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Research Note

Corticospinal projections from the medial wall of the hemisphere

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Summary. We injected wheat germ agglutinin conjugated to horseradish peroxidase into different segments of the spinal cord in order to examine the topographic organization of corticospinal projections from the medial wall of the hemisphere. We observed that substantial projections to the spinal cord originate not only from the supplementary motor area (SMA) in area 6, but also from 2 regions within the cingulate sulcus. The distribution of labeled neurons following tracer injections into different spinal cord segments indicates that corticospinal projections from the SMA and from the 2 cingulate regions are somatotopically organized. These findings together with other recent anatomical observations suggest that the corticospinal projections from the medial wall of the hemisphere provide the basal ganglia and limbic system with a somatotopically organized access to spinal cord mechanisms.

Key words: Supplementary motor area (SMA) – Cingulate cortex – Premotor areas – Medial wall of the hemisphere

Introduction

The corticospinal system originates not only from the primary motor cortex, but also from multiple areas in the frontal and parietal lobes (e.g., Liu and Chambers 1964; see Kuypers 1981 for a review). In fact, recent studies have demonstrated that corticospinal projections originate from 2 premotor areas in the frontal lobe, the supplementary motor area (SMA) (e.g., Biber et al. 1978; Murray and Coulter 1981; Macpherson et al. 1982a, b; Toyoshima and Sakai 1982; Nudo 1985; Martino and Strick 1987) and the arcuate premotor area (APA) (e.g., Toyoshima and Sakai 1982; Nudo 1985; Martino and Strick 1987). However, the precise origin and topographic organization of corticospinal projections from the SMA has been the subject of some controversy. Although some physiological studies have suggested that the SMA is somatotopically organized (e.g., Woolsey et al. 1952; Schlag and Schlag-Rey 1987; Mitz and Wise 1987), the results of other physiological and anatomical studies have been unclear regarding the topographic organization of SMA projections to cervical and lumbo-sacral segments of the spinal cord (e.g., Penfield and Welch 1951; Macpherson et al. 1982a, b).

In addition, corticospinal projections have been shown to originate from several areas on the medial wall of the hemisphere which are outside the SMA (Biber et al. 1978; Murray and Coulter 1981; Macpherson et al. 1982a, b; Toyoshima and Sakai 1982; Martino and Strick 1987). The topographic organization of these areas has not been clearly defined. Therefore, we examined the organization of corticospinal projections from cortical areas on the medial wall of the hemisphere to cervical and lumbo-sacral segments of the spinal cord.

Material and methods

The present study is based on the observations from 7 pig-tailed macaques (Macaca nemestrina). The origin of corticospinal projections to cervical and lumbo-sacral segments of the spinal cord was demonstrated using retrograde transport of wheat germ agglutinin conjugated to horseradish peroxidase (WGA-HRP). A description of the surgical procedures used for the spinal cord injections and details of the methods for demonstrating retrograde transport have been described previously (Schell and Strick 1984; Martino and Strick 1987). Briefly, injections of WGA-HRP were made into segments C3–T1 (n = 2), C2–C4 (n = 1), C5–C8 (n = 2), T12–L4 (n = 1) and L5–S2 (n = 1). After a 3, 4 or 7 day

