Motor functions of the Broca's region

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Abstract

Broca's region in the dominant cerebral hemisphere is known to mediate the production of language but also contributes to comprehension. This region evolved only in humans and is constituted of Brodmann's areas 44 and 45 in the inferior frontal gyrus. There is, however, evidence that Broca's region overlaps, at least in part, with the ventral premotor cortex. We summarize the evidence that the motor related part of Broca's area is localized in the opercular portion of the inferior frontal cortex, mainly in area 44 of Brodmann. According to our own data, there seems to be a homology between Brodmann area 44 in humans and the monkey area F5. The non-language related motor functions of Broca's region comprise complex hand movements, associative sensorimotor learning and sensorimotor integration. Brodmann's area 44 is also a part of a specialized parieto-premotor network and interacts significantly with the neighboring premotor areas.
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1. Introduction

Since the seminal case description by Broca (1864), it has been well known that damage to the inferior frontal cortex severely disrupts language production (Liberman, 1996; Mesulam, 1990). The advent of neuroimaging studies led to the insight that the posterior part of the inferior frontal cortex actively participates in language production (Kim, Relkin, Lee, & Hirsch, 1997; Petersen, Fox, Snyder, & Raichle, 1988; Swaab, Brown, & Hagoort, 1995; Wise et al., 1991; Zatorre, Evans, Meyer, & Gjedde, 1992). More recently its involvement in visual and auditory language comprehension and syntactic as well as phonological processing has been advocated (Chee, O'Kraven, Bergida, Rosen, & Savoy, 1999; Friederici, 1997; Pugh et al., 1996; Stromswold, Caplan, Alpert, & Rauch, 1996; Zatorre, Meyer, Gjedde, & Evans, 1996).

Broca's region consists of Brodmann's area 44 and 45 (Brodmann, 1909), of which area 44 exhibits a possible homology to the inferior premotor cortex in the monkey brain as was repeatedly pointed out in cytocharchitec-

tonic studies (Galaburda & Pandya, 1982; Petrides & Pandya, 1994; Preuss, Stepniewska, & Kaas, 1996; von Bonin & Bailey, 1947). It is known that in the macaque monkey there is a large representation of distal hand movements in the rostralmost part of ventral premotor cortex (area F5, according to the nomenclature proposed by Matelli, Luppino, & Rizzolatti (1985)) (Hepp-Reymond, Husler, Maier, & Ql, 1994; Kurata & Tanji, 1986; Rizzolatti, Scandolara, Matelli, & Gentilucci, 1981, 1988). More recently, physiological evidence was obtained that in the monkey area F5, at a comparable location to that of Broca's region in humans, there are neurons that discharge not only when the monkey executes goal-directed hand actions, but also when it observes the same or a similar action performed by another individual. These neurons are known as ''mirror neurons'' (Gallese, Fadiga, Fogassi, & Rizzolatti, 1996; Rizzolatti, Fadiga, Gallese, & Fogassi, 1996). Recent brain imaging studies strongly suggest that mirror neurons also exist in humans (Buccino et al., 2001, see for a review also Buccino, Binkofski, & Riggio, in this issue). Because Broca's region occurred only in human brain evolution, its functional role cannot be directly analysed by analogous experiments in non-human primates. However, there is also a growing evidence from lesion

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and neuroimaging studies, that the frontal opercular cortex participates in higher order motor control. Accordingly, Broca's region might thus not only be critical for speech but may play a more general role for motor control by interfacing external information about biological motion with internal motor representation of hand/arm and mouth actions.

Here we review the evidence from cytoarchitectonic studies, neurophysiological studies on monkeys and human lesions and neuroimaging studies that the frontal cortex, containing the ventral premotor cortex is engaged in many motor functions different from language production. The emphasis is put onto the similarity between the Brodmann's area 44 and monkey area F5.

2. Ventral premotor cortex in the macaque and Brocas area in humans

The search for homologies between Broca's region and ventral premotor areas of non-human primates is somewhat difficult, not only because Broca's region occurred first in human brain evolution. However, there is anatomical evidence that this region overlaps partly with motor areas identified previously in monkey studies. Because a great deal of information about the functional specialization of frontal motor areas was obtained from non-human primates studies it is worthwhile reviewing the evidence available about the homologies between monkey and man.

