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The primary motor and premotor areas of the human cerebral cortex

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Primary motor and premotor areas

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Abstract

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. Over 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 non-primary 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, we will 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). We will end this review by discussing how the premotor areas influence M1.
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 non-human 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 cyto-architecture between agranular cortex with large pyramidal cells in the anterior bank of the precentral sulcus (area 4) and 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 non-primary motor areas have been identified.

The non-primary 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 Welsh, 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 (M1)

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 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 ~75% of corticospinal neurons decussate in the pyramids, ~15% decussate in the spinal cord, and the remaining ~10% do not cross. Uncrossed 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). Extra-cellular recordings in the spinal ventral horn in response to cortical stimulation reveal that excitatory post-synaptic 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 (PMd)**

Patients with surgical excisions in the frontal lobes, including portions of the premotor cortex, have difficulty learning arbitrary associations. Petrides (1985a; 1997) have shown that these patients have difficulty learning a task in which six or nine different colored lights cued different hand gestures. Petrides (1982; 1985b), as well as Halsband and Passingham (1982; 1985), have 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 and 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 inter-mixed 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 (Figure 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 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 intra-parietal (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) 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 (Figure 2; center: X = −32, Y = −2, Z = 50; \( P_{\text{corrected}} < 0.01; 1,432 \text{ mm}^3 \)). In their meta-analysis, Picard and
Strick (2001) report average co-ordinates 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 inter-connected with the prefrontal cortex (Barbas and Pandya, 1987; Lu and others, 2004). 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 (Figure 2; center: X = −42, Y = −10, Z = 52; P_corrected < 0.01; 2,448 mm³). This portion of PMd has strong inter-connections 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**

PMv contributes significantly to the control of hand movements required for the manipulation of objects. When grasping objects, people pre-shape 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 intra-parietal (AIP) area and PMv (Rizzolatti and others, 1988; Murata and others, 1997). This pre-shaping 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). Neurons in PMv discharge as forces exerted during precision grip either increases or decreases (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 (Schimazu 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; Kutz-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 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 and others, 1996a). 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 and others, 1996b). Consistent with this notion, Umilta and others (2001) demonstrate 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.
In order 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 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 (Figure 4; center: X = −58, Y = 6, Z = 28; P_{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 M1**

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 (In: J Taylor, 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 or not the non-primary 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 non-primary motor areas have a weak direct influence on the spinal motor-neurons. The injection of anterograde tracers in the forelimb representation of the non-primary motor areas reveal that the majority of their corticospinal neurons terminate in the intermediate zone of the spinal cord (Dum and Strick, 1996; 2002). Excitatory post-synaptic potentials recorded in the lateral motor-nuclei
in response to electrical stimulation of the non-primary 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 non-primary 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 (≤ 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 (Gerschlager 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 non-primary 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 (Figure 5). These findings are consistent with known differences between M1 and PMd in the extent of their anatomical connectivity in the macaque monkey. M1 connects with the non-primary 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 non-primary 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 MIP (Colby and Duhamel, 1991; Galletti and others, 1996; Matelli and Luppino, 2000). Our TMS / PET study revealed a possible human homologue of the PMd-MIP circuit with changes in cerebral blood-flow in both the premotor area and medial intra-parietal cortex (Figure 5). PMv is strongly inter-connected with AIP in the anterior portion of the intra-parietal cortex (Luppino and others, 1999). Both PMv and AIP contain neurons that code for selective hand manipulations, grasping movements, and various visual characteristics of 3-D objects (Rizzolatti and others, 1988; Murata and others, 1997). Jeannerod and others (1995) suggest that this circuit may transform the 3-D characteristics of objects from sensory information into the appropriate hand movements for grasping. Our TMS / PET study revealed a possible human homologue of the PMv-AIP circuit with changes in cerebral blood-flow in both PMv and the anterior portion of the intra-parietal cortex (Figure 5). Repetitive TMS applied over PMd could have modulated PMv; both areas are strongly inter-connected (Marconi and others, 2002; 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 non-primary 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 post-synaptic 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 non-primary 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).
Table 1. Studies used to perform coordinate-based voxel-wise meta-analyses.