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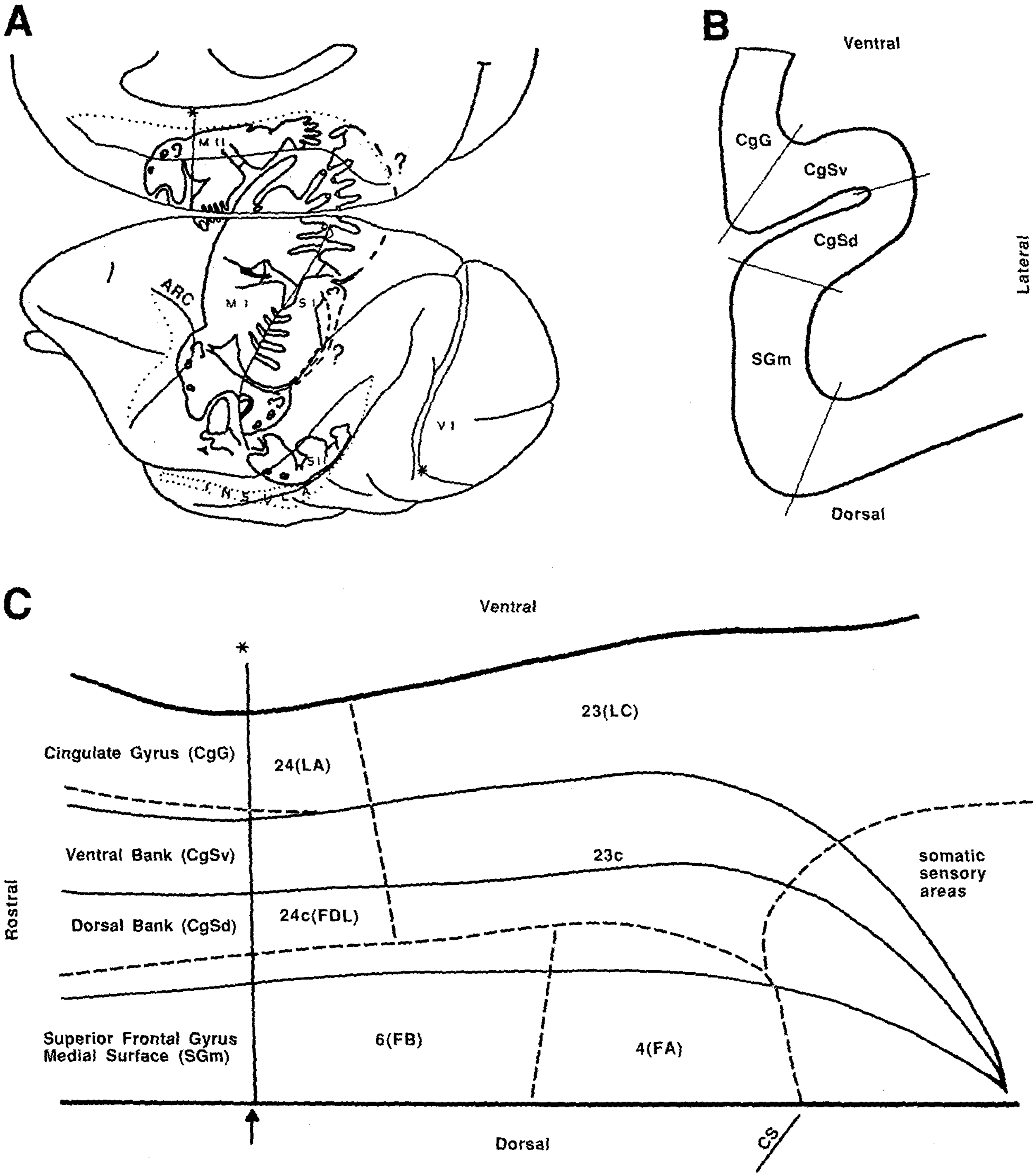

Fig. 1A–C. Cortex on the medial wall of the hemisphere. **A** Maps of body representation in the cerebral cortex according to Woolsey (1958). The medial wall of the hemisphere is reflected upwards to display the supplementary motor area (SMA). We have adopted this convention for the other sections of this figure and for Fig. 2. The cingulate sulcus is partially opened in this diagram; only the dorsal bank is shown. **B** A coronal section through the medial wall of the hemisphere at the level of the posterior extent of the arcuate sulcus (ARC). The level of this section is indicated by the vertical line in **A** marked by an asterisk. To unfold the medial wall it was divided into 4 segments indicated by the thin solid lines through the section. The abbreviations in **B** are defined in **C**. **C** Unfolded map of the medial wall of the hemisphere. Sulcal borders are indicated by solid lines and cytoarchitectonic borders are indicated by dashed lines. The vertical line indicates the level of the coronal section shown in **A** and **B**. The arrow indicates the posterior extent of the arcuate sulcus

