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# The Primary Motor and Premotor Areas of the Human Cerebral Cortex

PHILIPPE A. CHOUINARD and TOMÁŠ PAUS

Brodmann's cytoarchitectonic map of the human cortex designates area 4 as cortex in the anterior bank of the precentral sulcus and area 6 as cortex encompassing the precentral gyrus and the posterior portion of the superior frontal gyrus on both the lateral and medial surfaces of the brain. More than 70 years ago, Fulton proposed a functional distinction between these two areas, coining the terms *primary motor area* for cortex in Brodmann area 4 and *premotor area* for cortex in Brodmann area 6. The parcellation of the cortical motor system has subsequently become more complex. Several nonprimary motor areas have been identified in the brain of the macaque monkey, and associations between anatomy and function in the human brain are being tested continuously using brain mapping techniques. In the present review, the authors discuss the unique properties of the primary motor area (M1), the dorsal portion of the premotor cortex (PMd), and the ventral portion of the premotor cortex (PMv). They end this review by discussing how the premotor areas influence M1. *NEUROSCIENTIST* 12(2):143–152, 2006. DOI: 10.1177/1073858405284255

**KEY WORDS** *Primary motor area, Dorsal premotor area, Selection, Ventral premotor area, Object manipulation, Action observation, Coordinate-based voxel-wise meta-analysis, Activation likelihood-estimation*

Mapping of the motor cortex began in the late 19th century. The earliest experiments were performed on dogs; Fritsch and Hitzig (1870) demonstrated that electrical stimulation applied in the precentral cortex could induce movements in the limbs. In nonhuman primates, Leyton and Sherrington (1917) later applied electrical stimulation at different locations of the precentral cortex and reported that they could induce movements of specific parts of the body. Penfield and colleagues also applied electrical stimulation along the precentral cortex in patients during surgery for the removal of tumors and epileptic foci (Penfield and Boldrey 1937; Penfield and Rasmussen 1952). Their results revealed a disproportionate somatotopic map of the body as depicted by Penfield's famous homunculus.

Brodmann (1909) demonstrated differences in the cytoarchitecture between agranular cortex with large pyramidal cells in the anterior bank of the precentral sulcus (area 4) and the agranular cortex in the precentral gyrus and the posterior portion of the superior frontal gyrus on both the lateral and medial surfaces of the brain

(area 6). These findings, along with converging lines of evidence from clinical observations and cortical ablation experiments performed in monkeys, led Fulton (1935) to propose that the motor cortex could be divided into a primary motor area (area 4) and a premotor area (area 6). Today, the parcellation of the motor cortex has become more complex. Several distinct nonprimary motor areas have been identified.

The nonprimary motor areas encompass all areas in the frontal lobe that can influence motor output at the level of both the primary motor area (M1) and the spinal cord (Dum and Strick 1991). These include the premotor areas located on the lateral aspect of Brodmann area 6 (Picard and Strick 2001), the supplementary motor areas located on the medial aspect of Brodmann area 6 (Penfield and Welch 1951; Picard and Strick 1996), and the cingulate motor areas located along the dorsal and ventral banks of the cingulate sulcus (Luppino and others 1991; Paus and others 1993; Paus 2001). In this review, we will focus on motor areas located on the lateral surface of the precentral cortex. We will discuss the unique properties of M1, the dorsal portion of the premotor cortex (PMd), and the ventral portion of the premotor cortex (PMv). We will end this review by discussing how the premotor areas influence M1.

## Primary Motor Area

The strong presence of large corticospinal neurons is a unique feature of M1; 31% of corticospinal neurons that arise from M1 are considered large, and these neurons represent 79% of all large corticospinal neurons (Dum and Strick 1991). These neurons are important for the fractionation of independent finger movements because

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**Table 1.** Studies Used to Perform Coordinate-Based Voxel-Wise Meta-analyses

