

AFFERENT CORTICAL CONNECTIONS OF THE MOTOR CORTICAL LARYNX AREA IN THE RHESUS MONKEY

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Abstract—The present study describes the cortical input into the motor cortical larynx area. The retrograde tracer horseradish peroxidase-conjugated wheat germ agglutinin was injected into the electrophysiologically identified motor cortical larynx area in three rhesus monkeys (*Macaca mulatta*). Retrogradely labeled cells were found in the surrounding premotor cortex (areas 6V and 6D), primary motor cortex (area 4), primary somatosensory cortex (areas 3, 1 and 2), anterior and posterior secondary somatosensory cortex and the probable homologue of Broca's area (areas 44 and 45); furthermore, labeling was found in the supplementary motor area, anterior and posterior cingulate cortex (areas 24 and 23), prefrontal and orbital frontal cortex (areas 8A, 46V, 47/12L, 47/12O, 13), agranular, dysgranular and granular insula as well as in the cortex within the upper bank of the middle third of the superior temporal sulcus (area TPO). The majority of these regions are reciprocally connected with the motor cortical larynx area [Brain Res 949 (2000) 23]. The laryngeal motor cortical input is discussed in relation to the connections of other motor cortical areas and its role in vocal control. © 2004 IBRO. Published by Elsevier Ltd. All rights reserved.

Key words: motor cortex, larynx representation, vocal fold control, phonation, neuroanatomy.

The motor cortical larynx area is located in the most anterior part of the ventrolateral part of the motor cortex, bordering the tongue, lip and jaw representations. While functionally this area is considered as part of the primary motor cortex, cytoarchitecturally it belongs to area 6, not 4 (Brodmann, 1909). In the nomenclature of Vogt and Vogt (1919), the primate larynx area corresponds to area 6b α , in that of Von Bonin and Bailey (1947) to area FCBm and in that of Matelli et al. (1985) to area F5.

The motor cortical larynx area plays an important role in voluntary vocal fold control in humans. Bilateral lesions in this region cause a complete loss of voluntary phonation control, while non-verbal emotional vocalizations, such as laughing, crying or moaning, are preserved (for review, see

Jürgens, 2002). Brain imaging studies in humans, furthermore, report activation of the facial motor cortex (including the larynx area) during speaking and singing (Bookheimer et al., 2000; Perry et al., 1999). Electrical stimulation of the larynx area produces isolated bilateral vocal fold movements in man (Foerster, 1936) and non-human primates (Hast and Milojevic, 1966; Hast et al., 1974; Jürgens, 1974; Leyton and Sherrington, 1917; Sugar et al., 1948; Walker and Green, 1938). In non-primate mammals, electrical stimulation of the motor cortex does not yield isolated vocal fold movements (Milojevic and Hast, 1964).

Destruction of the laryngeal motor cortex in the monkey, in contrast to man, does not affect vocal communication (Kirzinger and Jürgens, 1982). The reason for this probably is that monkey calls are more or less completely genetically preprogrammed in their acoustic structure (Hammerschmidt et al., 2001). The production of such innate motor patterns does not seem to depend upon an intact motor cortex. The larynx area of the monkey's motor cortex thus probably serves non-vocal laryngeal functions, such as abdominal straining during defecation and delivery, or holding breath during forceful jumps and lifting of heavy weights, rather than vocal functions.

EXPERIMENTAL PROCEDURES

Three adult female rhesus monkeys (*Macaca mulatta*), weighing between 3.0 and 6.8 kg, were used. The animals were the same as in the accompanying paper on subcortical connections of the cortical larynx area.

All experimental procedures were approved by the Animal Ethics Committee of the district government Braunschweig, Lower Saxony, Germany. The experiments conformed to the National Institutes of Health guidelines on the ethical use of animals. Care was taken to minimize the number of animals used and their suffering.

Surgery and injection

All surgical procedures were carried out as described in the accompanying paper. Briefly, under general anesthesia, the head was fixed in a stereotaxic instrument and a craniotomy of a diameter of 15–20 mm was made above the inferior motor cortex. The motor cortex was explored with electrical brain stimulation, looking for sites yielding vocal fold adduction when stimulated. Effective sites were injected with 3% WGA-HRP (lectin from *Triticum vulgare* conjugated to horseradish peroxidase). After the injections, the bone defect was closed and the muscle fascia and skin were sutured.

Fixation and histological processing

Three days after the operation, the monkeys were perfused under deep narcosis with 0.9% saline, followed by 1% paraformaldehyde/1.25% glutaraldehyde buffer in 0.1 M phosphate buffer. The brains were removed and cut at 45 μ m in the stereotaxic frontal

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plane on a freezing microtome. Immunohistochemical tracer identification was carried out with tetramethylbenzidine, according to a modification of Mesulam (1978).

Data analysis

The sections were evaluated microscopically under bright and dark field illumination. Labeled structures were identified according to the stereotaxic atlas of the rhesus monkey brain of Paxinos et al. (2000). Photo documentation was made with the help of a digital camera and proper software.

RESULTS

The injection sites of all three animals were more or less round-shaped and were located with their center about 5 mm above the Sylvian fissure between the inferior

branch of the arcuate sulcus rostrally and the subcentral dimple posteriorly. There were slight differences in the anterior–posterior extent of the injections. While in the first animal, the injection site reached from A 28.2 to A 23.5, the injection site of the second animal reached from A 28.2 to A 22.8 and that of the third animal from A 27.8 to A 23.7. Cytoarchitecturally, the injection sites corresponded to areas 6VR and ProM of Paxinos et al. (2000) (Figs. 1A, 2A and 3, A 28–23.5). The tracer injection, in each case, involved all six cortical layers (Fig. 1A). In animal 3, the two injection sites merged into each other. All injection sites were characterized by an intensely labeled central core of homogeneous reaction product, surrounded by a broad halo. Retrogradely labeled cells outside of the injection site

