

Electrophysiology of Action Representation

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Abstract: We continuously act on objects, on other individuals, and on ourselves, and actions represent the only way we have to manifest our own desires and goals. In the last two decades, electrophysiological experiments have demonstrated that actions are stored in the brain according to a goal-related organization. The authors review a series of experimental data showing that this “vocabulary of motor schemata” could also be used for non-strictly motor purposes. In the first section, they present data from monkey experiments describing the functional properties of inferior premotor cortex and, in more detail, the properties of visuomotor neurons responding to objects and others’ actions observation (mirror neurons). In the second section, human data are reviewed, with particular regard to electrophysiological experiments aiming to investigate how action representations are stored and addressed. The specific facilitatory effect of motor imagery, action/object observation, and speech listening on motor excitability shown by these experiments provides strong evidence that the motor system is constantly involved whenever the idea of an action is evoked.

Key Words: Transcranial magnetic stimulation, Premotor cortex, Area F5, Mirror neurons, Motor imagery, Speech perception

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Neurophysiologic techniques, such as transcranial magnetic stimulation (TMS) (Barker et al. 1985) and electromyography (EMG), have traditionally been used to investigate the motor system, mainly from a clinical perspective. EMG, for example, is widely used to measure the conduction time of nerves (see Stalberg, 1990; Weber, 1990), to early diagnose myopathy (Jones and Darras, 2000), and to quantitatively investigate reflex circuits (Cruccu and Deuschl, 2000). TMS is clinically used to determine the central conduction time, to

diagnose central motoneuron diseases and damage to the myelin shield, or even to manage psychiatric diseases such as depression or schizophrenia (for recent general reviews, see Curra et al., 2002; Kobayashi and Pascual-Leone, 2003). All these clinical applications, however, functionally investigate the executive counterpart of the motor system. In contrast, here we deal not with motor execution, but focus on how electrophysiologic techniques can be used to investigate the way in which the brain represents actions, independently from their future execution. In the first part of this article, we will review data concerning single-neuron recordings in the monkey. Then, a parallel will be drawn with human data, mainly with those arising from electrophysiological experiments.

ACTION REPRESENTATION IN THE MONKEY BRAIN

Motor Properties of Monkey Ventral Premotor Cortex

Electrophysiologic evidence recently showed that actions are stored in the brain as goal-directed motor schemata. Microstimulation studies (Hepp-Reymond et al., 1994) and single-neuron recordings performed in the monkey ventral premotor cortex (area F5) demonstrated that neurons in this region selectively discharge during goal-directed hand/mouth actions (Rizzolatti et al. 1988). The specificity of the goal seems to be an essential prerequisite in activating these neurons. The same neurons that discharge during grasping, holding, tearing, and manipulating are silent when the monkey performs actions that involve a similar muscular pattern but with a different goal (e.g., grasping to put away, scratching, grooming). Further evidence in favor of such a goal representation is given by F5 neurons that discharge when the monkey grasps an object with its right or left hand or with its mouth. This observation suggests that some F5 premotor neurons are capable of generalizing the goal, independently from the acting effector. Using the action effective in triggering a neuron’s discharge as a classification criterion, F5 neurons can be subdivided into several classes. Among them, the most common are “grasping,” “holding,” “tearing,” and “manipulating” neurons. Grasping neurons form the most represented class in area F5. Many of them are selective for

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a particular type of prehension such as precision grip, finger prehension, or whole-hand prehension. In addition, some neurons show specificity for different finger configurations, even within the same grip type. Thus, the prehension of a large spherical object (whole-hand prehension, requiring the opposition of all fingers) is coded by neurons different from those coding the prehension of a cylinder (still whole-hand prehension but performed with the opposition of the four last fingers and the palm of the hand).

Typically, F5 premotor neurons begin to discharge before the contact between the hand and the object. Some of them stop firing immediately after contact, whereas others keep firing for a while after it. The temporal relation between grasping movement and neuron discharge varies from neuron to neuron. Some neurons become active during the initial phase of the movement (opening of the hand), some discharge during hand closure, and others discharge during the entire grasping movement from the beginning of fingers opening until their contact with the object.