Based on cytoarchitectural and histochemical data, a modern parcellation of the agranular frontal cortex (motor cortex) has been worked out in the macaque monkey by Matelli et al. (1985, 1991). In this terminology area F1 corresponds basically to Brodmann's area 4 (the site of the primary motor cortex), the other areas are mainly subdivisions of Brodmann's area 6. Areas F2 and F7, which lie in the superior part of area 6, are referred to collectively as "dorsal premotor cortex", while areas F4 and F5, which lie in the inferior area 6, are often referred to as "ventral premotor cortex" (Matelli & Luppino, 1996).

In humans the ventral sector of the premotor cortex is formed by two areas: the ventral part of area 6a alpha and BA 44 (Vogt & Vogt, 1919). The two areas share a common basic cytoarchitectonic structure, the main characteristics of which are the poverty of or lack of granular cells in BA 44 and BA 6 respectively (see Campbell, 1905; von Economo, 1929) and the presence of large pyramid cells in the third layer. Classically, both ventral BA 6 and BA 44 were thought of as areas controlling oro-laryngeal movements, but with a different specialization and selectivity. The most lateral part of BA 6 was considered to be responsible for the motor control of buccal and laryngeal movements, regardless of the movement purpose, while, in contrast, BA 44 was

considered to be the main speech motor area. A series of recent studies, reviewed in this article, showed that this view describes only partially the function of *these areas*. *A homology* between BA 44 and area F5 was suggested in the 1940s by von Bonin and Bailey (1947) on the basis of their cytoarchitectonic studies. (In their terminology, F5 was called FCBm.) This view was recently fully supported by Petrides and Pandya (1994) (see also Galaburda & Pandya, 1982; Preuss et al., 1996). A possible weakness of this homology (see Passingham, 1993) is the richness of the oro-laryngeal representation in BA 44, including that of speech control, in humans and, on the contrary, the presence of an important finger-movement representation in vPM in the monkey. Here, we will present some data showing that a hand/finger representation is indeed also present in human BA 44. Obviously, the relative cortical space for the two representations is not the same. However, the development of the cortex devoted to oro-laryngeal representations specifically in BA 44 is probably not a mere coincidence, but is due to the close evolutionary relation between action and speech (see Buccino et al., in this issue; Rizzolatti & Arbib, 1998).

3. Motor functions of ventral premotor cortex in monkeys

While it has been known since the 30s of the 19th century that independent finger movements depend on direct connections of the corticospinal tract with the spinal cord motoneurons (see Porter & Lemon, 1993), the mechanisms through which sensory information controls such movements as grasping and manipulatory movements began only recently to be understood. Recording and intracortical microstimulation studies showed that in the macaque monkey there is a large distal hand movements representation in the rostralmost part of ventral premotor cortex (area F5) (Hepp-Reymond et al., 1994; Kurata & Tanji, 1986; Rizzolatti et al., 1981, 1988). The neurons of this area discharge during specific goal-directed hand movements such as grasping, holding and tearing *an object*. Many of them become active also in response to visual presentation of 3-D objects provided that these are congruent with the type of prehension coded by the recorded neuron (Murata et al., 1997; Rizzolatti et al., 1988). Area F5 is directly connected with the primary motor cortex (F1) and receives rich input from the second somatosensory area (SII), from parietal area PF (7b), and from a parietal area located inside the intraparietal sulcus, the anterior intraparietal area (AIP) (Godschalk, Lemon, Kuypers, & Ronday, 1984; Luppino, Murata, Govoni, & Matelli, 1999; Matelli, Camarda, Glickstein, & Rizzolatti, 1986; Matsumura & Kubota, 1979; Muakkassa & Strick, 1979). The study of AIP showed that many of its neurons discharge during finger and hand movements,

others respond to specific visual 3-D stimuli and, finally, others discharge both during active finger movements and in response to 3-D stimuli congruent in size and shape with the coded grasping movement (Sakata, Taira, Murata, & Mine, 1995; Taira, Mine, Georgopoulos, Murata, & Sakata, 1990). Taken together, this data suggests that F5 and interaction between F5 and AIP plays a pivotal role in controlling the organization of hand ± object interaction (Jeannerod, Arbib, Rizzolatti, & Sakata, 1995; Binkofski et al., 1998).