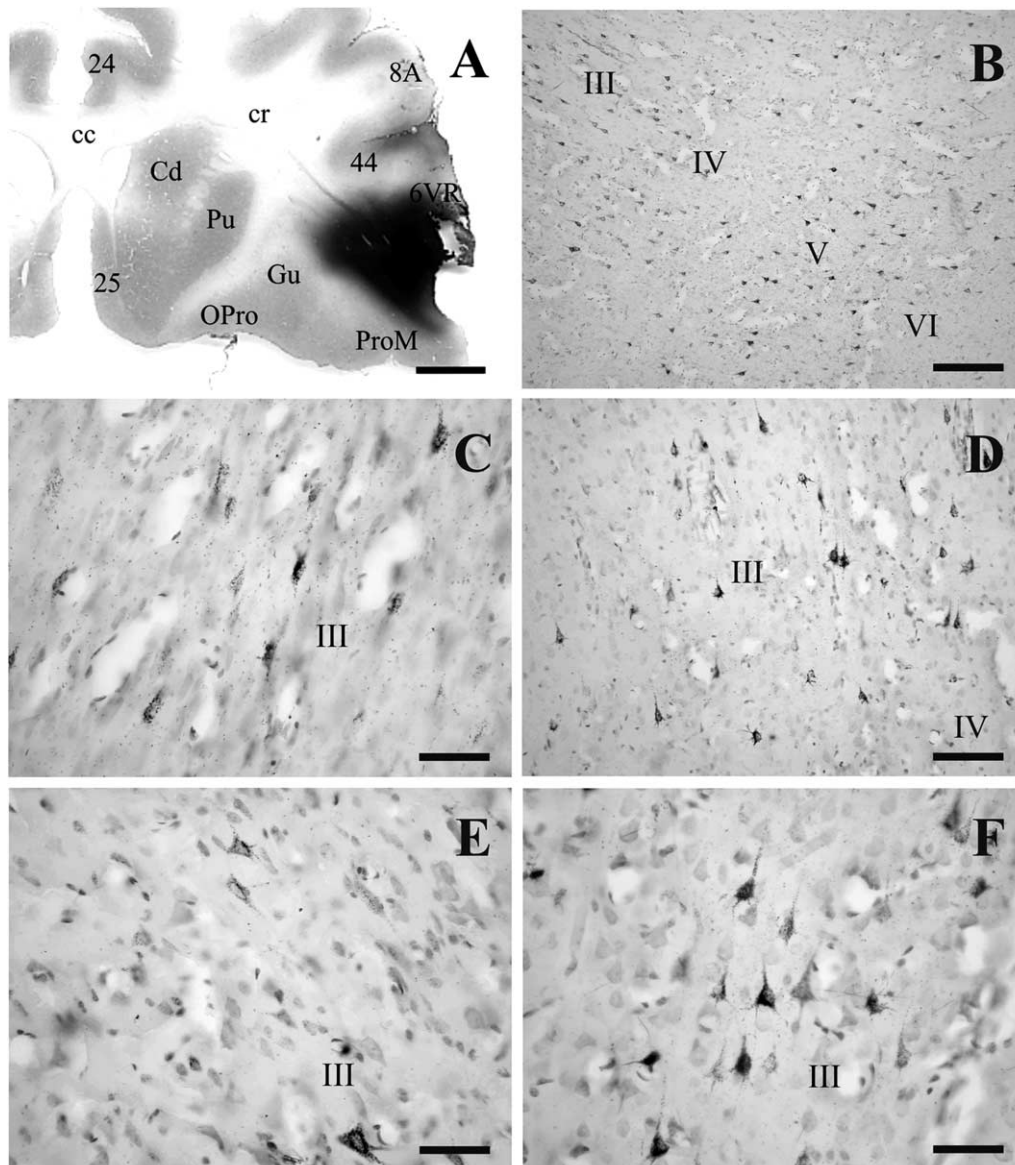


Fig. 1. (A) Photograph of the injection site within the laryngeal motor cortex, involving the rostral ventrolateral premotor cortex (6VR) and promotor area. (B–F) Microphotographs of ipsilateral dysgranular insula (B), ipsilateral ProM (C), ipsilateral area 4 (D), ipsilateral area 44 (E), and ipsilateral area 46V (F). Scale bars=5 mm (A); (B) 200 μm ; (D) 100 μm ; (C–F) 50 μm . All photographs were taken from animal 1. Nomenclature according to Paxinos et al. (2000). For abbreviations, see list.

mostly had pyramidal shape and were located in the third cortical layer. Lower densities of retrogradely labeled cells were found in the fifth layer (Fig. 1B–F). Anterograde labeling also was detected in various areas. As the anterograde projections have been reported already in an earlier study (Simonyan and Jürgens, 2002), we will limit ourselves in the following to the description of the retrograde projections.

Due to the somewhat different size of the injection sites, the number of retrogradely labeled cortical areas ranged between 29 and 40. As one or the other injection might have invaded non-laryngeal parts of the motor or premotor cortex, we accepted only those projections found in at least two of the three experimental animals. Altogether, 34 cytoarchitecturally distinguishable areas were found to be retrogradely labeled in at least two animals. These areas are listed in Table 1 and are presented in diagrammatic form in Figs. 2 and 3.

Retrograde labeling could be followed from the injection site along the upper bank of the Sylvian fissure into the rostral and caudal directions (Fig. 2A and 3). Intense labeling was found primarily in the lower rostral ventrolateral premotor cortex (area 6VR) and promotor area (area ProM) (Fig. 2A and Fig. 3, A, 28–22). Labeled cells were observed through the entire anterior–posterior distance in the second, third and fifth layers, with a dominance in the third layer. Caudal to the injection site, retrogradely labeled cells of lesser density extended to the inferior caudal ventrolateral premotor cortex (area 6VC; Fig. 2A and Fig. 3, A 20.5–17.5). Small clusters of labeled cells were found in the inferior and intermediate parts of the primary motor cortex (area 4) (Fig. 2A and Fig. 3, A 16–11.5). Labeled

cells in these areas are largely confined to the third layer, with some cells also in the fifth layer.

Further caudally, the laryngeal motor cortex is connected with the most inferior primary somatosensory cortex, involving all four subareas, that is, areas 3a, 3b, 1 and 2 (Fig. 2A and Fig. 3, A 22–13). Labeled cells are concentrated mainly in the third layer, with a few seen also in the fifth and sixth layers.

Dorsally to the injection site, small clusters of labeled cells in the third and fifth layers were observed in the intermediate part of the rostral dorsolateral premotor cortex (area 6DR) and caudal dorsolateral premotor cortex (area 6DC) in the region around the superior precentral dimple (Fig. 2A and Fig. 3, A 26.5–23.5 and A 20.5–17.5).

In the prefrontal cortex, heavy labeling was found in the ventral two thirds of the ventrolateral prefrontal cortex (area 47/12L), with a gradual decline toward the lateral orbital frontal cortex (area 47/12O), orbital preisocortex and central orbital frontal cortex (area 13) (Fig. 2A, D and Fig. 3, A 37–23.5). In the latter areas, labeled cells occur in discrete patches in both the third and fifth layers. Labeling did not invade the neighboring granular area 11.

Scattered labeling of medium density was detected in the lower prearcuate cortex and rostral bank of the inferior arcuate sulcus (area 45) as well as in the lower part of the caudal bank of the inferior arcuate sulcus (area 44) (Fig. 2B and Fig. 3, A 34–25). Labeled cells were located predominantly in the third layer of these regions.

Small clusters of labeled cells were also found in the upper prearcuate cortex in the region around the superior arcuate sulcus and in the depth of the arcuate sulcus spur (area 8A) as well as in the lower bank of the principal

Abbreviations used in the figures

AI	Agranular insula	OPAI	Orbital periallocortex
amt	Anterior middle temporal sulcus	OPro	Orbital preisocortex
ar	Arcuate sulcus	PE	Superior parietal cortex
arsp	Arcuate sulcus spur	PF	Anterior inferoparietal cortex
asd	Anterior subcentral dimple	PFG	Inferoparietal cortex
cc	Corpus callosum	PFOp	Anterior inferoparietal cortex
Cd	Caudate nucleus	PG	Posterior inferoparietal cortex
cg	Cingulum	PGOp	Posterior parietoopercular cortex
CG	Cingulate gyrus	ProM	Promotor cortex
cgs	Cingulate sulcus	ps	Principle sulcus
cr	Corona radiata	Pu	Putamen
cs	Central sulcus	PV	Anterior secondary somatosensory cortex
DI	Dysgranular insula	rf	Rhinal fissure
DIP	Depth intraparietal area	RG	Gyrus rectus
G, GU	Gustatory cortex	ros	Rostral sulcus
GI	Granular insula	sar	Superior arcuate sulcus
iar	Inferior arcuate sulcus	SII	Posterior secondary somatosensory cortex
iorb	Intermediate orbital sulcus	SMA	Supplementary motor area
ipd	Inferior precentral dimple	spcd	Superior precentral dimple
IPro	Insular preisocortex	STG	Superior temporal gyrus
ips	Intraparietal sulcus	sts	Superior temporal sulcus
lf	Lateral fissure	su	Superior postcentral dimple
lu	Lunate sulcus	TO	Temporoopercular cortex
lorb	Lateral orbital cortex	TPO	Temporal parietooccipital cortex
morb	Medial orbital cortex	TPPro	Temporopolar preisocortex
OG	Orbital gyrus	1....47	Brodman areas 1....47
ofs	Olfactory sulcus		