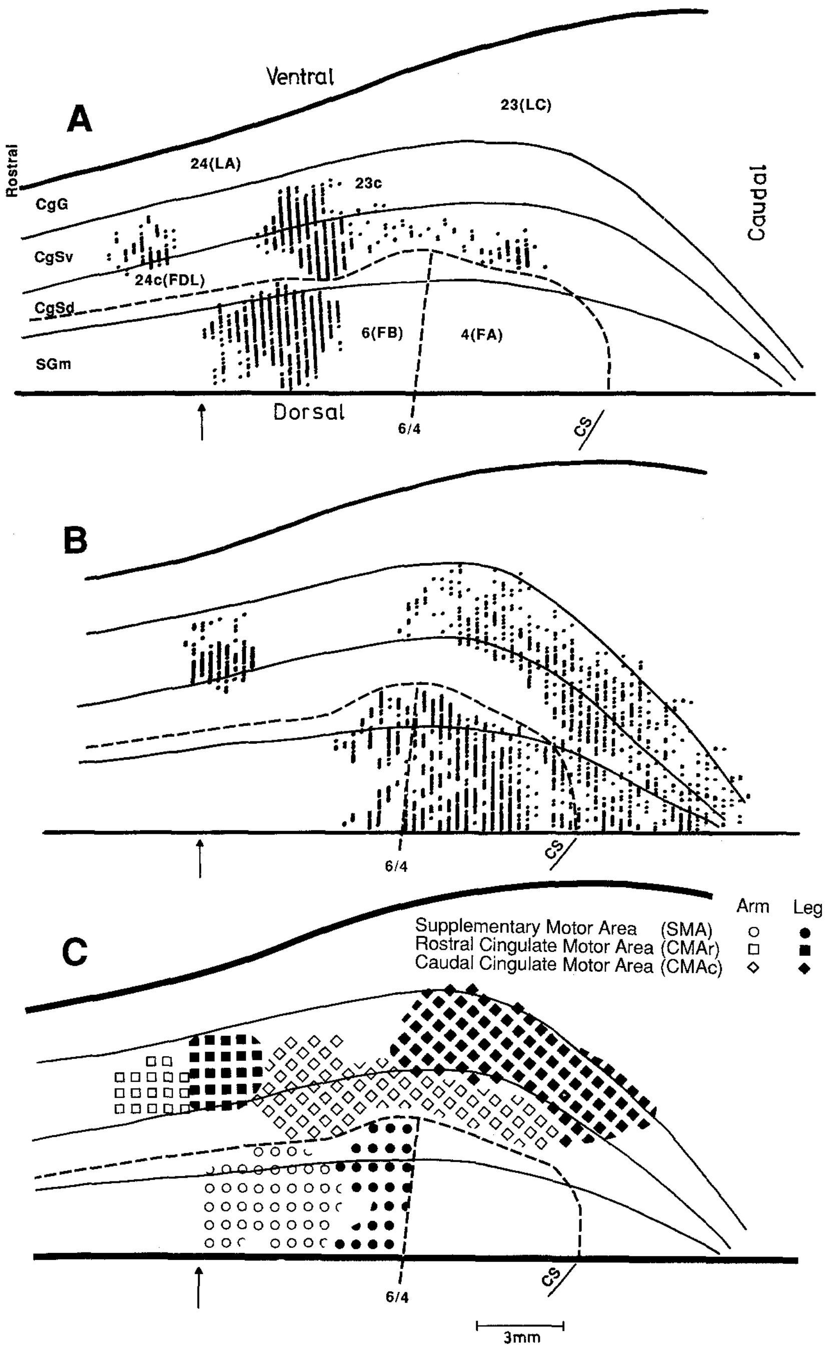

Fig. 2A–C. Topographic origin of corticospinal projections from the medial wall. The unfolded maps of the medial wall are displayed using the conventions presented in Fig. 1. Arrows in **A–C** indicate the posterior extent of the arcuate sulcus. **A** Distribution of labeled neurons following tracer injections into C5–C8. **B** Distribution of labeled neurons following injections into L5–S2. **C** Labeling shown in **A** and **B** has been plotted on a single unfolded map using symbols: Unfilled symbols, C5–C8 labeling; Filled symbols, L5–S2 labeling; Circles, labeling in the SMA; Squares, labeling in the rostral cingulate motor area (CMAr); Diamonds, labeling in the caudal cingulate motor area (CMAc). The labeled neurons in the hindlimb and tail representations in the primary motor cortex and various somatosensory areas are omitted from **C** to emphasize the pattern of projections from the premotor areas on the medial surface of the hemisphere

survival period animals were anesthetized and perfused with phosphate buffered aldehydes. Serial coronal sections of a block of brain (from the rostral margin of the arcuate sulcus to the lunate sulcus) and a large block of spinal cord (C1–T2 or T12–S3) were cut at 50 μm thickness. Every tenth section was postfixed and processed for cytoarchitecture (Mesulam 1982). The remaining sections were processed for HRP using the tetramethylbenzidine (TMB) technique (Mesulam 1982). The location of each labeled cortical neuron was charted using an X-Y plotter which was fed by two linear potentiometers coupled to movements of the microscope stage. Plots of individual sections were entered into a DEC PDP 11/03 computer using a high resolution X-Y tablet. The computer used the digitized sections to reconstruct unfolded maps of the medial wall of the hemisphere (Figs. 1C and 2).