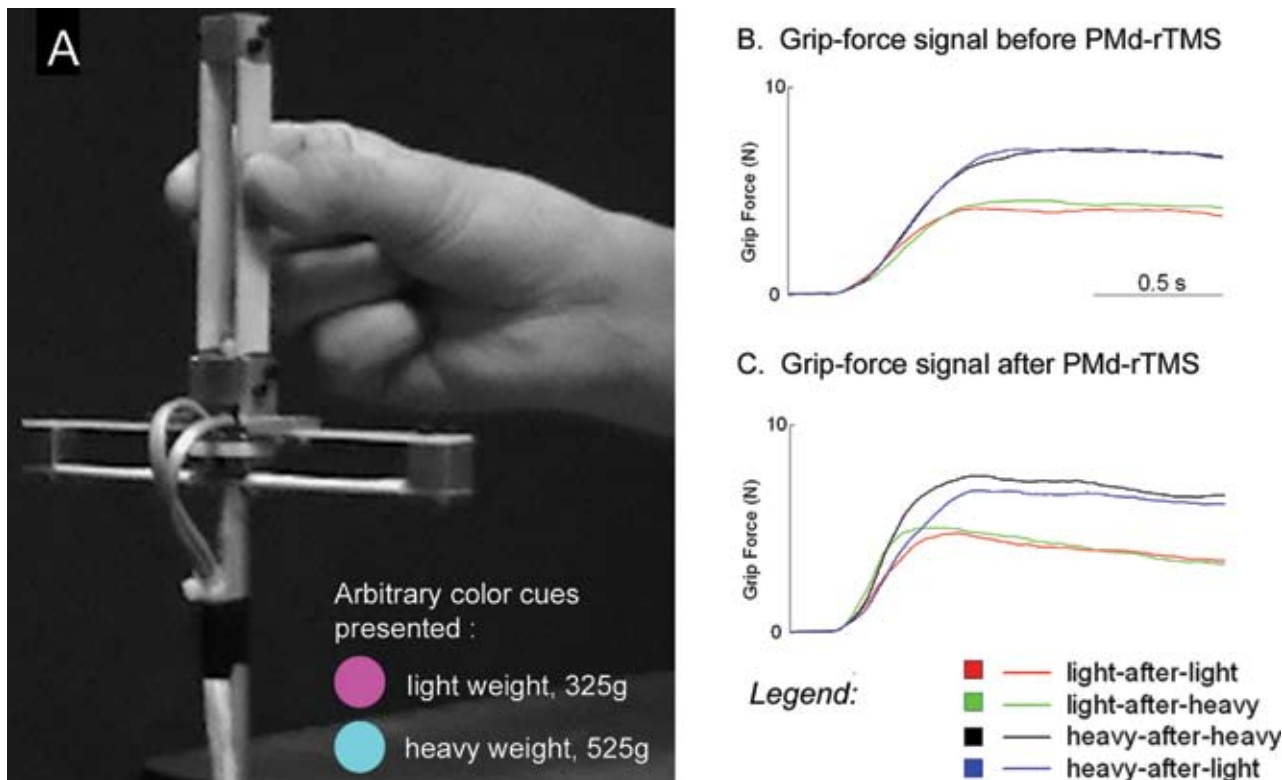
<b>Response Selection</b>	
Adam and others (2003)	Selective response to spatial cues > Rest
Grafton and others (1998)	Selective response to arbitrary color cues > Fixed response
Kertzman and others (1997)	Selective response to spatial cues > Rest
Kurata and others (2000)	Selective response to arbitrary tones > Fixed response
Sakai and others (2000)	Selective response to arbitrary color cues > Expected response
Schluter and others (2001)	Selective response to arbitrary tones > Expected response
Seidler and others (2004)	Selective response to arbitrary shapes > Fixed response
	Selective response to spatial cues > Rest
<b>Simple Responses</b>	
Cerasa and others (2005)	Fixed response to color cue > Viewing
Gerardin and others (2000)	Fixed response to auditory cue > Listening
Jancke and others (2000)	Fixed response to color cue > Rest
Kansaku and others (2004)	Fixed response to color, auditory, and air-puff cues > Base
Sugiura and others (2001)	Fixed response to color cue > Rest
	Fixed response to auditory cue > Rest
<b>Execution of Object-Related Hand Movements</b>	
Binkofski and others (1999)	Tactile manipulation (object) > Hold (object)
Bodegard and others (2001)	Tactile manipulation (object) > Rest
Ehrsson and others (2001)	Precision grip (gentle) > Precision grip (normal)
Kuhtz-Buschbeck and others (2001)	Precision grip (gentle) > Precision grip (normal)
	Precision grip (firm) > Precision grip (normal)
Stoeckel and others (2003)	Tactile manipulation (object) > Rest
<b>Observation of Object-Related Hand Movements</b>	
Buccino and others (2001)	Observation (grasp object) > Observation (static hand)
Buccino and others (2004)	Observation (grasp object) > Rest
Grafton and others (1996)	Observation (grasp object) > Observation (object)
Johnson-Frey and others (2003)	Observation (grasp object) > Observation (touch object)
Rizzolatti and others (1996)	Observation (grasp object) > Observation (object)

We performed coordinate-based voxel-wise meta-analyses using activation likelihood-estimation (ALE) mapping. Procedures related to this type of meta-analysis are described elsewhere (Laird and others 2005). Coordinates taken from studies that used the Montreal Neurological Institute template brain for spatial normalization were transformed further into the standard stereotaxic atlas of Talairach and Tournoux (1988) using an algorithm written by Dr. Matthew Brett ([www.mrc-cbu.cam.ac.uk/Imaging/Common/mnispace](http://www.mrc-cbu.cam.ac.uk/Imaging/Common/mnispace)).

they exert direct influence on the lateral motor-nuclei in the spinal cord (Evarts 1981; Muir and Lemon 1983). The effects of complete unilateral ablations of the sensorimotor cortex in the rhesus monkey exemplify the importance of M1 for generating movements of the distal forelimb muscles. Six months after lesioning the sensorimotor cortex, monkeys still fail to grasp small objects between the two fingers and make isolated movements of the wrist. When attempting to grasp small objects, the monkeys use their hand as a shovel and contract all their fingers simultaneously around the object (Passingham and others 1978, 1983).