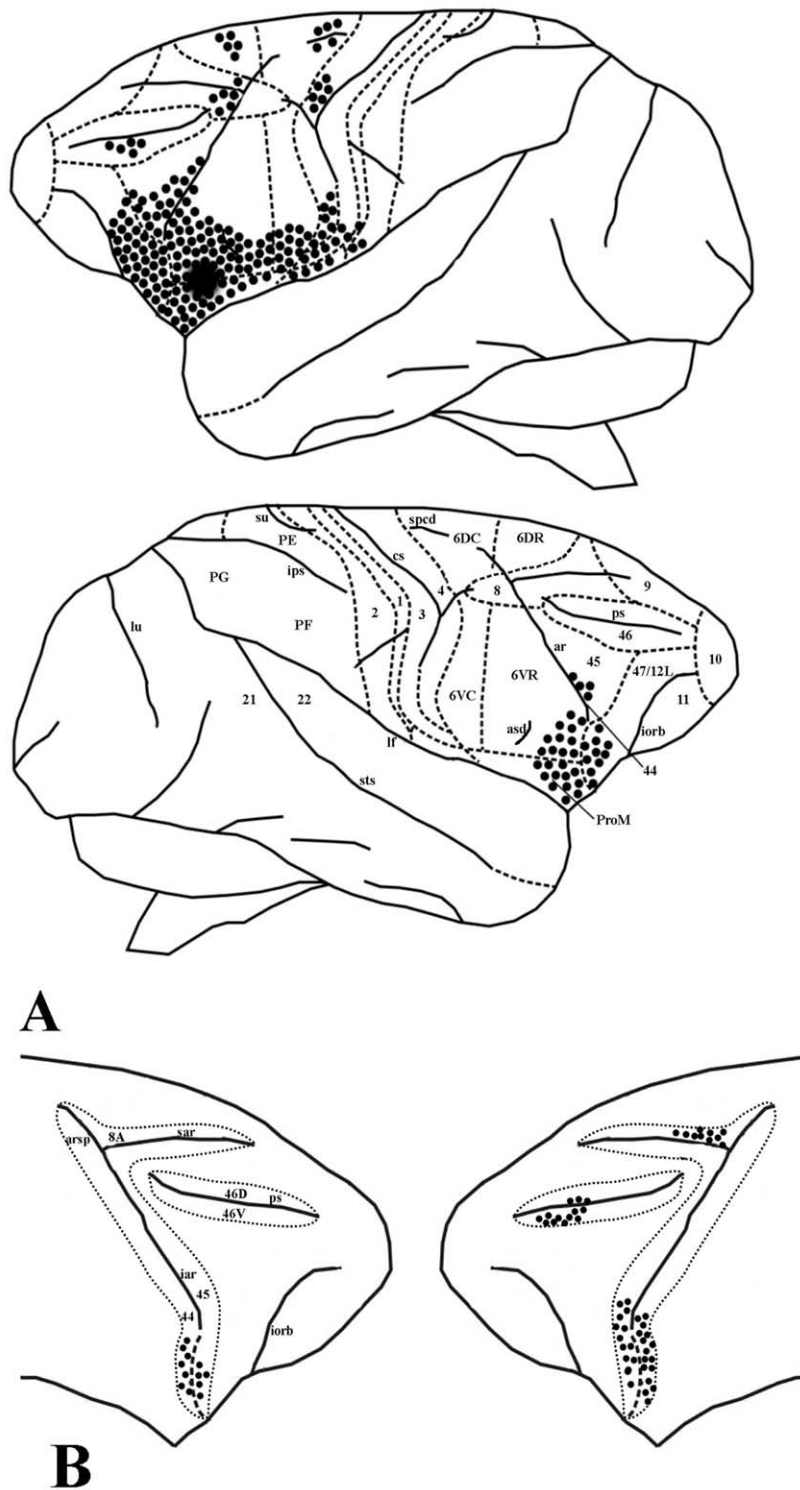


Fig. 2. Schematic diagrams of the rhesus monkey brain showing (A) lateral views of the left and right hemisphere, (B) unfolded cortex of the principal and arcuate sulci, (C) unfolded cortex within the Sylvian fissure, (D) ventral views of the left and right hemisphere, (E) medial views of the left and right hemisphere with unfolded sulcus cinguli. Dots indicate regions in which retrogradely labeled neurons were found in at least two of the three experimental animals (for quantitative differences between animals as well as structures, see Table 1). The injection site common to all three animals is indicated by the solid black area on the lateral view. In all diagrams, the left hemisphere represents the injection side. Brain diagrams and cytoarchitectonic nomenclature based on Paxinos et al. (2000). For abbreviations, see list.

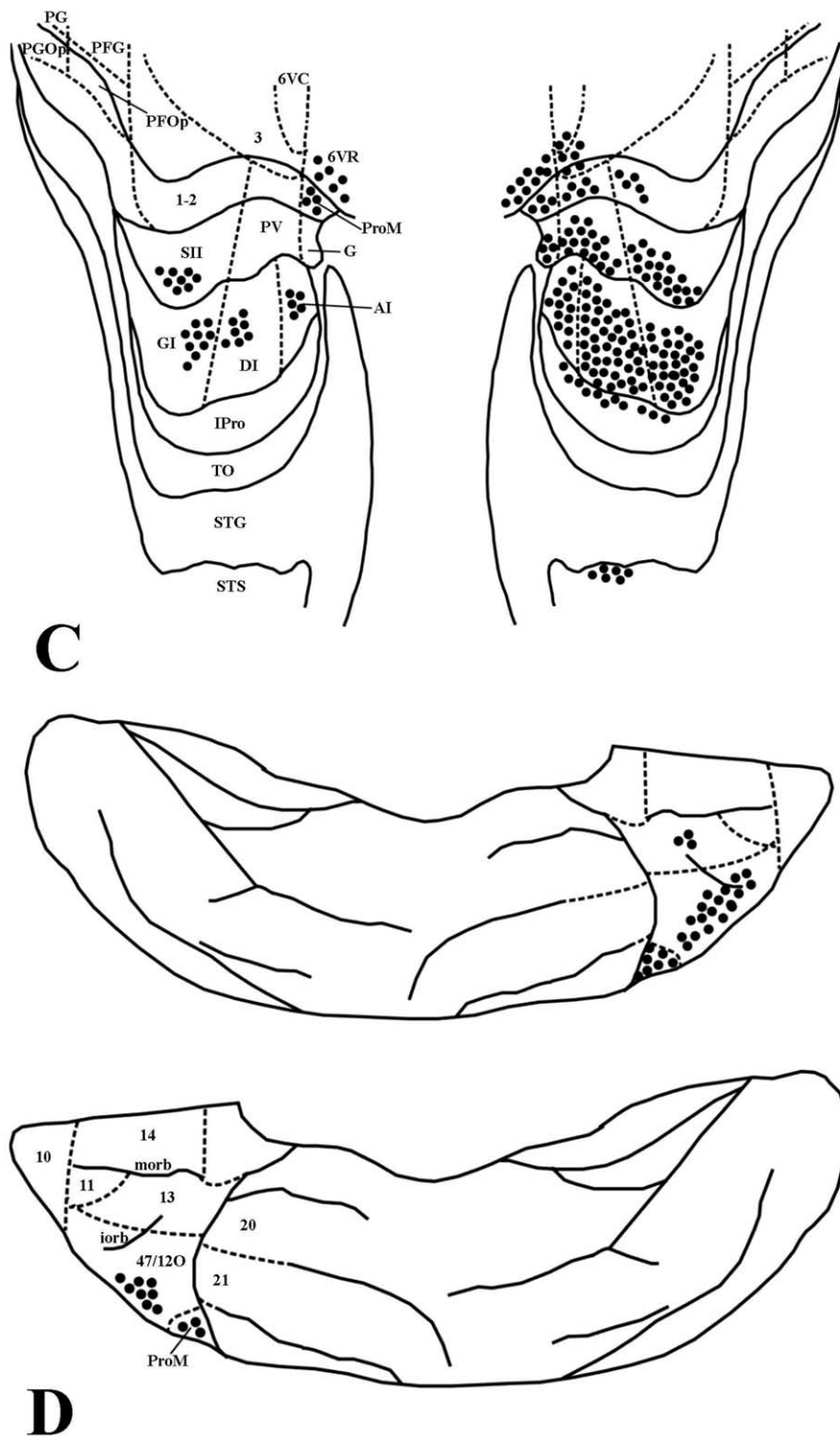
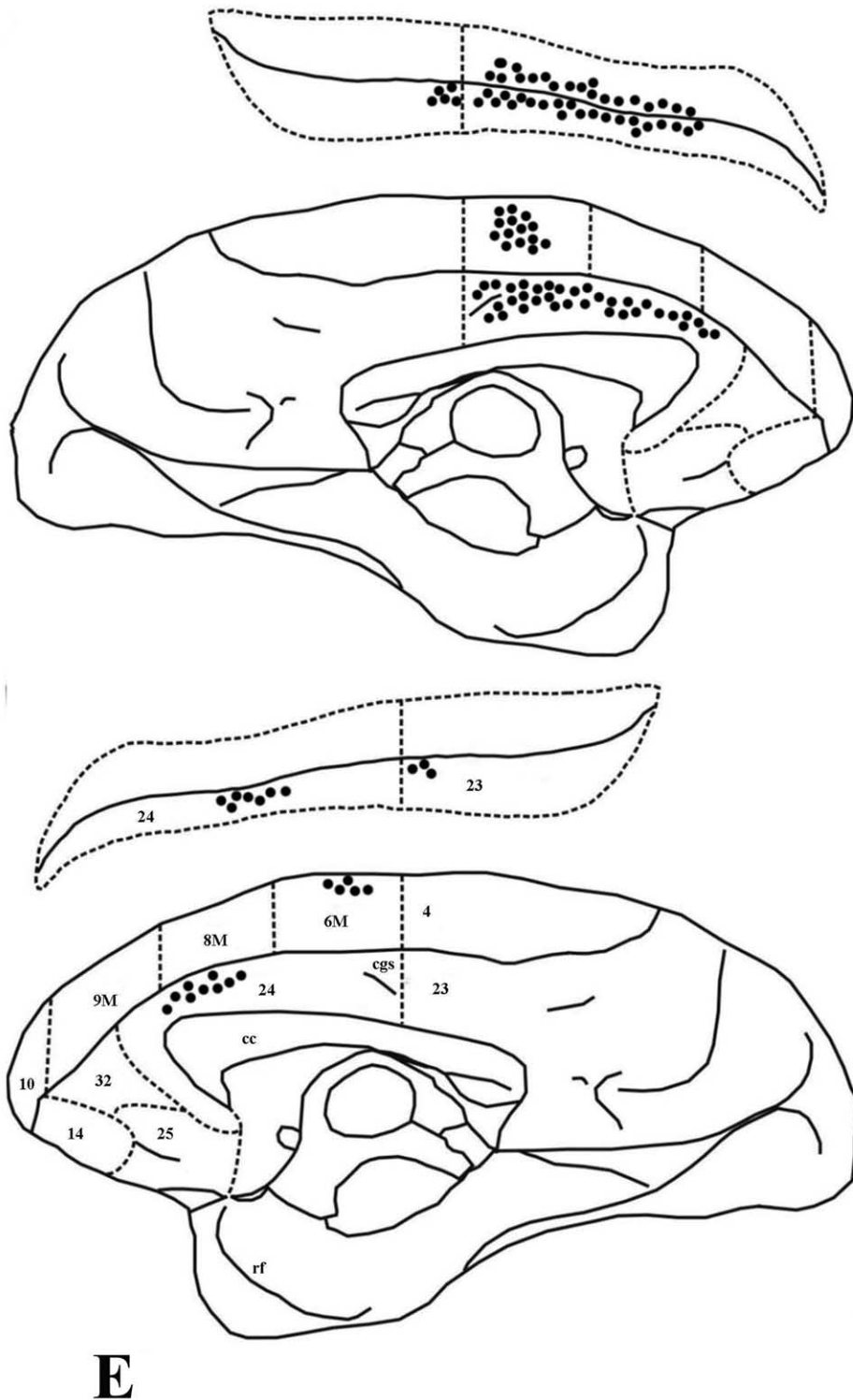