Our display of the cortical regions on the medial wall of the hemisphere is similar to that employed by Woolsey et al. (1952; see also Wise and Tanji 1981). The medial wall of the hemisphere is oriented with the dorsal surface of the brain downward (Figs. 1 and 2). In addition, we completely 'unfolded' the medial wall of the hemisphere by separating it into 4 segments: 1) the medial aspect of the superior frontal gyrus; 2) the dorsal bank of the cingulate sulcus; 3) the ventral bank of the cingulate sulcus; and 4) the cingulate gyrus. The cytoarchitectonic borders between areas 4, 6 and subfields of areas 23 and 24 (Figs. 1 and 2) were determined using the criteria employed by Wise and Tanji (1981); Macpherson et al. (1982a) and Vogt (1985).

Results

We will present the results of 2 animals, one with tracer injections into lower segments of cervical cord and the other with injections into lower segments of lumbar and sacral cord. These animals were chosen for display because they best illustrate some of the features of the topographic organization of the origin of corticospinal projections.

Lower cervical

In one animal, injections of WGA-HRP into lower cervical segments (C5–C8) resulted in 3 regions of labeled neurons on the medial wall of the hemisphere (Fig. 2A). A large group of labeled neurons was located in area 6 on the medial aspect of the superior frontal gyrus at a level just caudal to the posterior extent of the arcuate sulcus (arrow in Fig. 2A). A second, small cluster of labeled neurons was located at rostral levels of the cingulate sulcus in a region termed FDL by Von Bonin and Bailey (1947) and area 24c by Vogt (1985). This cluster was found predominantly on the ventral bank of the sulcus beginning approximately 1.6 mm rostral to the posterior extent of the arcuate sulcus. A third and more extensive group of labeled neurons was located at intermediate levels of the cingulate sulcus in a region termed LC by Von Bonin and Bailey (1947) and area 23c by Vogt (1985). In this area, labeled neurons were found on both the dorsal and ventral banks of the sulcus beginning approximately 2.8 mm caudal to the posterior extent of the arcuate sulcus.

Lower lumbar

In another animal, tracer injections were made into lower segments of lumbar and sacral spinal cord (L5–S2). Many labeled neurons were found on the medial wall of the hemisphere caudal to the area 4/6 border (e.g., Wise and Tanji 1981; Macpherson et al. 1982a) in the hindlimb and tail representations of the primary motor and somatic sensory cortex (Fig. 2B). Three additional areas on the medial wall of the hemisphere contained labeled neurons. One group of labeled neurons was located in a posterior portion of area 6 on the medial aspect of the superior frontal gyrus. This region of labeled neurons is just anterior to the primary motor cortex (e.g., Wise and Tanji 1981). A second, small cluster of labeled neurons was located rostrally in the cingulate sulcus in area 24c (FDL). This cluster was located predominantly on the ventral bank of the cingulate sulcus beginning at the level of the posterior extent of the arcuate sulcus (arrow in Fig. 2B). A third and more extensive group of labeled neurons was located caudally in the cingulate sulcus in area 23c. In this area, labeled neurons were found predominantly on the ventral bank of the cingulate sulcus beginning approximately 9.2 mm caudal to the posterior extent of the arcuate sulcus.

The observations in these 2 animals indicate that both lower cervical and lumbo-sacral segments of spinal cord receive projections from 3 cytoarchitectonically distinct regions on the medial wall of the hemisphere, i.e., a medial portion of area 6, a subfield of area 24 (24c or FDL) and a subfield of area 23 (23c). In order to examine the topographic organization of corticospinal projections from these areas we overlapped the maps of labeled neurons from the animals described above (Fig. 2C). Labeled neurons found in regions of cortex outside of areas 6, 23 and 24 (i.e., in the hindlimb and tail representations of the primary motor cortex and in the somatic sensory cortical areas on the medial wall of the hemisphere) were omitted from the diagram to emphasize the pattern of projections from the premotor areas on the medial surface of the hemisphere. This procedure demonstrated that, in each of the 3 cortical areas, neurons labeled following tracer injections into cervical segments of spinal cord were located rostral to those labeled following injections into lower lumbar and sacral segments of spinal cord. This result suggests that the origins of corticospinal projections from medial area 6, area 24c and area 23c are somatotopically organized.

Discussion

The results of the present study indicate that there are 3 distinct regions on the medial wall of the hemisphere in the frontal lobe which project directly to the spinal cord. Each of these regions is located in a different cytoarchitectonic area of cortex. One of these regions is located in area 6 largely on the medial aspect of the superior frontal gyrus. Another region with corticospinal projections is located more rostrally in the ventral bank of the cingulate sulcus within a subfield of area 24 (24c or FDL). A third region with corticospinal projections is located more caudally in the depths of the dorsal and ventral banks of the cingulate sulcus within a subfield of area 23 (23c).

The region of medial area 6 which projects to the spinal cord lies within the supplementary motor area (SMA) as defined by Woolsey and his colleagues (Woolsey et al. 1952; see also Wise and Tanji 1981; Macpherson et al. 1982a, b). We have confirmed the results of prior studies which demonstrated direct projections from the SMA to the spinal cord (Biber et al. 1978; Murray and Coulter 1981; Macpherson et al. 1982a, b; Toyoshima and Sakai 1982; Martino and Strick 1987). Furthermore, our results provide additional evidence that the SMA is topographically organized. Tracer injections that were limited to lower cervical segments of the spinal cord labeled neurons in the SMA which were largely rostral to those labeled following injections that were limited to lower lumbar and sacral segments. Substantial overlap in the origin of projections from the SMA to cervical and lumbar segments was observed only with more widespread injections into the spinal cord. Thus, our results suggest that the SMA contains an arm representation which is largely rostral to a leg representation. We believe that the controversy concerning the topographic organization of the SMA is due, in part, to 2 factors: 1) prior studies did not focus on projections to lower cervical and lower lumbar and sacral segments; and 2) some prior studies included corticospinal projections from the 2 areas within the cingulate sulcus as part of the system which originates from the SMA.

Our observations also support prior reports of projections to the spinal cord from cortex within the cingulate sulcus (Biber et al. 1978; Murray and Coulter 1981; Macpherson et al. 1982a; Toyoshima and Sakai 1982; Martino and Strick 1987). In addition, our results indicate that the origins of corticospinal projections from the 2 cingulate areas are topographically organized. Neurons in each area which innervate lower cervical segments are located largely rostral to those which innervate lower lumbar and sacral segments. This suggests that each of the cingulate regions is somatotopically organized and contains a distinct arm and leg representation. It should be noted, however, that injections of tracers into different segments of the spinal cord can provide only a relatively gross measure of the topographic organization of corticospinal projections. Thus, the full extent of the somatotopic organization of the SMA and the 2 regions in the cingulate sulcus remains to be determined with alternative methods.

The 2 cingulate areas with corticospinal projections have a number of features in common with the SMA: 1) both cingulate regions project directly to the primary motor cortex and these projections are somatotopically organized (Muakkassa and Strick 1979; Primrose and Strick 1985); and 2) the limited evidence available suggests that surface and intracortical stimulation of the 2 cingulate areas can evoke motor effects (Showers 1959; Mitz and Wise 1987; see for review Vogt 1985). Although few studies have specifically examined the anatomy and physiology of the regions buried in the cingulate sulcus, we believe that it may be useful to consider these regions as motor areas like the SMA. Thus, we propose that the rostral region in the cingulate sulcus with corticospinal projections be termed the rostral cingulate motor area (CMAr) and that the caudal region within the cingulate sulcus be termed the caudal cingulate motor area (CMAc). This nomenclature is meant to reflect the hypothesis that the 2 cingulate motor areas are directly involved in the control of movement in some as yet undetermined fashion (e.g., Ward 1948; Gemba et al. 1986).

In summary, our results indicate that 3 areas on the medial wall of the hemisphere, i.e., the SMA, CMAr and CMAc, have somatotopically organized projections to the spinal cord. Schell and Strick (1984) recently proposed that the SMA is the major cortical site of termination for basal ganglia outputs related to limb movement (see also Alexander et al. 1986 and Wiesendanger and Wiesendanger 1985). Thus, the corticospinal projections from the SMA may be particularly important because they provide the basal ganglia with a somatotopically organized route to the spinal cord. Little is known about the anatomy and physiology of the cingulate motor areas. However, their proximity to the cingulate gyrus and the well known associations between cingulate cortex and the limbic system (see Vogt 1985 for a review) suggest that the corticospinal projections of the CMAr and CMAc represent a potential route by which the limbic system gains access to spinal cord mechanisms.

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