Taken together, the functional properties of F5 neurons suggest that this area stores a set of motor schemata (Arbib, 1997) or, as proposed previously (Rizzolatti and Gentilucci, 1988), contains a “vocabulary” of motor acts. The “words” composing this vocabulary are constituted by populations of neurons. Some of them indicate the general category of an action (hold, grasp, tear, manipulate). Others specify the effectors that are appropriate for that action. Finally, a third group is concerned with the temporal segmentation of the actions. What differentiates F5 from the primary motor cortex (M1, BA4) is that whereas F5 motor schemata code for goal-directed actions (or fragments of specific actions), in the primary motor cortex are represented movements that are independent from the action context in which they are used. In comparison with F5, M1 could therefore be defined as a “vocabulary of movements.”

All F5 neurons share similar motor properties. In addition to their motor discharge, however, several F5 neurons discharge also to the presentation of visual stimuli (visuomotor neurons). Two radically different categories of visuomotor neurons are present in area F5. Neurons of the first category discharge when the monkey observes graspable objects (“object observation” visuomotor neurons), whereas neurons of the second category discharge when the monkey observes hand actions performed by other individuals. These neurons have been named “mirror neurons” (Gallese et al., 1996; Rizzolatti et al., 1996a) and will be referred to here as “action observation” visuomotor neurons. The two categories of F5 visuomotor neurons are located in two different subregions of area F5: “object observation” neurons are mainly found in the bank of arcuate sulcus, whereas “action observation” neurons are almost exclusively recorded from the cortical convexity. Area F5 receives visual information from different sectors of the parietal cortex (mainly the inferior

parietal lobule). The description of these anatomical data goes behind the scope of this article. Readers interested in these more specialistic aspects could refer to Rizzolatti et al. (1998).

Visuomotor Properties of Monkey Ventral Premotor Cortex: “Object Observation” Visuomotor Neurons

As we outlined in the previous section, the motor vocabulary of actions stored in area F5 can be addressed not only during action execution. Recent experiments have shown that several F5 neurons (about 20%) discharge at the mere presentation of objects whose shape and size is congruent with the type of grip motorically coded by the same neurons. Recently, the visual responses of F5 object observation neurons have been reexamined using a formal behavioral paradigm that allowed the investigators to separately test the response related to object observation, during the waiting phase between object presentation and movements onset and during movement execution (Murata et al., 1997). The results showed that among object observation visuomotor neurons recorded in area F5, two thirds were selective to one or few specific objects. When visual and motor properties of F5 object observation neurons are compared, it becomes clear that there is a strict congruence between the two types of responses. Neurons that become active when the monkey observes small objects discharge also during precision grip. On the contrary, neurons selectively active when the monkey looks at a large object discharge also during actions directed toward large objects (e.g., whole-hand prehension).

The most likely interpretation for visual discharge in these visuomotor neurons is that, at least in adult individuals, there is a close link between the most common three-dimensional stimuli and the actions necessary to interact with them. Thus, every time a graspable object is visually presented, the related F5 neurons are addressed and the action is “automatically” evoked. Under certain circumstances, it guides the execution of the movement; under others, it remains an unexecuted representation of it that might be used also for semantic knowledge.

Visuomotor Properties of Monkey Ventral Premotor Cortex: “Action Observation” Visuomotor Neurons

Neurons that become active when the monkey acts on an object and when it observes another monkey or the experimenter making a similar goal-directed action (mirror neurons) (di Pellegrino et al., 1992; Gallese et al., 1996) constitute the second class of F5 visuomotor neurons. Mirror neurons appear, therefore, to be identical to “object observation” neurons in terms of motor properties, but they radically differ from them as far as visual properties are concerned (Rizzolatti and Fadiga, 1998).

To be triggered by visual stimuli, mirror neurons require an interaction between a biologic effector (hand or mouth) and an object. The sights of an object alone, of an agent mimicking an action, or of an individual making intransitive (non-object-directed) gestures are all ineffective. The object significance for the monkey has no obvious influence on mirror-neuron response. Grasping a piece of food or a geometric solid produces responses of the same intensity. Mirror neurons show a large degree of generalization. Largely different visual stimuli, but representing the same action, are equally effective. For example, the same grasping mirror neuron that responds to a human hand grasping an object responds also when the grasping hand is that of a monkey. Similarly, the response is, typically, not affected if the action is done near or far from the monkey, despite the fact that the size of the observed hand is obviously different in the two conditions. It is also of little importance for neuron activation if the observed action is eventually rewarded. The discharge is of the same intensity if the experimenter grasps the food and gives it to the recorded monkey or to another monkey introduced in the experimental room. Typically, mirror neurons show congruence between the observed and executed action. This congruence can be extremely strict, i.e., the effective motor action (e.g., precision grip) coincides with the action that, when seen, triggers the neurons (e.g., precision grip). For other neurons, the congruence is broader. For them, the motor requirements (e.g., precision grip) are usually stricter than the visual ones (any type of hand grasping).