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sulcus (area 46V) and in the depth of the central third of the principal sulcus (area 46V/46D) (Fig. 2B and Fig. 3, A 37–32.5 and 20.5). Here, labeling was restricted to the third layer.

In the mediofrontal cortex, retrogradely labeled cells were found in the central third of the supplementary motor area

(SMA; area 6M) and the underlying cingulate cortex (Fig. 2E and Fig. 3, A 34–11.5). Here, labeling reached from the level of the genu of the corpus callosum (area 24) to the posterior cingulate gyrus (area 23). A major part of the labeled cells were located in the depth of the cingulate sulcus, invading the



E

Fig. 2. (Continued).

upper as well as lower lips of the sulcus, with the most dense labeling in the areas 24b, 24c, and medium to weak labeling in the areas 24d, 24a, 23c and 23b. Labeling within the cingulate cortex was predominantly of pyramidal cells in the third layer with fewer cells in the fifth layer.

The cortical larynx area also receives an extensive input from the cortex within the Sylvian fissure. In the frontoparietal operculum, labeling of medium density was found in a scattered form from the most rostral part of the anterior secondary somatosensory cortex (area PV) into

Table 1. Brain structures with output to the cortical larynx area^a

Brain structure	Animal I		Animal II		Animal III	
	Ipsi	Contra	Ipsi	Contra	Ipsi	Contra
Upper prearcuate cortex (area 8A)	++	+	+	–	+/-	–
Lower bank of principal sulcus (area 46V)	++	+	–	–	+	–
Cortex within principal sulcus (46V/46D)	+	–	+	–	+	–
Ventrolateral prefrontal cortex (area 47/12L)	+++	++	++	+/-	+++	+
Lateral orbital frontal cortex (area 47/12O)	+++	++	+	–	++	+
Orbital proisocortex (OPro)	+	–	–	–	+	–
Central orbital frontal cortex (area 13)	+	–	+	–	+	–
Lower postarcuate cortex (area 44)	++	+	+	–	++	+
Lower prearcuate cortex (area 45)	++	+	+	–	++	+
Promotor cortex (ProM)	+++	++	++	+	+++	++
Rostral ventrolateral premotor cortex (area 6VR)	+++	++	+++	+	+++	+
Caudal ventrolateral premotor cortex (area 6VC)	++	+	+	–	++	–
Caudal dorsolateral premotor cortex (area 6DC)	++	+	+	–	–	–
Rostral dorsolateral premotor cortex (area 6DR)	++	–	+	–	–	–
Supplementary motor area (area 6M)	++	+	+	+	+	–
Anterior cingulate cortex (area 24a)	+	–	+	–	+	–
Anterior cingulate cortex (area 24b)	+++	++	++	+	++	–
Anterior cingulate cortex (area 24c)	+++	+	++	+	++	–
Anterior cingulate cortex (area 24d)	++	+	+	–	+	–
Posterior cingulate cortex (area 23c)	++	+	+	+	–	–
Posterior cingulate cortex (area 23b)	+	–	+	–	–	–
Primary motor cortex (area 4)	++	+	+	–	+	–
Primary somatosensory cortex (area 3a)	+	–	+	–	+	+
Primary somatosensory cortex (area 3b)	+	–	+/-	–	+	+
Primary somatosensory cortex (area 1)	+	–	+/-	–	+	+/-
Primary somatosensory cortex (area 2/1)	++	–	+	–	+	+
Primary somatosensory cortex (area 2)	+/-	–	–	–	+	–
Anterior secondary somatosensory cortex (PV)	++	–	+	–	+++	+
Posterior secondary somatosensory cortex (SII)	+++	+	++	+	++	–
Agranular insula (AI)	+++	+	++	+	+++	+
Dysgranular insula (DI)	+++	+	++	+	+++	+
Granular insula (GI)	+++	+	++	+	+++	+
Insular proisocortex (IPro)	+++	–	+	–	++	+
Cortex within superior temporal sulcus (TPO)	+	–	–	–	+	–

^a +++, Heavy projection; ++, medium projection; +, weak projection; +/-, questionable projection; –, no projection. Only those structures are listed that contained labeled cells in at least two of the three animals on at least one side. Categorization of labeling is based on the average labeling across all animals.

the inferior part of the posterior secondary somatosensory cortex (area SII) (Fig. 2C and Fig. 3, A 20.5–17.5 and 14.5–7). Heavy labeling was found in the agranular, dysgranular and granular insula (areas AI, DI, GI) throughout its entire rostro-caudal extent. In the insular proisocortex, labeled cells formed a narrow band along the upper part of this area (Fig. 2C and Fig. 3, A 23.5–7). Labeled cells were prominent in the third layer with a few cells in the fifth layer.

Very few labeled cells were found within the central part of the dorsal bank of the superior temporal sulcus (Fig. 2C and Fig. 3, A 17.5). These cells were mainly found in the third layer.

Contralateral to the injection side, only 14 out of the 34 regions labeled ipsilaterally contained labeled cells in at least two animals (Table 1). All these regions showed a much weaker labeling than the corresponding ipsilateral regions. Crossing anterogradely labeled WGA-HRP fibers were only found in the corpus callosum, not the anterior commissure. The contralateral labeling was limited almost

exclusively to the third and fifth layer; but these laminae were not always labeled together in the same region.

Scattered groups of labeled cells were found in the rostral ventrolateral premotor cortex (area 6VR), promotor cortex (ProM), lower post- and prearcuate cortex (areas 44, 45), ventrolateral prefrontal cortex (area 47/12L), lateral orbital frontal cortex (area 47/12O), agranular, dysgranular and granular insula as well as secondary somatosensory cortex (area SII) (Fig. 2A, B, D and Fig. 3, A 32.5–17.5 and 13).

On the medial surface, some labeled cells were located in the SMA (area 6M), anterior cingulate cortex (areas 24b, c) and lower bank of posterior cingulate sulcus (area 14; Fig. 2E and Fig. 3, A 32.5–13).

DISCUSSION

Motor input

The cortical larynx area receives input from essentially five cortical motor control structures. These are the bordering,