Another sector of ventral premotor cortex localized adjacent to area F5 and playing an important role in the sensorimotor control of actions is area F4. While recording from F4 neurons, Fogassi et al. (1996) and Graziano, Hu, and Gross (1997a) found that this region is involved in coding space relevant for action. Visual receptive fields anchored to the arm can encode stimuli location in "arm-centered" coordinates and are useful for guiding arm movements, whereas visual receptive fields anchored to the head can likewise encode stimuli in "head centered" coordinates and are useful for guiding head movements. Both suggesting that "body-part-centered" coordinates provide a general solution to a problem of sensorimotor integration: sensory stimuli are located in a coordinate system anchored to a particular body part (Graziano et al., 1997a). The same authors recorded in the ventral premotor cortex neurons exhibiting "object permanence", encoding the presence of an object that is no longer visible (Graziano, Hu, & Gross, 1997b).

4. Motor functions of the ventral premotor cortex and pars opercularis of the inferior frontal gyrus in humans–evidence from neuroimaging

Recent experiments carried out with brain imaging techniques contributed to extend our understanding of functions of the frontal opercular cortex, different from speech. Activation of the inferior frontal gyrus was found during overt and covert production of *actions* (Bonda, Petrides, Frey, & Evans, 1995; Decety et al., 1994, 1997; Parsons et al., 1995), especially during mental rotations necessary for hand recognition (Parsons et al., 1995), during mental imagery of grasping movements (Decety et al., 1994; Grafton, Arbib, Fadiga, & Rizzolatti, 1996), during preparation of finger movements on the basis of a copied movement (Krams, Rushworth, Deiber, Frackowiak, & Passingham, 1998), during imagery and performance of visually guided movements (Binkofski et al., 2000; Toni, Ramnani, Josephs, Ashburner, & Passingham, 2001; Toni, Rushworth, & Passingham, 2001) and the vPMC was also found to be of importance for motor tasks with high motor execution demands (Winstein, Grafton, & Pohl, 1997). Ventral premotor cortex seems to play a crucial

role in motor imagery as repeatedly shown in neuroimaging studies (Binkofski et al., 2000; Decety et al., 1994; Stephan et al., 1995). Common to all these tasks was the preparation for the performance of complex motor acts with a high degree of sensorimotor control. This notion is backed by the finding of Ehrsson, Fagergren, Jonsson, Westling, and Johansson (2000) that the frontal operculum becomes active during the performance of precision grip and not of much more coarse power grip.

The frontal opercular cortex was also shown to be critically involved in the learning of explicit and implicit motor sequences (Hazeltine, Grafton, & Ivry, 1997; Rauch et al., 1995; Seitz & Roland, 1992). The frontal opercular region seems also to be involved in initial learning of novel visuomotor associations (Toni, Ramnani, et al., 2001; Toni et al., 2002), while overlearned performance is likely to rely on dorsal premotor cortex (Toni, Ramnani, et al., 2001; Toni et al., 2001; Toni, Rowe, Stephan, & Passingham, 2002). A sustained activity in the ventral premotor cortex can also be found during motor preparation in the context of learned arbitrary associations (Toni & Passingham, 1999; Toni, Ramnani, et al., 2001; Toni et al., 2001).

The involvement of the ventral premotor cortex and pars opercularis of the inferior frontal gyrus in higher cognitive motor functions like the observation and recognition of action performed by others (Buccino et al., 2001; Decety et al., 1997; Grafton, Fagg, Woods, & Arbib, 1996; Grèzes, Costes, & Decety, 1998; Rizzolatti et al., 1996), and, to some extent, by individuals belonging to other species (Buccino et al., in press), the observation and imitation of action (Binkofski, Buccino, Freund, & Fink, in press-a) and supramodal processing of object related actions (Binkofski, Buccino, Zilles, & Fink, in press-b) will be reviewed by Buccino et al. (in this issue).

5. Combination of cytoarchitectonic and imaging data for identification of similarities between human area 44 and monkey area F5

While investigating motor imagery under different conditions we found that the posterior opercular part of the human inferior frontal cortex became specifically engaged during imagery of abstract movements (Binkofski et al., 2000). This imagery of abstract movement was limited to conditions in which movement had to be imagined from a third person's perspective. The imagery of the observation of one's own movement was associated with activation of the left ventral opercular cortex, while the imagery of a moving target caused activation of the right ventral opercular cortex. After transformation of our data into the standardized reference brain atlas by Roland and Zilles (1994), we were able to

superimpose our activation data onto the cytoarchitectonic data of the Brodmann areas 44 and 45 (Amunts et al., 1999). The superimposition of our activation data with the probabilistic maps of areas 44 and 45 obtained from cytoarchitectonic data of ten individual brains allows for exact localization of the activation foci within one of these areas. Here, we could clearly demonstrate that during imagery of one's own limb motion, from an observer's perspective there was left-hemispheric activation of area 44, whereas during imagery of spatial target motion in extrapersonal space, significant activation of the right area 44 became apparent (see Fig. 1).

Moreover, we showed that the center of gravity of activation in area 44 was significantly caudal to area 45 and rostral to lower area 6 of premotor cortex. These data support the view that the left-hemispheric activation of Broca's region reflected "pragmatic" motor processing, while the right-hemispheric activation of Broca's homologue was related to explicit motor processing of motion. Interestingly, in our study the inferior frontal cortex was not activated by imagery of finger movements but of more derived concepts of motion. Imagery of visually guided finger movements was associated with activation of more dorsal parts of lateral premotor cortex, possibly in the homologue to monkey area F4.

The specific motor activation of the area 44 could be demonstrated in another experiment in which volunteers were asked to manipulate complex objects and an indifferent object (a sphere) (Binkofski et al., 1999). In one condition the subjects were asked to merely manipulate the objects and avoid covert naming and in the other condition they were explicitly asked to covertly name the explored objects. In the contrast between both conditions containing manipulation of complex objects and manipulation of a sphere ventral premotor activations were found. The comparison of the coordinates of the activated foci located around the opercular and triangular parts of the inferior frontal gyrus with the coordinates of the probability maps of BAs 44 and 45 (Amunts et al., 1999) demonstrated that the activation foci located in the pars triangularis related to covert naming of objects fitted entirely into BA 45. The foci activated during complex object manipulation without naming and located in vPMC fitted into the borders of BA 44. These results underline the notion, that within Broca's region the area 44 is relevant for motor activity.

We suggest that these frontal opercular activations in humans within the cytoarchitectonical borders of Brodmann's area 44 may correspond to neuronal activations related to action perception and recognition as reported for a set of neurones in the ventral premotor cortex in the area F5 of macaques (Gallese et al., 1996; Rizzolatti et al., 1996). This notion is strongly supported in a recent review by Rizzolatti, Fogassi, and Gallese (2002).

6. Clinical data in humans

Lesions of the frontal operculum in man are often associated with paresis of the oro-facial, laryngeal and tongue muscles (Förster, 1936). This author also described that after removal of area 4 electrical stimulation of lower area 6aα patients could elicit complex contralateral arm movements. These movements included pronation of the hand and closure of fingers to form a fist. However, much higher stimulation strength was needed to elicit these complex movements in comparison to stimulation of area 4, where rather simple movements were evoked. Förster (1936) could further observe more prominent motor deficits in a series of more than 40 patients with excision of the area 6a beta. These patients exhibited an initial temporal contralateral hemiparesis
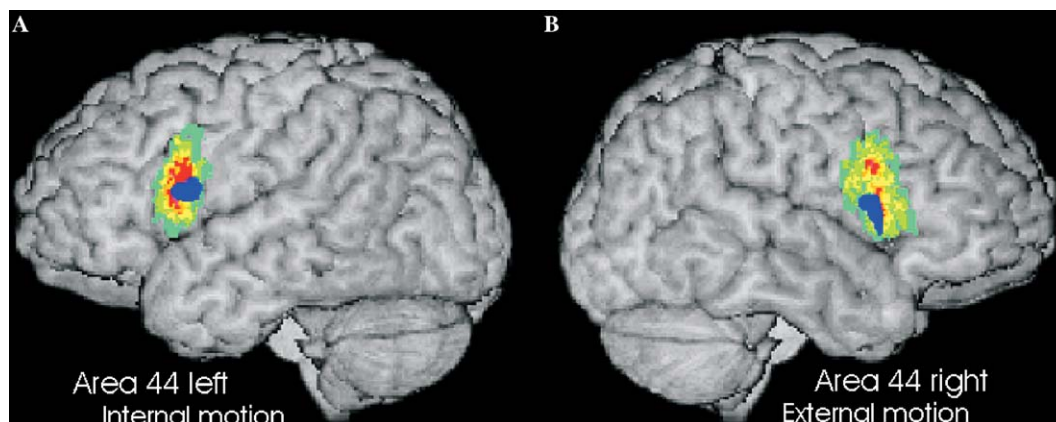

Fig. 1. Activation of the left area 44 during performance of a task containing processing of internal motion (A) and of the right area 44 during performance of a task containing processing of external motion (B). Superposition of the corresponding activation foci (blue, from Binkofski et al., 2000) on the probablilistic cytoarchitectonic map of area 44 (Amunts et al., 1999) (with permission of Katrin Amunts, Research Center Jülich GmbH, Jülich, Germany).

with proximally accentuated slowing and impoverishment of movements. Such lesions were also associated with the loss of "kinetic melody", disintegration of complex skilful movements, derangement of the kinetic structure of movements, motor perseveration (Fulton, 1935; Kleist, 1911; Luria, 1966), motor hemineglect (Berti & Frassinetti, 2000; Halligan & Marshall, 1991; Lappane & Degos, 1983) or limbkinetic apraxia (Kleist, 1911; Liepmann, 1920). Accordingly, we found in a population of patients with premotor lesions a loss of regularity of exploratory finger movements during manipulation of objects (Binkofski, Kunesch, Classen, Seitz, & Freund, 2001). Patients with lateral premotor lesions have also marked difficulties to reproduce rhythms from memory (Halsband, Ito, Tanji, & Freund, 1993). However, the ability to discriminate rhythms seems to be preserved in these patients.

The role of the lateral premotor cortex for sensorimotor integration was emphasized by the finding of Halsband and Passingham (1982) showing that monkeys with lesions of this region showed a marked disturbance in associative sensorimotor learning. This finding could be replicated in humans with lesions of the lateral premotor cortex (Halsband & Freund, 1990). These patients exhibited marked difficulties in learning associations between *actions* and certain sensory stimuli, like colors.

Description of isolated lesions around the Broca's area in the inferior frontal gyrus causing focal motor deficits are rare. Very recently, we could observe a 50-jear old patient with a focal lesion of the right frontal operculum, most probably including to the ventral premotor cortex, who exhibited a complete inability to establish associations between simple gestures (like making a fist, or pronating the palm) and colors. This finding suggests that the ventral premotor cortex is playing a substantial role at least in the initial phase of visuomotor associative learning. In the light of these findings the importance of the premotor cortex as a high order sensorimotor interface becomes evident. A further patient, a 58-years old teacher, had a lesion of the rostral part of the right inferior frontal gyrus. The primary motor cortex was not affected by this lesion and by means of transcranial magnetic stimulation we could assess the intactness of the pyramidal tract. Despite the preserved grip force and the preserved ability to perform individual finger movements, this patient had enormous difficulties to grasp an object. Especially the precision grip was markedly disturbed, whereas the whole hand prehension was only slightly impaired. There was also a marked discrepancy between the well preserved transportation phase of the arm and the inappropriate formation of the finger aperture during reaching for grasping movements (Dettmers, Liepert, Hamzei, Binkofski, & Weiller, 2003). This finding stresses the importance of the hu-

man ventral premotor cortex for grasping actions (Jeannerod et al., 1995).

Adjacent to Broca's speech region the existence of a highly specialized area for writing (Exner's writing area (Exner, 1881)) was proposed. Exner's writing area lies within a small region along the lateral convexity, near the foot of the second frontal convolution of the left hemisphere, occupying the border regions of Broadmans areas 46, 8, 6. Both areas maintain extensive connections and Exner's writing area appears to be coextensive with Broca's area (Lesser, Lueders, Dinner, Hahn, & Cohen, 1984). Electrical stimulation in this region in awake moving patients resulted in the arrest of ongoing motor acts, including the capacity to write or perform rapid alternating finger movements and sometimes writing and speech arrest (Lesser et al., 1984). Broca's area, that possibly emerged from a former hand area, seems to organize and relay impulses received from posterior language zones to Exner's writing area and transforms them into appropriate writing programs. Those programs are then sent to the primary motor cortex for final execution of writing movements. Although some authors have denied the existence of Exner's area, this region appears to be the final common pathway where linguistic impulses are transferred into writing programs; i.e., the formation of graphemes and their temporal sequential expression. Lesions or seizure activity around this area may result in agraphia (Penfield & Roberts, 1959; Ritaccio, Hickling, & Ramani, 1992; Tohgi et al., 1995). Interestingly, writing of single letters do not activate Broca's region (Seitz et al., 1997; Siebner et al., 2001).

7. Summary

In this review we summarize the evidence that a part of the ventral premotor cortex in the monkey, especially area F5, corresponds to the pars opercularis of the inferior frontal gyrus in humans (area 44) and possibly to the ventralmost part of area 6. This part of Broca's region, classically considered as devoted to the motor control of oro-laryngeal movements and speech production, rather constitutes a high level sensorimotor interface integrating sensory stimuli and cognitive tasks with the related motor representations of hand- and face-related actions.

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