The most likely interpretation for visual discharge in mirror neurons is that it evokes an internal representation of the observed action. In other terms, the observed action selects, in the F5 motor vocabulary, a congruent "motor word," a potential action.

It seems plausible that the visual response of both object observation and action observation visuomotor neurons address the same motor vocabulary, the words of which constitute the monkey motor repertoire. What is different is the way in which "motor words" are selected: in the case of object observation neurons, they are selected by the sight of an object or, in the case of mirror neurons, by the sight of an action. Thus, the visuomotor coupling shown by object observation neurons could be at the basis of the sensorimotor transformation that adapts the hand to a given object. The visuomotor discharge that characterizes mirror neurons could be at the basis of action imitation and action understanding (see Fadiga and Gallese, 1997; Rizzolatti et al., 1996b). The possible role of mirror neurons will be discussed more in detail later in this article.

ACTION REPRESENTATION IN THE HUMAN BRAIN

In the last two decades, the picture of how the human brain plans and executes actions has become clearer, thanks

to the development of noninvasive techniques such as brain imaging (fMRI), magnetoencephalography (MEG), high-resolution EEG and TMS. If, on the one side, these techniques significantly contributed to the knowledge of the physiology of the motor system, human neuroanatomy did not proceed with the same velocity, mainly because of the absence of noninvasive techniques for tracing neural pathways. For this reason, a comparative analysis with monkey data should take into account functional categories more than anatomical (and hodological) ones. In the next sections, we will review some recent data demonstrating in humans the existence of visuomotor responses similar to those found in monkeys. In addition, the involvement of action representation in peculiarly "human" situations, such as during thinking to act or during verbal communication, will be described.

Motor Imagery: The Brain Process of Action Simulation

One of the properties that most typically characterizes and differentiates human beings from other animals is the possibility to mentally represent "things" (actions, objects, emotions, etc.) by means of the *voluntary* process of thought, also in the absence of external triggers. It is a common experience that we can mentally represent actions simply by thinking about them. This process of mental representation is usually defined as motor imagery.

It is possible that the voluntary thinking about actions uses only cognitive tools, associating, for example, visual memories of the performed action with the emotional content typical of the context in which that particular action is usually performed. However, it is possible that motor imagery necessarily implies the involvement of the motor system, being it the fundamental source of the internal information about the evoked action. There is, indeed, a general agreement on the idea that the motor system plays a crucial role on motor imagery, that is supported by several data demonstrating that during the internal rehearsal of an action the individual "feels" as he were moving. For instance, the main vegetative parameters, such as heart rate, blood pressure, and breath frequency significantly increase. Moreover, the involvement of the vegetative system correlates with the strength of the effort (see Décety et al., 1993). The duration of imagined actions is similar to that of the same actions when actually executed, indicating a strict dependency of motor imagery on the physical and mechanical constraints driving action actual execution (Décety et al. 1989; Oishi and Maeshima, this issue). Many brain imaging studies showed an increase of regional blood flow (rCBF) in various cortical motor areas and cerebellum during motor imagery tasks (Décety et al., 1990; Fox et al., 1987; Grafton et al., 1996; Porro et al., 1996; Roland et al., 1980; Roth et al., 1996; Sanes, 1994; Stephan et al., 1995). Similar results were recently achieved by magneto-encephalography (Hari et al., 1997; Schnitzler et al.,

1997) and movement related potentials (Beisteiner et al., 1995; Cunnington et al. 1996). The involvement of the motor system during motor imagery, however, could be due to unspecific factors, such as intention or readiness to move, rather than to a true internal dynamic simulation of movement. Only in the latter case the motor system should be influenced in different ways according to the effector involved in motor imagery, to the type of imagined movement, and to the phase of the imagined movement. To discriminate between these two alternatives it is necessary to achieve a precise dynamic description of the excitation/inhibition pattern present in the corticospinal system during motor imagery. This purpose is easily addressed by using TMS that allows measurement of the corticospinal excitability with high temporal resolution.