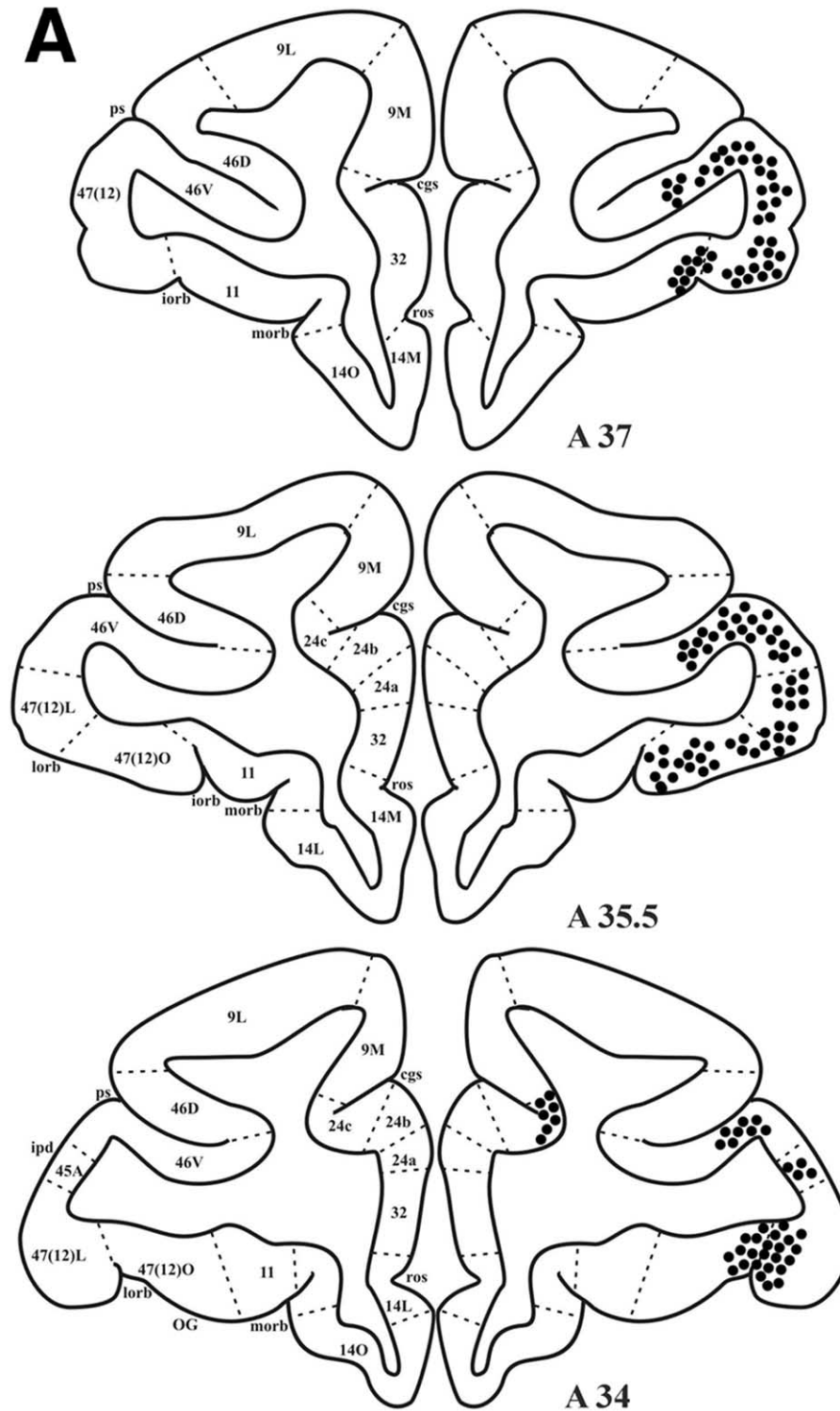


Fig. 3. Frontal sections of the rhesus monkey brain, showing the retrogradely labeled areas in animal 1. Each dot represents one to several labeled cells. Each section shows the distribution of labeled cells at the plane indicated as well as planes up to 0.5 mm anterior and posterior to it. Brain diagrams and nomenclature are based on Paxinos et al. (2000). For abbreviations, see list.

non-laryngeal primary motor cortex, supplementary motor area, anterior and posterior cingulate motor areas and the ventrolateral premotor cortex. Input from the primary motor

cortex comes from its tongue, lip and jaw representation. These regions border the larynx area caudally and caudomedially. Their electrical stimulation induces movements of the

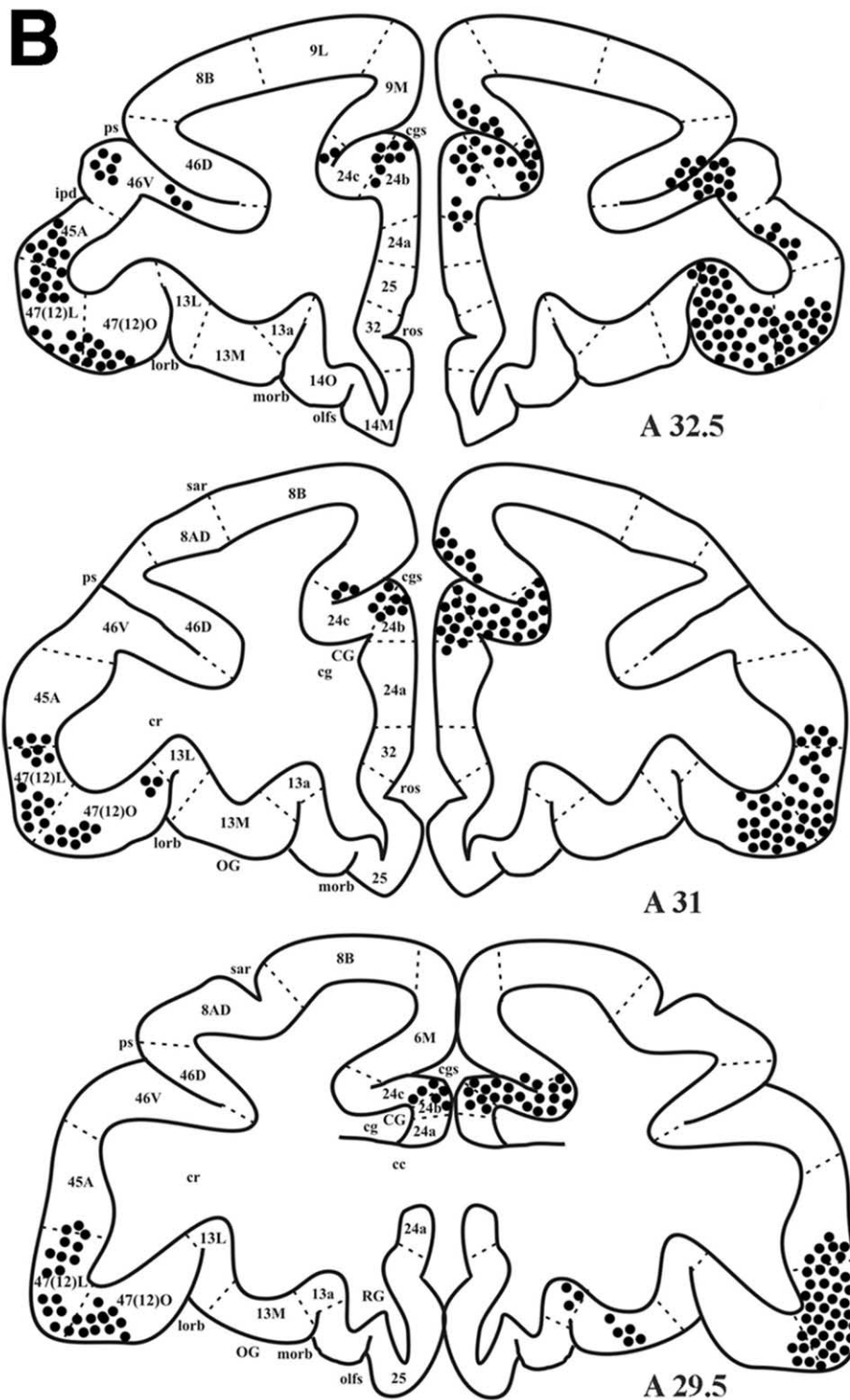


Fig. 3. (Continued).

respective organs (Huang et al., 1988; Woolsey et al., 1952). Single-unit recording reveals tongue, lip and jaw movement-related neuronal activity (Murray and Sessle, 1992). Inactivation of these regions affects learned oral movements (Murray et al., 1991). In addition to the input from the motor cortical

face area, we found an input from a motor cortical region higher up in the precentral cortex, probably representing trunk muscles (Woolsey et al., 1952). As several behavior patterns, such as phonation, coughing, swallowing, abdominal pressing and breath holding, demand the cooperation of