<table>
<thead>
<tr>
<th>Response selection</th>
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<tbody>
<tr>
<td><strong>Adam and others, 2003</strong></td>
<td>Selective response to spatial cues &gt; Rest</td>
</tr>
<tr>
<td><strong>Grafton and others, 1998</strong></td>
<td>Selective response to arbitrary color cues &gt; Fixed response</td>
</tr>
<tr>
<td><strong>Kertzman and others, 1997</strong></td>
<td>Selective response to spatial cues &gt; Rest</td>
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<tr>
<td><strong>Kurata and others, 2000</strong></td>
<td>Selective response to arbitrary tones &gt; Fixed response</td>
</tr>
<tr>
<td><strong>Sakai and others, 2000</strong></td>
<td>Selective response to arbitrary color cues &gt; Expected response</td>
</tr>
<tr>
<td></td>
<td>Selective response to arbitrary tones &gt; Expected response</td>
</tr>
<tr>
<td><strong>Schluter and others, 2001</strong></td>
<td>Selective response to arbitrary shapes &gt; Fixed response</td>
</tr>
<tr>
<td><strong>Seidler and others, 2004</strong></td>
<td>Selective response to spatial cues &gt; Rest</td>
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<tr>
<td></td>
<td><strong>Simple responses</strong></td>
</tr>
<tr>
<td><strong>Cerasa and others, 2005</strong></td>
<td>Fixed response to color cue &gt; Viewing</td>
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<tr>
<td><strong>Gerardin and others, 2000</strong></td>
<td>Fixed response to auditory cue &gt; Listening</td>
</tr>
<tr>
<td><strong>Janke and others, 2000</strong></td>
<td>Fixed response to color cue &gt; Rest</td>
</tr>
<tr>
<td><strong>Kansaku and others, 2004</strong></td>
<td>Fixed response to color, auditory, and air-puff cues &gt; Base</td>
</tr>
<tr>
<td><strong>Suguira and others, 2001</strong></td>
<td>Fixed response to color cue &gt; Rest</td>
</tr>
<tr>
<td></td>
<td>Fixed response to auditory cue &gt; Rest</td>
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<td></td>
<td><strong>Execution of object-related hand movements</strong></td>
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<tr>
<td><strong>Binkofski and others, 1999</strong></td>
<td>Tactile manipulation (object) &gt; Hold (object)</td>
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<tr>
<td><strong>Bodegard and others, 2001</strong></td>
<td>Tactile manipulation (object) &gt; Rest</td>
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<tr>
<td><strong>Ehrsson and others, 2001</strong></td>
<td>Precision grip (gentle) &gt; Precision grip (normal)</td>
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<tr>
<td><strong>Kutz-Buschbeck and others, 2001</strong></td>
<td>Precision grip (gentle) &gt; Precision grip (normal)</td>
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<tr>
<td></td>
<td>Precision grip (firm) &gt; Precision grip (normal)</td>
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<tr>
<td><strong>Stoeckel and others, 2003</strong></td>
<td>Tactile manipulation (object) &gt; Rest</td>
</tr>
<tr>
<td></td>
<td><strong>Observation of object-related hand movements</strong></td>
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<tr>
<td><strong>Buccino and others, 2001</strong></td>
<td>Observation (grasp object) &gt; Observation (static hand)</td>
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<tr>
<td><strong>Buccino and others, 2004</strong></td>
<td>Observation (grasp object) &gt; Rest</td>
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<tr>
<td><strong>Grafton and others, 1996</strong></td>
<td>Observation (grasp object) &gt; Observation (object)</td>
</tr>
<tr>
<td><strong>Johnson-Frey and others, 2003</strong></td>
<td>Observation (grasp object) &gt; Observation (touch object)</td>
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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 MNI template brain for spatial normalization were transformed further into the standard stereotaxic atlas of Talairach and Tournoux (1998) using an algorithm written by Dr. Matthew Brett (www.mrc-cbu.cam.ac.uk/Imaging/Common/mnispace).
Figure 1. The effects of low-frequency repetitive TMS applied over PMd on object lifting. In one of our TMS studies, subjects lifted “light” and “heavy” weights in a series of inter-mixed 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 200g 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 20 to 12 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.
Figure 2. *Cerebral activity during the selection of responses versus simple responses.* The figure illustrates results from comparing 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 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 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 PMv 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 in a volume that exceeded 100 mm$^3$. 
Figure 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 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 in a volume that exceeded 100 mm$^3$. 
Figure 4. PMv activity common to both the execution and observation of object-related hand movements. A conjunction analysis between ALE 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. Abbreviations: PrCS = precentral sulcus.
Figure 5. *The effects of low-frequency repetitive TMS applied over 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 lend also 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 it then communicates 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. Abbreviations: PMd = dorsal premotor area, MIP = medial intra-parietal area, DL-PFC = dorsolateral prefrontal cortex, PMv = ventral premotor area, AIP = anterior intra-parietal area, VL-PFC = ventrolateral prefrontal cortex.
References