Several TMS experiments indicated that facilitation of motor-evoked potentials (MEPs) by motor imagery appears to be largely limited to the target muscle, and is not due to a global arousal effect (Abbruzzese et al., 1996, 1999; Izumi et al., 1995; Kiers et al., 1997; Rossini et al., 1999). In the forearm, muscle-specific facilitation of MEP amplitude has been demonstrated during imagery of both tonic (Kasai et al., 1997; Rossi et al., 1998) and phasic (Hashimoto and Rothwell, 1999) wrist flexion and extension. Corticospinal excitability has been also studied during mental simulation of leg extension movements (Tremblay et al., 2001). These authors recorded EMG in both knee extensors (quadriceps) and flexors (biceps femoris) showing that, during motor imagery, the size of TMS-induced MEPs in the quadriceps, but not in the biceps femoris, increased significantly. Rossini and colleagues (1999) recorded MEPs from right abductor digiti minimi and first dorsal interosseus (FDI) during either mental simulation of selective index finger or little finger abduction. Their results showed that the increase of MEP amplitude induced by the task was confined to the muscle acting as "prime mover" for the mentally simulated movement, according to the motor program dispatched but not executed by the subject. Finally, a recent study (Facchini et al., 2002) indicated that imagery of unilateral simple movements is associated with a very specific increase of the excitability of contralateral primary motor cortex.

Although several groups demonstrated that the act of imagining to move facilitates the corticospinal system, only few investigated the temporal dynamic of this facilitation during motor imagery. Our group (Fadiga et al., 1999) investigated the specificity of action representation and temporal dynamics during motor imagery, by assessing the excitability of one arm muscle (biceps brachialis [BB], agonist for elbow flexion) and two hand muscles (opponens pollicis [OP], agonist for hand closing; extensor digitorum communis, antagonist of hand closing) during mental simulation of right forearm extension and flexion and right hand opening and closing. Imagined movements were continuously guided by a

frequency-modulated sound: the phase with increasing frequency indicated to the subjects to imagine to open their right hand or to flex their right forearm, whereas the phase with decreasing frequency guided the imagined hand closing or forearm extension. In some subjects, the association between sound and imagined movement was reverted. As a control, subjects were asked to generate the visual imagery of a previously seen cartoon showing a schematic man going down a schematic mountain (visual imagery task). This task was associated to the same sound used during the motor imagery task. The visual imagery condition was introduced to assess the degree of nonspecific activation (arousal) of the corticospinal system during the task. Motor potentials were evoked by TMS on the left precentral cortex. Results showed that: (1) during motor imagery of proximal arm movements, MEP amplitude of the BB muscle was larger during mental simulation of forearm flexion than during mental simulation of forearm extension (Fig. 1A), whereas OP muscle excitability recorded during motor imagery of the same proximal movements was not significantly influenced by the task (Fig. 1B). These data indicate the specificity of the motor imagery process: motor imagery of proximal movements involves proximal muscles only. (2) During hand motor imagery, whereas OP muscle excitability was higher during imagined hand closing than during imagined hand opening (Fig. 1C), extensor digitorum communis muscle excitability followed a reversal pattern of that exhibited by OP muscle during the same task (Fig. 1D). These data indicate that specific corticospinal channels are selectively influenced by the internal simulation of movement: motor imagery affects only MEPs of muscles that are involved during actual execution of that movement.

Similar results have been also achieved by Hashimoto and Rothwell (1999). These authors instructed subjects to imagine repetitive wrist flexion and extension movements at 1 Hz, whose flexion timing was given by an auditory signal (1.6-kHz tone burst of 20-millisecond duration). Surface EMG responses were recorded from the FDI, the flexor carpi radialis, and the extensor carpi radialis muscles. Results showed that MEPs in the flexor carpi radialis (agonist for wrist flexion) were larger during the period of imagined wrist flexion, whereas those in the extensor carpi radialis (agonist for wrist extension) were larger during imagined wrist extension. Finally, MEPs in the FDI, a muscle not involved in the task, were unaffected by imagined wrist movements. Taken together, these data strongly support the view that during motor imagery, the motor system is dynamically simulating the activation pattern occurring during actual execution, and that the specificity of the observed effect is effector related. In a very recent study, Stinear and Byblow (2003) confirmed that the influence of motor imagery on corticospinal excitability is specifically related both to the phase of the imagined movement and to the muscles involved in that movement.