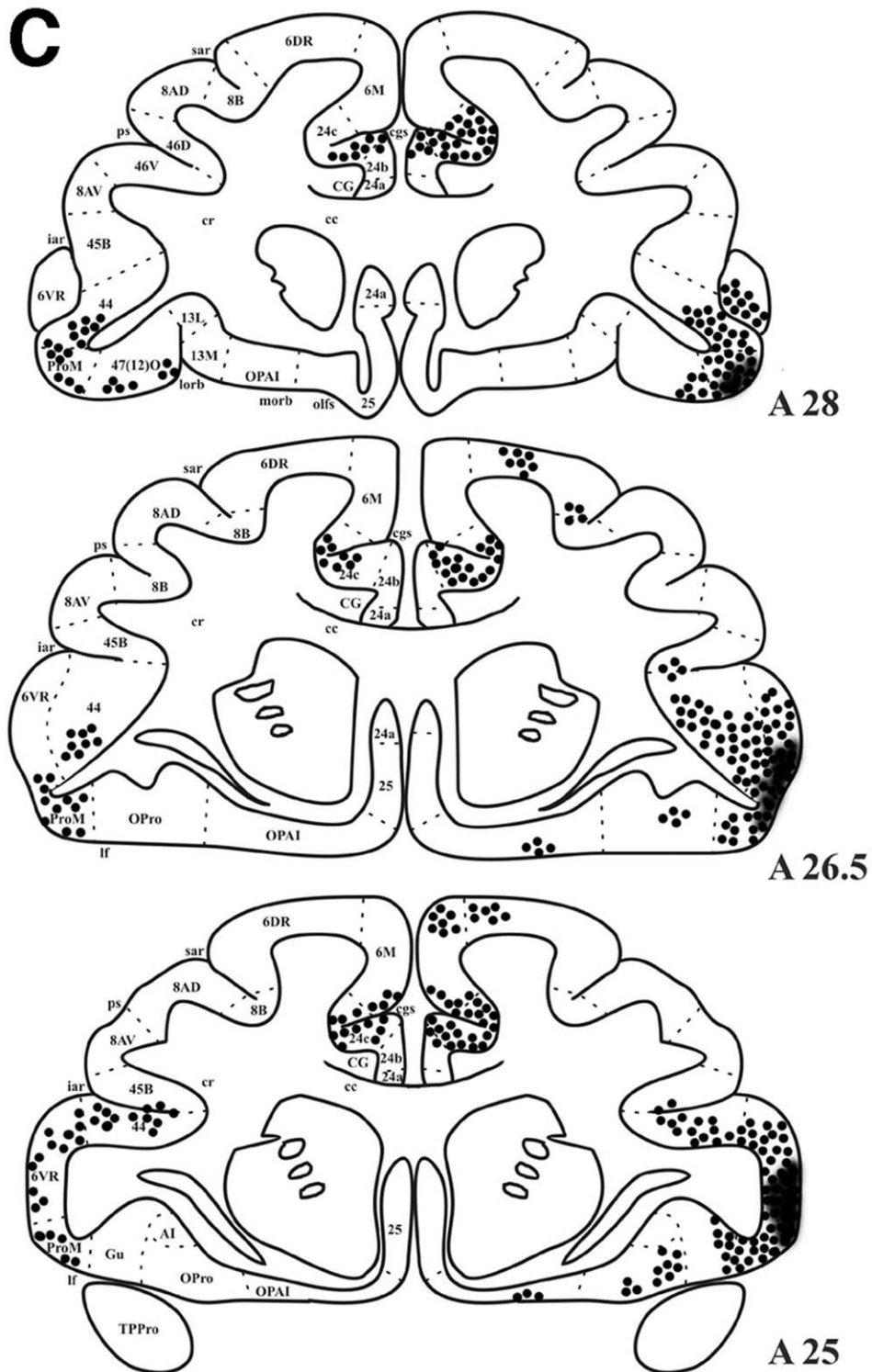


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laryngeal with oral and respiratory muscles, it makes sense that the motor cortical larynx area is connected with the tongue, lip, jaw and trunk area of the motor cortex.

Recent brain imaging studies, furthermore, have shown that during speaking, there is a global activation of the facial

and laryngeal motor area, together with the trunk motor area (Bookheimer et al., 2000; Herholz et al., 1994; Hirano et al., 1996). Brain activation during speaking is bilateral. In the present study, the left cortical larynx area received a direct input from the right cortical larynx area. A comparison with

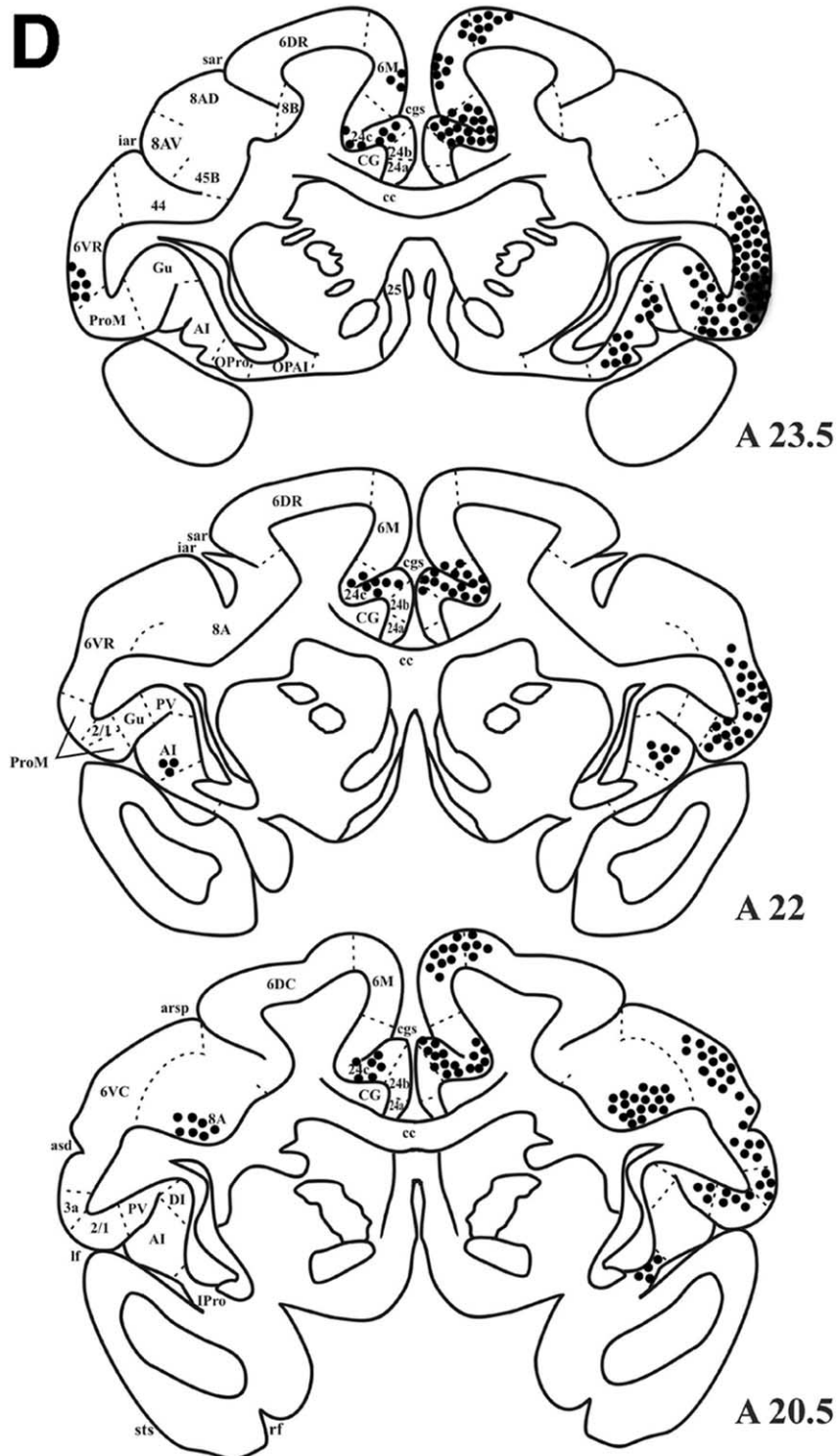


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our anterograde projection study (Simonyan and Jürgens, 2002) makes clear that left and right cortical areas are reciprocally connected. No reciprocal projections, however, seem to exist between cortical larynx area of the one side and face or trunk area of the other side.

The SMA is another source of cortical input into the motor cortical larynx area. The input is not limited to the larynx area, but connects all parts of the primary motor cortex with the SMA (Luppino et al., 1991; Muakkassa and Strick, 1979). The connections are reciprocal (Wiesendan-