Brinkman and Kuypers (1973) demonstrated in macaque monkeys with split brains that each half of

the brain controls distal movements of the forelimb contralaterally and proximal movements of the forelimb bilaterally. They examined movements of either forelimb in retrieving food pellets while restricting visual input to one hemisphere. Their results indicate that the seeing hemisphere could control reaching and grasping movements of the contralateral forelimb and reaching but not grasping movements of the ipsilateral forelimb. Axonal degeneration studies (Liu and Chambers 1964) and studies injecting anterograde tracers in M1 (Ralston and Ralston 1985) reveal that approximately 75% of corticospinal neurons decussate in the pyramids, approximately 15% decussate in the spinal cord, and the remaining approximately 10% do not cross. Uncrossed



**Fig. 1.** The effects of low-frequency repetitive transcranial magnetic stimulation (TMS) applied over the dorsal premotor cortex (PMd) on object lifting. In one of our TMS studies, subjects lifted “light” and “heavy” weights in a series of intermixed trials before and after we applied low-frequency repetitive TMS over PMd (Chouinard and others 2005). *A*, Illustrates the manipulandum that we used to measure precision grip. An aluminum rod passed through a hole in the table that held a weight carrier at its bottom end. This allowed us to add or remove from the carrier a 200-g weight without the subject seeing us change weights. Color cues were presented on a computer screen to provide subjects with advance information about which of the two weights they would have to lift. *B*, Represents average traces for grip forces 12 to 20 minutes before repetitive stimulation over PMd. Before repetitive TMS, subjects could scale appropriate forces for a current weight. *C*, Represents average traces for grip forces 12 to 20 minutes after repetitive stimulation over PMd. Repetitive TMS over PMd resulted in the scaling of forces based on a previous trial. In the switch trials, the rates in force increased after the weight became lighter, that is, light-after-heavy was faster than light-after-light, and decreased after the weight became heavier, that is, heavy-after-light was slower than heavy-after-heavy.

corticospinal neurons terminate in either the medial motor-nuclei or intermediate zones of the spinal cord (Liu and Chambers 1964; Ralston and Ralston 1985) and innervate proximal-forelimb muscles in the shoulder. Terminations of uncrossed corticospinal neurons in the lateral motor-nuclei, which innervate distal-forelimb muscles, have yet to be demonstrated.

It is believed that the corticospinal tract evolved as primates became more dexterous with their hands. Comparative anatomical studies reveal that as primates developed precision grip, the corticospinal tract increased in its overall size (Heffner and Masterton 1983; Nudo and others 1995), and this was accompanied by the emergence of corticospinal terminations in the ventral horn where the lateral motor-nuclei are located (Bortoff and Strick 1993). Cebus monkeys can use precision grip between the thumb and index finger to manipulate small objects and have abundant corticospinal terminations in the ventral horn. In contrast, squirrel monkeys cannot use precision grip and must instead use the whole hand to manipulate small objects; these monkeys have sparse corticospinal terminations in the ventral horn (Bortoff and Strick 1993). Extracellular recordings in the spinal

ventral horn in response to cortical stimulation reveal that excitatory postsynaptic potentials are smaller and rise more slowly in primate species that cannot use precision grip compared with those that do (Maier and others 1997, 1998).

### Dorsal Premotor Area

Patients with surgical excisions in the frontal lobes, including portions of the premotor cortex, have difficulty learning arbitrary associations. Petrides (1985b, 1997) showed that these patients have difficulty learning a task in which six or nine different colored lights cued different hand gestures. Petrides (1982, 1985a), as well as Halsband and Passingham (1982, 1985), examined in the monkey the effects of frontal cortex ablations on similar conditional associative tasks. They discovered that the removal of PMd disrupts the ability to use arbitrary cues to withhold or make particular movements. Other studies provide further evidence that PMd is critical for implementing associations between arbitrary cues and motor responses. PMd neurons discharge after the presentation of an arbitrary cue that instructs the monkey to make a

particular motor response (Kurata and Wise 1988; Mitz and others 1991; Kurata and Hoffman 1994). Also, injections of GABA<sub>A</sub>-agonist muscimol in PMd diminish the monkey's ability to select correct responses based on previously learned arbitrary associations (Kurata and Hoffman 1994).

In one of our transcranial magnetic stimulation (TMS) studies, subjects lifted two different weights in a series of intermixed trials before and after we applied low-frequency repetitive TMS over PMd (Chouinard and others 2005). Color cues provided subjects with advance information about which of the two weights they would have to lift. Repetitive TMS applied over PMd disrupted the subjects' ability to use the arbitrary color cues to scale forces for a current weight (Fig. 1). Before repetitive TMS, the arbitrary color cues provided subjects with information about which of the two weights they had to lift, and subjects were then able to use this information to apply faster rates in grip-force for the heavier weight compared with the lighter weight. After repetitive TMS, subjects could no longer select appropriate motor programs for the lifting of the two different weights based on the arbitrary color cues that they saw. Instead, they scaled forces based on the weight they had lifted in the previous trial.

PMd also selects motor responses based on spatial cues (Wise 1985). The firing activity of a number of PMd neurons increases after a spatial cue is presented to instruct monkeys to make a particular response in one direction (Weinrich and Wise 1982; Weinrich and others 1984; Wise 1985). These neurons show specificity regardless of whether spatial cues are presented in the visual or auditory modality (Weinrich and Wise 1982). These findings indicate that PMd can direct movements based on sensory information. This has certain importance for behavior. We often attend to an object while we prepare to reach towards it and grasp it and continue to do so until the task is accomplished. PMd receives a combination of somatosensory and visual information for the visual guidance of arm movement trajectories from the medial intraparietal (MIP) area in the superior parietal lobule (Colby and Duhamel 1991; Galletti and others 1996).