F1

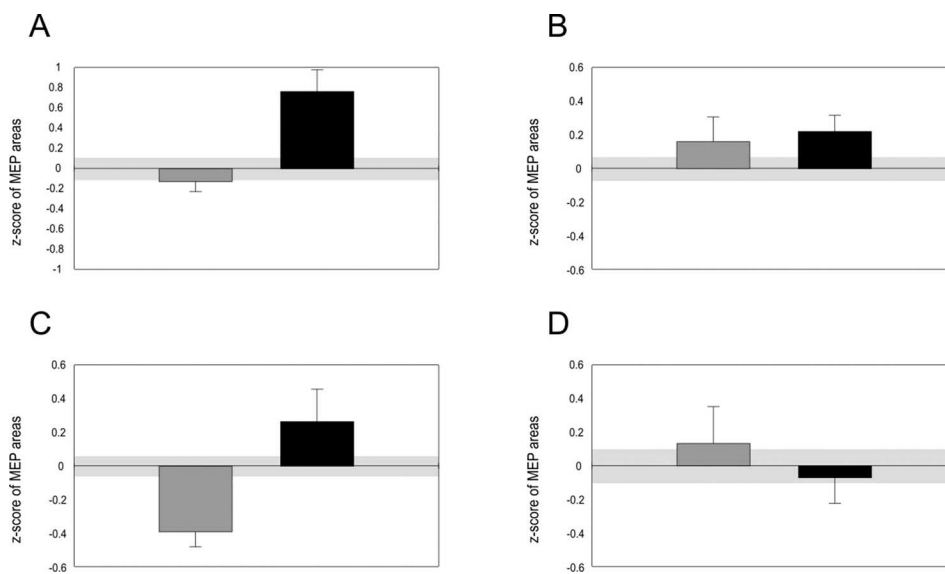


FIGURE 1. Mean values (\pm standard error) of motor-evoked potentials (MEPs) recorded from biceps brachialis muscle (A) and from opponens pollicis muscle (B) during motor imagery of forearm extension (gray bar) and flexion (black). Mean values (\pm standard error) of MEPs recorded from opponens pollicis (C) and extensor digitorum communis (D) during motor imagery of hand opening (gray bar) and closing (black). Ordinates: z-score of MEP total areas. Data are represented as difference from the control condition, whose standard error is shown by the gray strip along the horizontal axis.

The authors explored the temporal characteristics of corticospinal excitability modulation during motor imagery of a phasic task involving a single digit. MEPs were recorded in abductor pollicis brevis and abductor digiti minimi during actual execution and simulation of an isometric contraction of the thenar muscles. Magnetic stimuli were delivered during the “on” and “off” phases of the movement. Results showed that, during motor imagery, for abductor pollicis brevis, the MEP amplitudes recorded during the “on” phase of the task were significantly higher than during the “off” phase, whereas MEPs recorded from abductor digiti minimi were not modulated by the different phases of the task. This result mirrors the changes in cortical excitability found during actual task performance (Stinear and Byblow, 2003). Thus, these data indicate that motor imagery produces a temporally modulated increase in the excitability of the M1 representation of an intrinsic hand muscle involved in a phasic task. Moreover, the temporal modulation of cortical excitability was limited to the representation of the muscle involved in the task, and was not observed in the control muscle.

In addition to the investigation of the specific effect induced by imagined movements on hand/arm muscles, we also investigated how the two brain hemispheres are involved during motor imagery of ipsilateral and contralateral hand movements (Fadiga et al., 1999). In two different experimental sessions, left and right motor cortices were stimulated, and MEPs were recorded from the OP muscle contralateral to the stimulated hemisphere. Similar to the previously described

experiment, subjects were instructed to imagine the opening or closing their right or their left hand. Figure 2 shows the results.

F2

During stimulation of the left hemisphere, MEP amplitude increased during motor imagery of both contralateral and ipsilateral hand closing and decreased during motor imagery of both contralateral and ipsilateral hand opening. The influence of the task on corticospinal excitability was however significantly larger during imagery of contralateral movements. During stimulation of the right hemisphere, MEP amplitude increased during imagined hand closing, and decreased during imagined hand opening of the contralateral hand only. In agreement with various brain-imaging studies (Kim et al., 1993; Porro et al., 2000), our data indicate that left and the right hemispheres are differently involved during motor imagery: the left hemisphere is active during imagination of movements involving both the contralateral and the ipsilateral hand, whereas the right hemisphere is involved only during motor imagery of the contralateral hand. The pragmatic role of left hemisphere in right dominant individuals may account for this effect.

In conclusion, all these data support the evidence that during motor imagery, the motor system becomes active in a very specific way, as if it were really involved in action execution. The specificity relates to both aspects of motor control: effector recruitment and temporal dynamics. Does motor imagery involve the same neural populations that are active during execution or depend on the activation of a

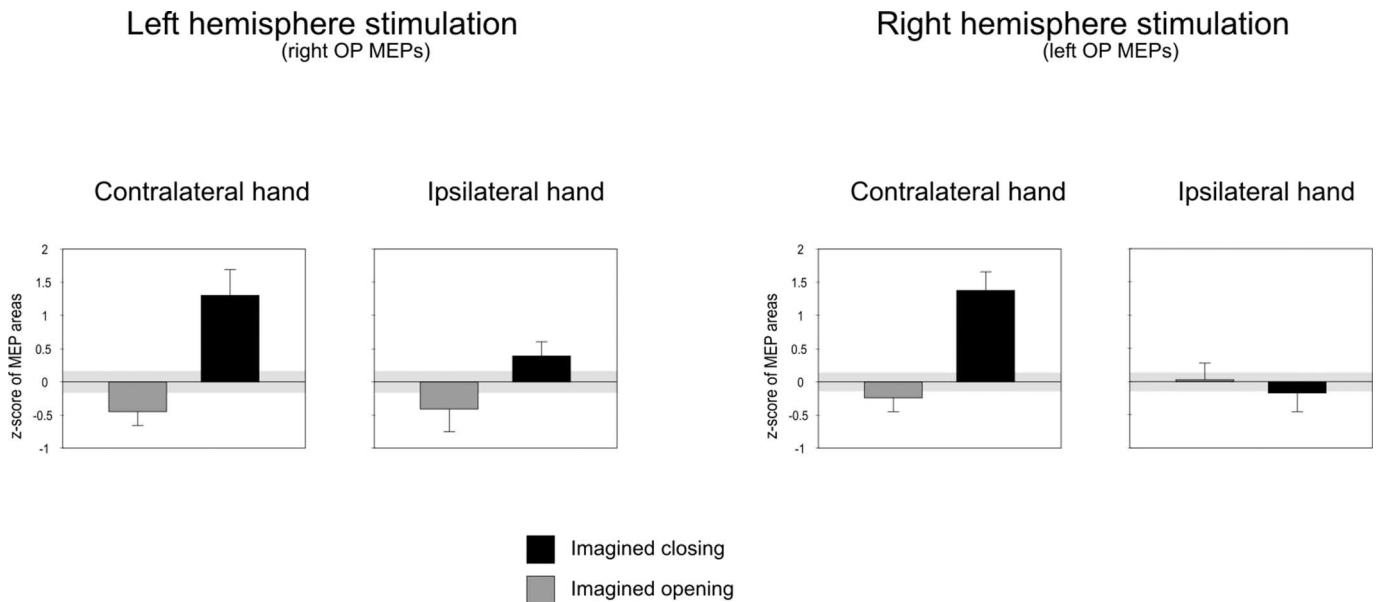


FIGURE 2. Mean values (\pm standard error or the mean) of motor-evoked potentials (MEPs) in the four experimental conditions. Abscissae: imagined movement. Ordinates: z-scores of MEP total areas. Data are represented as difference from the control condition, whose standard error is shown by the gray bar on the horizontal axis.

specifically devoted neural circuitry? Porro et al. (1996) specifically investigated this question by using fMRI during execution (motor performance, MP) and imagination (motor imagery, MI) of finger movements and by comparing the activated regions both in terms of spatial extension and differences in intensity of activated voxels. Their conclusion is that “percentage increases in signal intensity during MI were on average 30% as great as increases during MP. The pixels activated during both MP and MI appear to represent a large fraction of the whole population activated during MP. These results support the hypothesis that MI and MP involve overlapping neural networks in perirolandic cortical areas.”