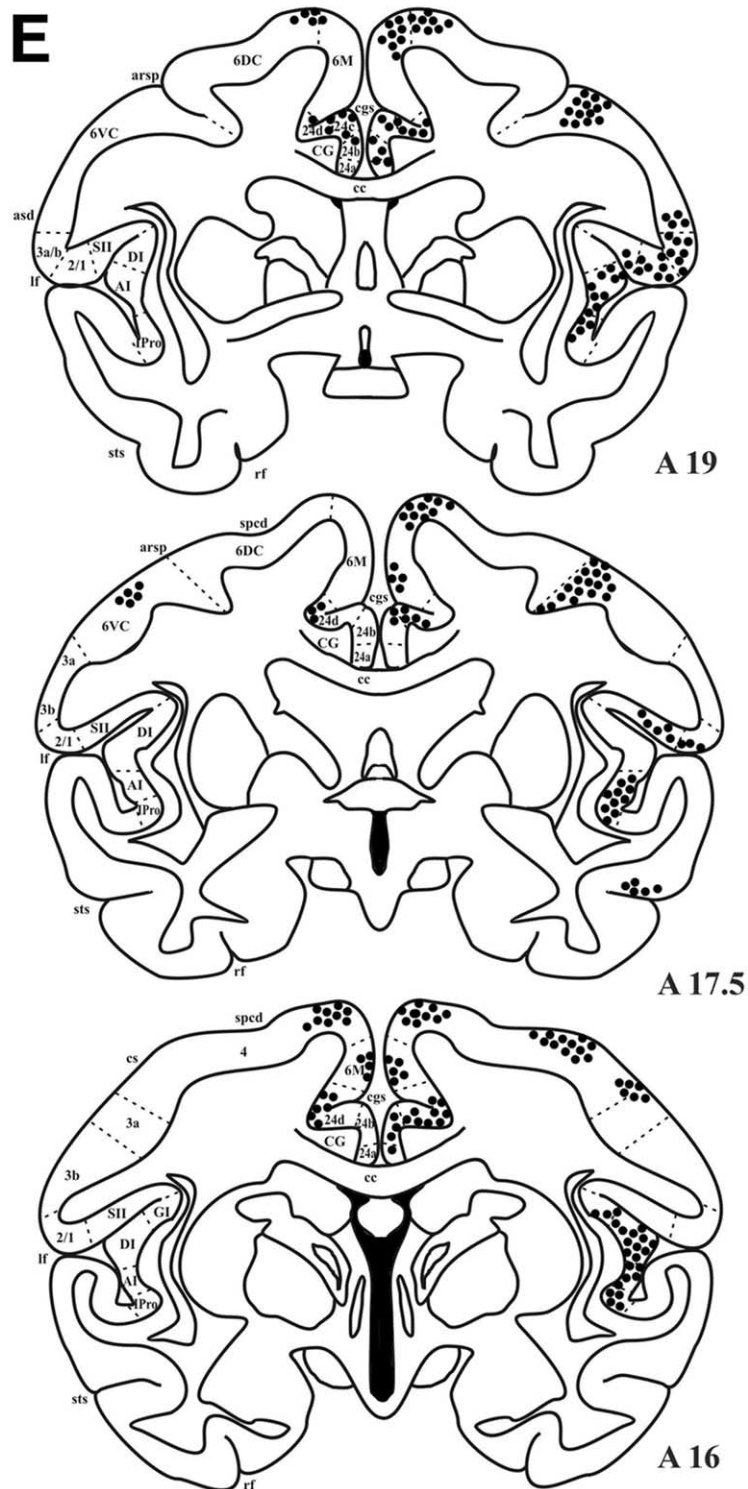


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ger, 1986). There is some disagreement in the literature about the existence of a somatotopy in SMA. While some authors describe a gross somatotopy, with the head represented rostrally and the legs caudally (Luppino et al., 1991; Muakkassa and Strick, 1979; Woolsey et al., 1952),

others deny such a somatotopy (Macpherson et al., 1982; Penfield and Welch, 1951). In the present study, retrogradely labeled cells were limited to the central third of the SMA. In brain imaging studies, the SMA has been shown to be active during the execution of learned complex motor

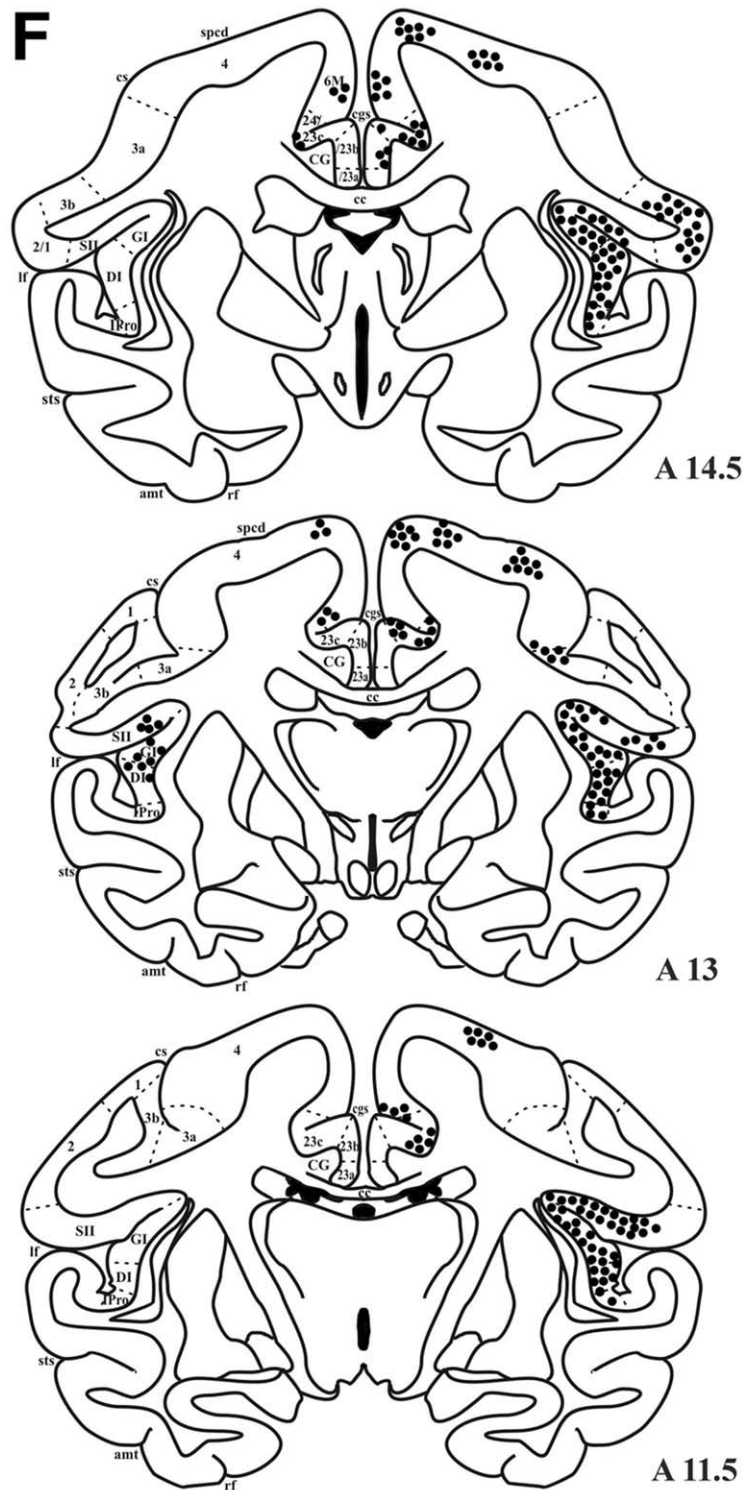


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sequences, including speech and singing (Bookheimer et al., 1995; Herholz et al., 1994; Hirano et al., 1996; Perry et al., 1999; Price, 2000). By electrical stimulation of the SMA, vocal utterances can be produced in human patients, but not in monkeys (Jürgens and Ploog, 1970; Pen-

field and Welch, 1951). Bilateral lesions in the SMA do not affect monkey call production (Kirzinger and Jürgens, 1982), but severely reduce the motivation to speak in humans, a syndrome called transcortical motor aphasia (Erickson and Woolsey, 1951; Gelmers, 1983; Rubens,

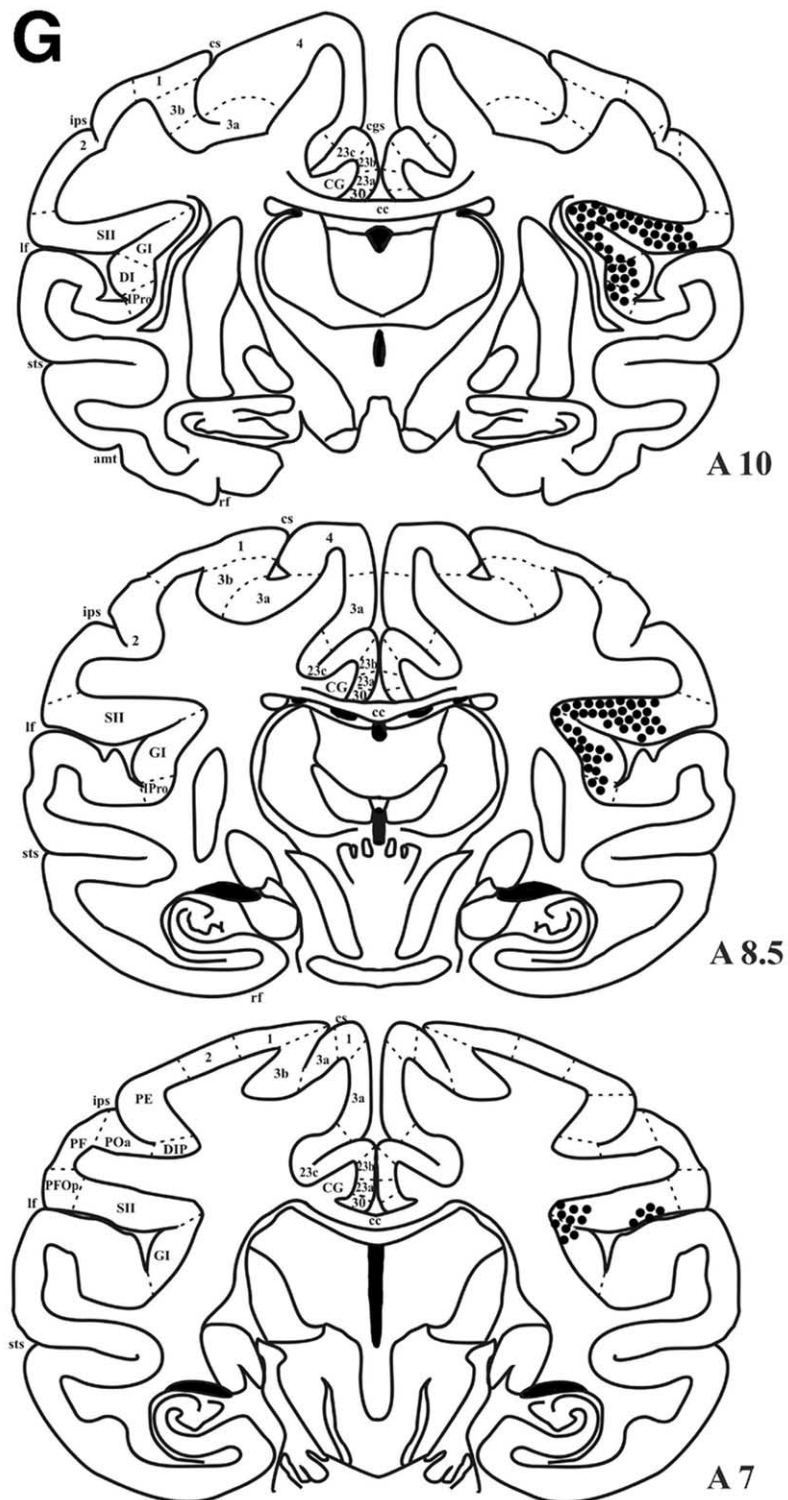


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1982). These findings suggest that the SMA is involved in the control of speech and song, but not in monkey call production.

In the cingulate cortex, two motor areas have been distinguished: one in the lower lip of the anterior cingulate

sulcus, corresponding to area 24c; the other in the lower lip of the posterior cingulate sulcus, corresponding to area 23c (Morecraft and Van Hoesen, 1992; Picard and Strick, 1996). Both areas contained retrogradely labeled cells in the present study. Marked labeling, in addition, was found

in the anterior cingulate cortex below the cingulate sulcus (area 24b). This area has been shown in electrical stimulation experiments to produce species-specific vocalization in the rhesus monkey, squirrel monkey, cat and bat (for review, see Jürgens, 2002). Bilateral lesions in the anterior cingulate cortex have been reported to abolish conditioned, but not unconditioned, vocalization in the rhesus monkey (Aitken, 1981; Sutton et al., 1974) and reduce the number of spontaneous vocal utterances in the squirrel monkey (MacLean and Newman, 1988). In humans, bilateral lesions in the anterior cingulate cortex affect the voluntary control of emotional vocal utterances (Jürgens and Von Cramon, 1982).

Cortical input reaches the motor cortical larynx area also from the rostrally bordering peri-arcuate cortex. This region is considered by some authors to be homologous to Broca's area (areas 44 and 45) (Paxinos et al., 2000; Petrides and Pandya, 1994, 2001). From single-unit recording studies, it is known that the neurons in the rostral ventrolateral premotor cortex have very complex reaction characteristics. Some of them are active during the execution of specific mouth movements and, at the same time, to the observation of corresponding oral movements in conspecifics (Ferrari et al., 2003). In humans, brain imaging studies have shown an activation in Broca's area during complex, but not simple, speech tasks. Specifically, if a person is asked to repeat simple phonemes or the months of the year, no activity using positron emission tomography (PET) is found in Broca's area. If, in contrast, a person is asked to recite a memorized prose passage, activity is found (Bookheimer et al., 2000). Lesions in Broca's area, contrary to those in the lower primary motor cortex, do not cause a paresis of the oral muscles (Mohr et al., 1978). Broca's area in humans and its counterpart, the inferior peri-arcuate cortex in the monkey, seem to provide the motor cortex with information necessary for the imitation of oral behavior and the long-term organization of learned oromotor sequences.

Sensory input

Somatosensory input of cortical origin reaches the larynx area from the primary and secondary somatosensory cortices. Within the primary somatosensory cortex, retrogradely labeled cells were limited to its lateralmost part. This region receives somatosensory input from the face and intraoral regions (Dreyer et al., 1975; Lin et al., 1994). Labeling was found in all four subareas, that is, Brodmann areas 3a, 3b, 1 and 2. Area 3a is known to receive input mainly from deep receptors, such as muscle spindles and tendon organs, while areas 3b and 1 receive primarily input from surface receptors, such as Merkel cells and Meissner's corpuscles, and area 2 receives mixed input (Jones and Porter, 1980; Kaas et al., 1979; Manger et al., 1996; Nelson et al., 1980; Pons et al., 1985; Wiesendanger and Miles, 1982). The fact that the cortical larynx area receives an input from all four subareas suggests that vocal fold control relies on information coming from various types of mechanoreceptors.

Somatosensory input reaches the cortical larynx area also from two areas hidden in the depth of the Sylvian fissure: the anterior secondary somatosensory area PV and the posterior secondary somatosensory area SII. According to Krubitzer et al. (1995), both areas show a somatotopy, with the face representation bordering the face representation of the primary somatosensory cortex and the arm and leg representation following the face representation toward the insula. In the present study, labeled cells were distributed over large parts of PV and SII.

The larynx area does not only receive sensory information of the somatosensory type. A small group of retrogradely labeled cells was also found in the depth of the superior temporal sulcus. This region represents multimodal association cortex, receiving auditory, visual as well as somatosensory input (Baylis et al., 1987; Hikosaka et al., 1988). It is still unclear in which way this multimodal information is used by the cortical larynx area in laryngeal control. Brain imaging studies show that the cortex of the superior temporal sulcus is active during listening to words as well as reading a text. The activation is stronger during speaking than during listening to words (Price, 2000). This points to an interaction between language perception and language production in the superior temporal sulcal cortex.

Prefrontal, orbital frontal and insular input

While the premotor cortex, SMA, primary and secondary somatosensory cortices as well as cingulate sulcal cortex represent "classical" input structures of the primary motor cortex, this does not hold for the prefrontal, orbital frontal and insular cortices (Ghosh et al., 1987; Godschalk et al., 1984; Leichnetz, 1986; Muakkassa and Strick, 1979; Pandya and Kuypers, 1969). The reason that the latter structures contained retrogradely labeled cells in the present study, but were not found by other authors to project to the primary motor cortex, is the special position of the larynx representation within the motor cortex. While all the other motor cortical body representations (face, arms, trunk, legs, tail) are lined up along the central sulcus, the larynx representation lies far more rostrally, occupying area 6, instead of area 4. Laterally as well, the larynx area takes an extreme position. Together with the caudally adjacent tongue representation, the larynx representation has the lateralmost position of all body representations. As a consequence, the larynx area shows projections, which have been considered to be typical of the premotor and peri-Sylvian cortex, but not the motor cortex. Specifically, the premotor cortex is one of the classical target structures of the prefrontal cortex, the insula is directly connected with the peri-Sylvian cortex, and the orbital frontal cortex has been shown to project to regions combining a peri-Sylvian with a premotor position (Augustine, 1996; Barbas and Pandya, 1987; Deacon, 1992; Matelli et al., 1986; Morecraft and Van Hoesen, 1993; Tokuno et al., 1997).

While the prefrontal and orbital frontal cortex is assumed to be involved in vocal control only in a very indirect way (Price, 1996), the insula seems to play a more specific role. The insula, similar to the facial sensorimotor cortex and SMA, is regularly activated in PET studies during

speaking, singing and whispering (Bookheimer et al., 2000; Paus et al., 1996; Perry et al., 1999). Lesions in the insula cause speech apraxia, a syndrome characterized by impairment in the coordination of speech movements (Dronkers, 1996).

Reciprocal connections

A comparison between the retrograde projections of the present study and the anterograde projections reported in our previous study (Simonyan and Jürgens, 2002) shows that almost all cortical connections of the motor cortical larynx area are reciprocal. More specifically, the larynx area receives massive projections from and projects heavily into the neighboring inferior premotor, prefrontal and motor cortex, anterior cingulate cortex, secondary somatosensory cortex and insula. Weaker reciprocal connections exist, in addition, with the dorsolateral premotor, prefrontal and motor cortex, the SMA, primary somatosensory cortex and cortex within the superior temporal sulcus. The only region projecting to the larynx area without receiving an input from it is the central orbital frontal cortex (area 13). This projection, however, is a very weak one. Anterograde projections of the larynx area, that are not reciprocated, go to the inferior parietal cortex (areas inferior parietal cortex, posterior inferior parietal cortex), posterior parieto-occipital cortex (areas anterior inferior parietal cortex, posterior parieto-occipital cortex) and cortex within the intraparietal sulcus.

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