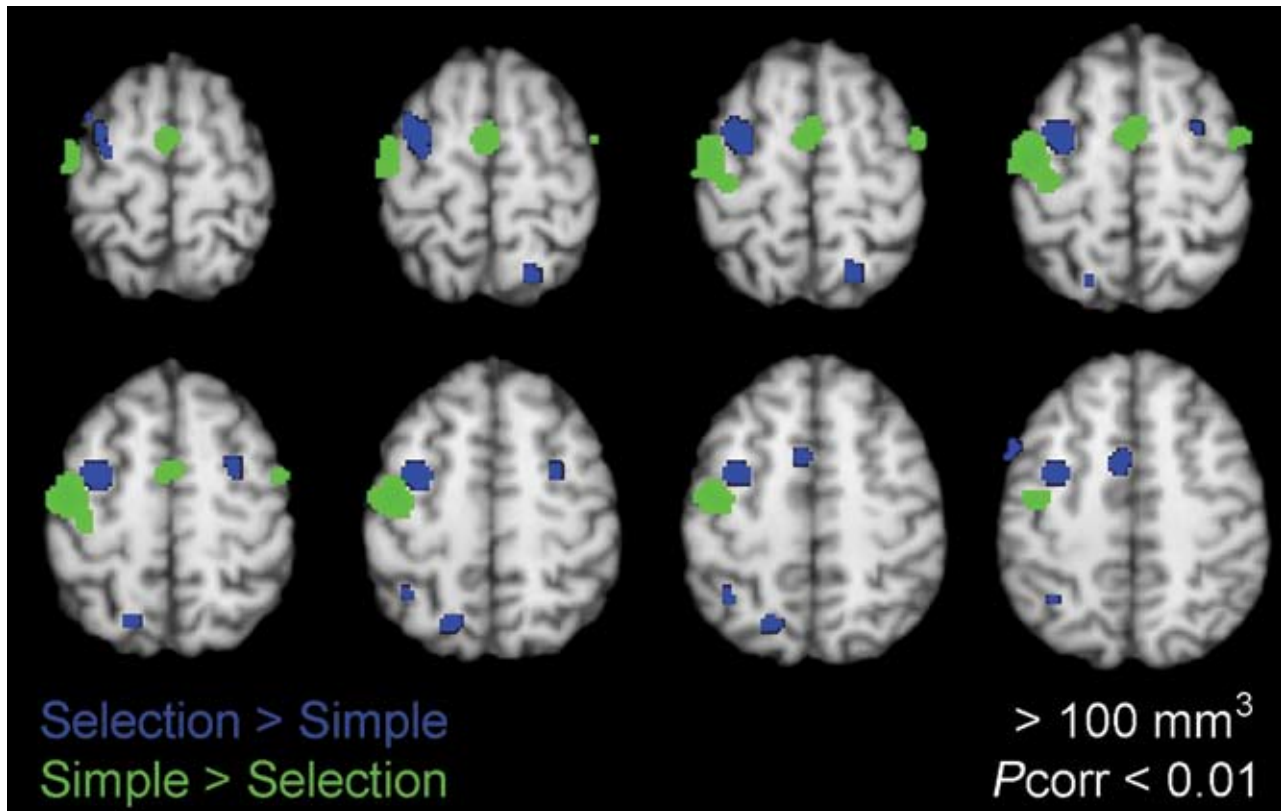
In a meta-analysis of neuroimaging studies, Picard and Strick (2001) revealed that the caudal and rostral portions of the human PMd each have unique functional specializations. Changes in cerebral activity related to more cognitively demanding tasks were present, on average, 19 mm anterior to movement-related tasks. These findings could correspond to two distinct PMd areas, namely, those identified in the monkey as the rostral PMd area F7 and the caudal PMd area F2 (Rizzolatti and others 1998). We found a similar dissociation when we performed a coordinate-based voxel-wise meta-analysis based on activation likelihood-estimation (ALE) mapping (Laird and others 2005). We used the software Search & View ([www.brainmap.org](http://www.brainmap.org)) to subtract two ALE maps derived from neuroimaging studies that measured changes in cerebral activity during the selection of motor responses with those during the execution of simple

(fixed) responses to visual, auditory, or somatosensory cues (Table 1). Our analysis yielded a cluster unique for the selection of motor responses in the left PMd in the superior frontal sulcus (Fig. 2; center: X = -32, Y = -2, Z = 50;  $P_{\text{corrected}} < 0.01$ ; 1432 mm<sup>3</sup>). In their meta-analysis, Picard and Strick (2001) reported average coordinates for the rostral PMd (Y = 5) that are more anterior than the one yielded from our analysis (Y = -2). This may relate to their inclusion of more anterior coordinates in Brodmann area 8 derived from contrasts not related to response selection. The rostral PMd is strongly interconnected with the prefrontal cortex (Barbas and Pandya 1987; Lu and others 1994). The prefrontal cortex has access, through its connections with other brain structures, to sensory and spatial aspects of the environment and mnemonic information acquired through experience (Barbas 2000; Petrides 2000). Our analysis yielded a cluster unique for the execution of simple responses in the left caudal PMd on the precentral gyrus (Fig. 2; center: X = -42, Y = -10, Z = 52;  $P_{\text{corrected}} < 0.01$ ; 2448 mm<sup>3</sup>). This portion of PMd has strong interconnections with M1 (Barbas and Pandya 1987; Dum and Strick 2005) and is therefore well placed to influence the generation of movements.