“Object Observation”–Related Visuomotor Responses

Humans, similarly to monkeys, can access the internal representation of an action whenever a cue relative to that action is presented. For example, the internal representation of the action “to eat an apple” is immediately activated when we see someone else eating an apple, when we just see an apple, when somebody describes the fabulous taste of a particular apple and, of course, when we are eating an apple. Experimental evidence coming from TMS and psychophysics experiments support the view that, similar to monkey’s object-observation visuomotor neurons, motor representations are specifically facilitated by the mere observation of objects. During the previously reported study by Fadiga et al. (1999) the authors, in a preliminary version of the experiment, used as a control a visual imagery task apparently devoid of motor

content. Subjects were asked to visually imagine an expanding/shrinking light bar that was previously shown on a computer screen (unpublished data). Imagery of the expanding/shrinking phases was guided by the same frequency-modulated sound successively used to guide motor imagery. During visual imagery, EMGs were recorded from right proximal arm muscle BB and from right intrinsic hand muscle OP, and TMS was delivered on left primary motor cortex in correspondence of arm and hand motor representations. Figure 3 shows EMG data recorded during this visual imagery task.

F3

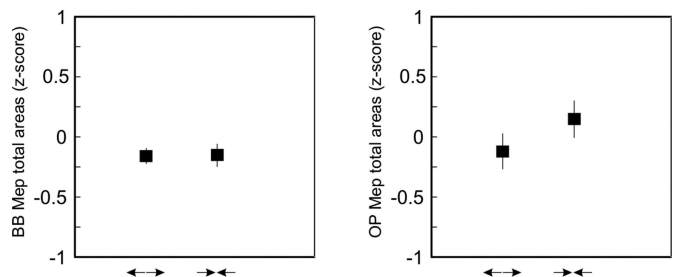


FIGURE 3. Mean values (\pm standard error) of motor-evoked potentials (MEPs) recorded from biceps brachialis muscle (biceps brachialis [BB], left panel) and from opponens pollicis muscle (opponens pollicis [OP], right panel) during visual imagery of the expanding (\longleftrightarrow) and shrinking ($\rightarrow\leftarrow$) light bar. Abscissae: imagined movement. Ordinates: z-scores of MEP total areas.

Curiously, as it appears clearly from the figure, the visual imagery of the expanding/shrinking visual bar exerted an effect on corticospinal excitability and, moreover, it differently modulated MEPs recorded from BB and OP muscles. Whereas BB muscle excitability was not affected by the phase of the imagined movement, MEP amplitude of the OP muscle was larger during mental simulation of bar shrinking than during mental simulation of bar expanding. These data indicate that during visual imagery of a dynamic shape modification of a light bar, intrinsic hand muscles are specifically facilitated. The interpretation we favor is that the imagination of the visual bar involves in humans a mechanism similar to that of monkey's "object observation" visuo-motor neurons, which become active when the monkey acts on an object and when it observes that object. However, further experiments are necessary to investigate this point.

Convincing evidence that an automatic link between objects and motor programs exists also in humans was provided by reaction-time experiments performed in normal subjects (Craighero et al., 1996, 1998). In these experiments, drawings of differently oriented rectangles were presented on a computer screen around a fixation point before (−100 milliseconds), simultaneously with (0 milliseconds), or after (+100 milliseconds) a go signal, which consisted in a change in color of the fixation point (see Fig. 4A). At the appearance

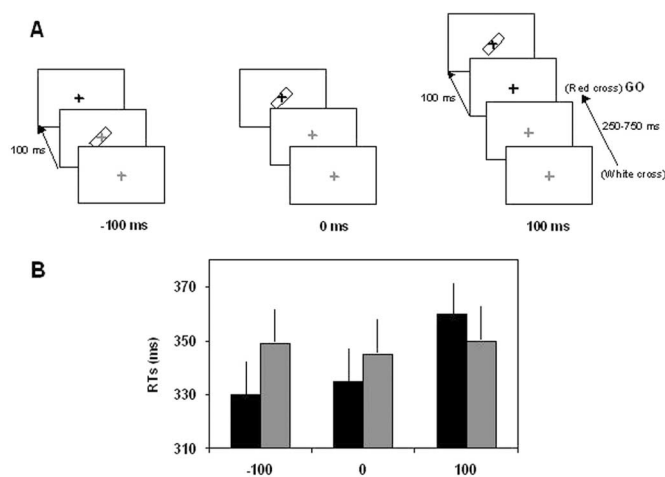


FIGURE 4. (A) Schematic representation of the experimental procedure. At the beginning of each a white (here gray) fixation cross appeared at the center of the screen. After a variable interval (250 to 750 milliseconds), the fixation cross became red (here black), giving the signal to execute the grasping response. Before (−100 milliseconds), simultaneously with (0 milliseconds), or after (100 milliseconds) the go signal, drawings representing differently oriented rectangles were depicted around the fixation cross. (B) Mean reaction times (RTs) for congruent and incongruent trials in the three experimental conditions. The solid lines above each bar represent standard errors of the mean.

of the go signal, the subject had to respond, as fast as possible, by grasping an object whose orientation was either the same or different from that of the presented drawing. The results showed a difference in reaction times when the drawings were presented before the go signal. Reaction times decreased when the orientation of the drawing was the same as the orientation of the object to be grasped (congruent trials) (see Fig. 4B).

The facilitatory effect of congruent visual stimuli on grasping execution was present only when the drawing was presented before the go signal. Note that, being the response exclusively determined by the go signal, the analysis of the drawing has no utility for task solution. The effect of the congruent stimulus indicates, therefore, that the mere observation of a task-irrelevant visual stimulus automatically facilitates the grasping of a real object when the intrinsic properties of the latter are congruent with those of the drawing.

Further evidence that the presentation of an object may automatically facilitate actions directed to it is given by a study of Tucker and Ellis (1998). These authors presented normal human subjects with photographs of common graspable objects. The subjects had to decide, by pressing a key either with the left or the right hand, whether the presented object was upright or inverted. The results showed that the reaction times were faster when the key press response was executed by the hand best suited to grasp the presented object. This suggests that visual objects potentiate actions that may be performed on them, even in the absence of explicit intentions to act.

Direct evidence of an activation of premotor areas during observation of graspable objects was provided by a positron emission tomography experiment (Grafton et al., 1997). Normal right-handed subjects were scanned during observation of bidimensional colored pictures (meaningless fractals), during observation of three-dimensional objects (real tools attached to a panel), and during silent naming of the presented tools and of their use. The most important result was that the premotor cortex became active during the simple observation of the tools. This premotor activation was further augmented when the subjects named the tool use. This result shows that, as in the case of object observation F5 monkey neurons, also in the absence of any overt motor response or instruction to use the observed stimuli, the presentation of graspable objects increases automatically the activity of premotor areas.

A very recent positron emission tomography study conducted by Grèzes and Décety (2002) indicated that the perception of objects, irrespective of the task required to the subject (judgment of the vertical orientation, motor imagery, and silent generation of the noun or of the corresponding action verb), versus perception of nonobjects, was associated with activation of a common set of cortical regions. The occipitotemporal

junction, the inferior parietal lobule, the supplementary motor area proper, the pars triangularis in the inferior frontal gyrus, and the dorsal and ventral precentral gyri were engaged in the left hemisphere. The ipsilateral cerebellum was also involved. These activations are congruent with the idea of an involvement of motor representation already during the perception of objects, providing evidence that the perception of objects automatically affords actions that can be made toward them.

“Action Observation”–Related Visuomotor Responses

In a TMS experiment, Fadiga et al. (1995) provided the first evidence in favor of the existence of mirrorlike visuomotor activity in humans. The motor cortex of normal human participants was magnetically stimulated and MEPs were recorded from intrinsic and extrinsic hand muscles. It was reasoned that if the observation of a hand movement activates the premotor cortex, this should, in turn, induce an enhancement of MEPs elicited by the magnetic stimulation of the hand representation of the motor cortex. MEPs were recorded from extensor digitorum communis, flexor digitorum superficialis (FDS), FDI, and OP muscles. There were four different experimental conditions. (1) Grasping observation. The subject had to observe the experimenter grasping an object. Objects of different size and shape (e.g., spheres, boxes, and commonly used objects) were used in different trials. (2) Object observation. The same objects as above were presented to the subject, who had to observe them attentively for about 3 seconds. (3) Arm movement observation. The subject had to observe the experimenter who traced in the air a relatively complex geometric shape with his arm extended and the hand relaxed in a prone position. In different trials, different shapes were drawn (e.g., squares, crosses, Greek-alphabet letters: alpha, omega, etc.). (4) