), and therefore, it is likely to contain multiple motor areas in addition to the SMA (e.g., Colebatch et al., 1991; Deiber et al., 1991; Grafton et al., 1992, 1993; Paus et al., 1993; Rao et al., 1993). Little information is available on the location, extent and motor maps within these areas in humans. Such information will be critical to further progress in understanding medial wall function.

The SMA, CMAr, CMA_d, and CMA_v are members of a set of premotor areas in the frontal lobe, all of which project directly to the primary motor cortex (Dum and Strick, 1991b). In the past, the premotor areas have been viewed as hierarchically superior to the primary motor cortex, in part, because they were thought to be more remote from the spinal cord circuits which generate motor output. According to this view, the premotor areas were concerned with the goal of movement, rather than the control of specific movement parameters. This conceptual framework included the notion that the premotor areas lacked well-defined maps of the body. The absence of such maps would endow these cortical areas with the ability to conceive of movement in terms of the ultimate goal of a task, without regard to the specific patterns of muscle activity necessary to perform the

task (Orgogozo and Larsen, 1979; Roland et al., 1980; Eccles, 1982; Goldberg, 1985).

It is now clear that the premotor areas, including those on the medial wall, have more in common with the primary motor cortex than previously suspected. Like the primary motor cortex, each of the premotor areas projects directly to the spinal cord (Dum and Strick, 1991a,b). In addition, the results of the present study and the preceding report (He et al., 1993; see also Luppino et al., 1991) indicate that maps of the body exist in most of the premotor areas. Furthermore, the relative amount of cortex in some of the premotor areas allotted to the representation of the distal forelimb is comparable to and, in some instances greater than, that in the primary motor cortex. While these features do not preclude a role for the premotor areas in generating higher order aspects of motor behavior, they are appropriate for motor areas involved in generating commands that control specific movement parameters.

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