### Ventral Premotor Area

PMv contributes significantly to the control of hand movements required for the manipulation of objects. When grasping objects, people preshape their hand to match the three-dimensional structure of the object. This behavior requires a transformation from the visual representation of the object's geometrical properties to the motor commands acting on the muscles of the hand. Several studies in the monkey demonstrate that this transformation relies on a parieto-frontal circuit composed of connections between the anterior intraparietal (AIP) area and PMv (Rizzolatti and others 1988; Murata and others 1997). This preshaping of the hand, however, is not enough to ensure proper manipulation of objects. When lifting objects, people must also apply forces that match the expected weight of the object (Johansson and Westling 1984). Firing activity in a number of PMv neurons either increase or decrease as a function of the amount of grip forces applied during precision grip (Hepp-Reymond and others 1994, 1999). This dexterous control of forces by PMv is mediated through M1. PMv by itself exerts little detectable corticospinal output but can produce robust changes in the corticospinal output arising from M1 (Shimazu and others 2004).

A number of neuroimaging studies report changes in cerebral activity in PMv when subjects either alter grip forces during precision grip (Ehrsson and others 2001; Kuhtz-Buschbeck and others 2001) or change finger configurations while manipulating objects by tactile exploration (Binkofski and others 1999; Bodegard and others 2001; Stoeckel and others 2003). The *left* panel of Figure 3 provides results from an ALE map that we produced from neuroimaging studies that measured changes in cerebral activity during the execution of object-related



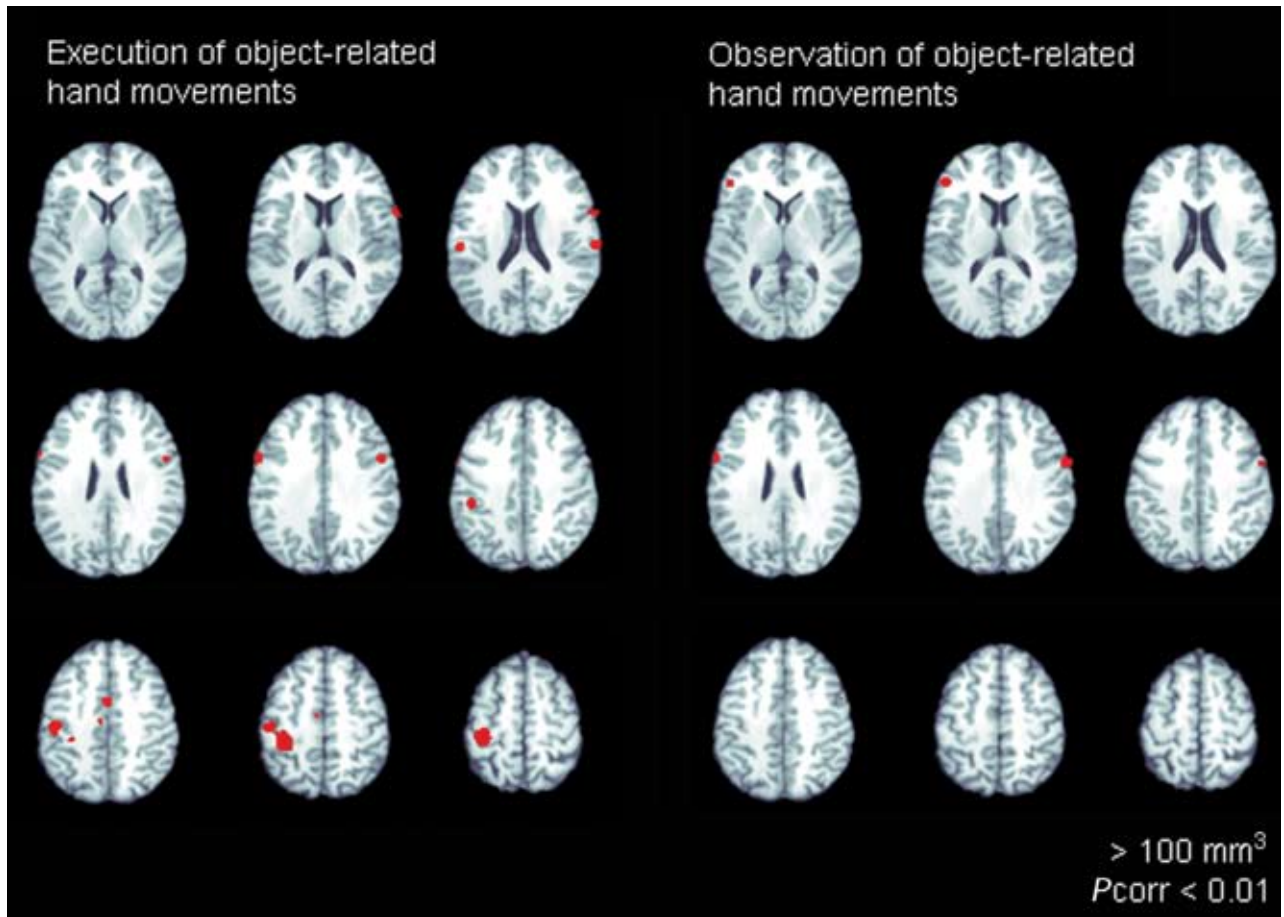
**Fig. 2.** Cerebral activity during the selection of responses versus simple responses. The figure illustrates results from comparing two activation likelihood-estimation maps derived from neuroimaging studies that measured changes in cerebral activity during the selection of motor responses with those during the execution of simple responses. Blue represents clusters unique for the selection of responses, and green represents clusters unique for simple responses. Clusters unique to the selection of responses reached significance in the left dorsal premotor cortex (PMd) in the superior frontal sulcus ( $-32, -2, 50$ ), the left cingulate sulcus ( $-6, 4, 46$ ), the left middle frontal gyrus ( $-50, 10, 42$ ), the left ventral premotor cortex at the opening of the precentral sulcus ( $-54, 6, 32$ ), the right parahippocampal gyrus ( $20, -50, -8$ ), the left posterior superior parietal lobule ( $-16, -64, 50$ ), the right posterior superior parietal lobule ( $18, -60, 56$ ), and the right PMd at the junction of the precentral and superior frontal sulci ( $28, 0, 52$ ). Clusters unique to simple responses reached significance in the left PMd on the precentral gyrus ( $-42, -10, 52$ ), the supplementary motor area ( $-2, -2, 56$ ), the right PMd on the precentral gyrus ( $44, -2, 54$ ), and the right postcentral operculum ( $58, -22, 12$ ). All clusters had false discovery rates of below 0.01 after correction for multiple comparisons in a volume exceeding  $100 \text{ mm}^3$ .

hand movements. It should be noted that some neuroimaging studies fail to demonstrate changes in PMv during object-related hand movements (e.g., Grafton and others 1996; Rizzolatti, Fadiga, Matelli, and others 1996). The lack of change in PMv might relate to the fact that these studies subtracted cerebral activity acquired while subjects viewed objects from cerebral activity acquired while subjects grasped the same objects. Neurons in PMv discharge both when monkeys view and grasp the same object (Murata and others 1997). The effects of seeing an object and grasping the same object might therefore cancel activity in PMv. In fact, one neuroimaging study reports common activity in PMv during the viewing and grasping of objects as determined by conjunction analysis (Grezes and others 2003).

PMv is also thought to underlie more cognitive-related functions including the understanding of actions. In the macaque monkey, PMv contains a class of neurons called *mirror neurons* (Rizzolatti and Luppino 2001). Mirror neurons discharge both when monkeys make a particular action and when they observe another monkey

or human make the same action. Actions that activate mirror neurons most effectively are the grasping and manipulation of objects (Gallese and others 1996). Importantly, mirror neurons discharge for one action only. It has been suggested that these neurons might mediate the understanding of actions made by others (Rizzolatti, Fadiga, Gallese, and others 1996). Consistent with this notion, Umiltà and others (2001) demonstrated that mirror neurons discharge when monkeys observe an action directed towards an object hidden behind a screen but do not discharge when monkeys see the beginning of the same action with no object present behind the screen. In recent years, the number of human brain mapping studies devoted to understanding action observation has increased. The *right* panel of Figure 3 provides results from an ALE map that we produced from neuroimaging studies that measured changes in cerebral activity during the observation of object-related hand movements.

To locate areas in the brain that may have a dual role in both the execution and observation of object-related hand movements, we performed a conjunction analysis



**Fig. 3.** Cerebral activity during the execution (*left side*) and observation (*right side*) of object-related hand movements. For the execution of object-related hand movements, clusters reached significance in the left sensorimotor area in the central sulcus ( $-38, -28, 52$ ), the left postcentral gyrus ( $-48, -20, 44$ ), the left ventral premotor cortex (PMv) over the precentral sulcus ( $-60, 8, 30$ ), the right PMv in the precentral operculum ( $62, 10, 12$ ), the right postcentral operculum ( $60, -18, 18$ ), the left cingulate gyrus ( $-2, 0, 42$ ), the right PMv in the precentral sulcus ( $48, 6, 28$ ), the left postcentral operculum ( $-56, -20, 18$ ), and the left cingulate sulcus ( $-8, -16, 42$ ). For the observation of object-related hand movements, clusters reached significance in the right PMv on the precentral gyrus ( $56, 4, 30$ ), the left inferior frontal gyrus in the prefrontal cortex ( $-48, 34, 10$ ), and the left PMv over the precentral sulcus ( $-62, 6, 22$ ). All clusters had false discovery rates of below 0.01 after correction for multiple comparisons in a volume exceeding  $100 \text{ mm}^3$ .

between ALE maps produced from neuroimaging studies that measured changes in cerebral activity during the execution of object-related hand movements with those during the observation of object-related hand movements. The analysis resulted in a cluster in the left PMv common to both maps over the precentral sulcus (Fig. 4; center:  $X = -58, Y = 6, Z = 28$ ;  $P_{\text{corrected}} < 0.05$ ). This finding suggests that PMv fulfills a dual role in both the execution and observation of object-related hand movements. Consistent with this finding, Grezes and others (2003) demonstrated changes in cerebral activity in the left PMv as subjects both grasped objects and watched other people grasp the same objects as determined by a conjunction analysis.

#### How the Premotor Areas Influence the Primary Motor Area

Hughlings Jackson viewed the central nervous system as a sensorimotor machine (York and Steinberg 1994).

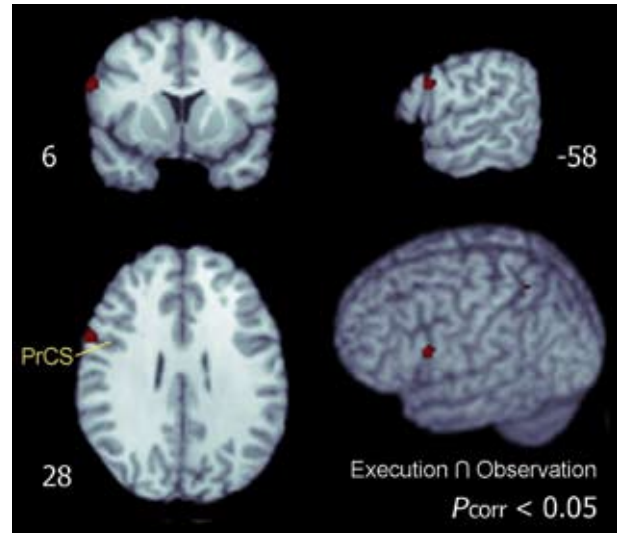
By this, he meant that all functions in the brain could be described exclusively in terms of processing sensory input and generating motor output. He believed that the central nervous system was composed of a number of hierarchical levels: each level containing a complete set of representations of the next lower level that enables it to exert influence on motor behavior (see Hughlings Jackson 1958). This hierarchical organization of the motor system was challenged in the 1990s with the emergence of anatomical studies in the monkey that demonstrate a number of cortical areas other than M1 with direct projections to the spinal cord (Dum and Strick 1991; He and others 1993, 1995; Galea and Darian-Smith 1994). The question then arises whether the nonprimary motor areas could have the capacity to act in parallel when generating movements.

Yet cortical projections to the spinal cord do not mandate necessarily a direct influence on the spinal motor-neurons. In fact, all nonprimary motor areas have a weak direct influence on the spinal motor-neurons. The injec-

tion of anterograde tracers in the forelimb representation of the nonprimary motor areas reveals that the majority of their corticospinal neurons terminate in the intermediate zone of the spinal cord (Dum and Strick 1996, 2002). Excitatory postsynaptic potentials recorded in the lateral motor-nuclei in response to electrical stimulation of the nonprimary motor areas are much smaller and rise more slowly compared with electrical stimulation of M1 (Lemon and others 2002; Maier and others 2002). M1 lesions produce force deficit, abnormal muscle tone, and impairments in generating fractionated finger movements (Porter and Lemon 1993). In contrast, motor disturbances ascribed to lesions restricted to the premotor cortex include weakness of proximal arm muscles and limb-kinetic apraxia (Freund and Hummelsheim 1985). Together, these findings demonstrate that the influence of the nonprimary motor areas on the spinal cord may reflect the preparation and modulation of intrinsic spinal circuitry (Prut and Fetz 1999; Bizzi and others 2000) rather than the generation of independent finger movements that requires a direct excitatory influence on the spinal motor-neurons (Lemon and others 2002; Maier and others 2002).

Brain mapping studies demonstrate also a hierarchical organization of the motor system in humans. TMS studies have examined functional connectivity between PMd and M1. TMS applied in multiple pulses can modulate the output of the motor system in a temporary fashion lasting beyond the duration of stimulation. Low-frequency ( $\leq 2$  Hz) repetitive TMS over M1 typically reduces motor excitability as assessed by motor-evoked potentials recorded in the contralateral hand muscles (Chen and others 1997; Maeda and others 2000; Muellbacher and others 2000). Low-frequency repetitive TMS over PMd can also reduce motor excitability (Gerschlag and others 2001; Munchau and others 2002; Chouinard and others 2003, 2005). Cortico-cortical connections between PMd and M1 are thought to mediate these effects. Munchau and colleagues (2002) demonstrated that a reduction in motor excitability induced by repetitive TMS over PMd coincides with lasting effects in the cortical circuitry of M1 as assessed by paired-pulse TMS and changes in the cortical silent period.

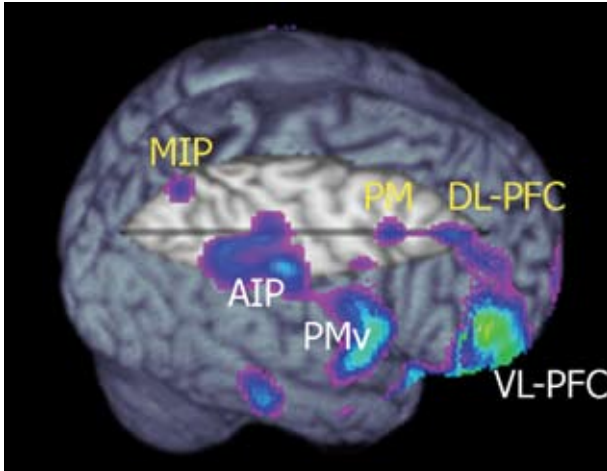
In a TMS/positron emission tomography (PET) study, we examined the effects of applying low-frequency repetitive TMS over M1 and PMd on cerebral blood flow (Chouinard and others 2003). We mapped networks of brain regions in which changes in cerebral blood flow correlated with changes in motor excitability. We interpreted these correlations as an index of *neural modulation* induced by repetitive TMS. Neural modulation occurred in a small number of brain regions after M1 stimulation, many of these confined to the nonprimary motor areas and subcortical motor structures. In contrast, neural modulation occurred in multiple regions after PMd stimulation; these include motor areas in the frontal cortex as well as more associational regions in the parietal and prefrontal cortices (Fig. 5). These findings are consistent with known differences between M1 and PMd in the extent of their anatomical connectivity in



**Fig. 4.** The ventral portion of the premotor cortex (PMv) activity common to both the execution and observation of object-related hand movements. A conjunction analysis between activation likelihood-estimation maps derived from neuroimaging studies that measured changes in cerebral activity during the execution of object-related hand movements with those during the observation of object-related hand movements yielded common changes in activity in the left PMv at the opening of the precentral sulcus ( $-58, 6, 28$ ).  $P$  values were corrected for multiple comparisons using a method based on false discovery rate. PrCS = precentral sulcus.

the macaque monkey. M1 connects with the nonprimary motor and somatosensory cortices; connections between M1 and other cortical structures are sparse (Matelli and Luppino 1997). Visual and/or auditory information that influence movements must first be processed by associational and/or higher order sensory cortices and then be communicated to the nonprimary motor areas (Ghez and others 1991).

Parieto-frontal circuits provide an anatomical basis for the transformation of sensory information into actions (Rizzolatti and others 1998; Matelli and Luppino 2000). The parietal lobes receive somatosensory and visual inputs and encompass several subdivisions that have reciprocal connections with motor areas in the frontal cortex, each with a specific target with which it is most densely connected. PMd receives information for the visual guidance of arm movement trajectories from the MIP (Colby and Duhamel 1991; Galletti and others 1996; Matelli and Luppino 2000). Our TMS/PET study revealed a possible human homolog of the PMd-MIP circuit with changes in cerebral blood flow in both the premotor area and medial intraparietal cortex (Fig. 5). PMv is strongly interconnected with AIP in the anterior portion of the intraparietal cortex (Luppino and others 1999). Both PMv and AIP contain neurons that code for selective hand manipulations, grasping movements, and various visual characteristics of three-dimensional objects (Rizzolatti and others 1988; Murata and others 1997). Jeannerod and others (1995) suggested that this circuit may transform the three-dimensional characteris-



**Fig. 5.** The effects of low-frequency repetitive transcranial magnetic stimulation (TMS) applied over the dorsal portion premotor cortex (PMd) on cerebral activity. In one of our previous TMS/PET studies (Chouinard and others 2003), repetitive TMS applied over PMd induced changes in cerebral blood flow in a number of premotor, prefrontal, and parietal areas. The results presented in this figure could reflect parieto-premotor and premotor-prefrontal circuits that are known to exist in the macaque monkey and also lend support to the notion of PMd being involved in selecting actions based on sensory information. The parietal lobes integrate sensory information about the environment, which they then communicate to both the premotor and prefrontal cortices. The prefrontal cortex plays a prominent role in executive functions and has access through other brain structures to mnemonic information acquired through experience. MIP = medial intraparietal area; DL-PFC = dorsolateral prefrontal cortex; PMv = ventral premotor area; AIP = anterior intra-parietal area; VL-PFC = ventrolateral prefrontal cortex.

tics of objects from sensory information into the appropriate hand movements for grasping. Our TMS/PET study revealed a possible human homolog of the PMv-AIP circuit with changes in cerebral blood flow in both PMv and the anterior portion of the intraparietal cortex (Fig. 5). Repetitive TMS applied over PMd could have modulated PMv; both areas are strongly interconnected (Marconi and others 2003; Dum and Strick 2005).

## Conclusions

The parcellation of the motor cortex has become more complex since Fulton (1935) suggested that it can be divided into distinct functional areas. Today, several distinct nonprimary motor areas have been identified. The caudal PMd has strong connections with M1 and is well placed to influence the generation of movements. In contrast, the rostral PMd has strong connections with the prefrontal cortex and selects responses based on arbitrary and spatial cues. In recent years, the number of human brain mapping studies devoted to understanding action observation has increased. A conjunction analysis reveals that the human PMv has a dual role in both the execution and observation of object-related hand movements. The premotor areas all have a weak direct influence on the spinal motor neurons. The majority of their

corticospinal neurons terminate in the intermediate zone (Dum and Strick 1996, 2002), and electrical stimulation of these areas results in weaker postsynaptic activity in the lateral motor-nuclei compared with electrical stimulation of M1 (Lemon and others 2002; Maier and others 2002). Finally, M1 is connected with fewer cortical structures than the premotor areas. Visual and/or auditory information that influence movements must first be processed by associational and/or higher-order sensory cortices and then be communicated to the nonprimary motor areas. The premotor areas in turn can use this information to coordinate output at the level of both M1 and the spinal cord (Dum and Strick 1991).

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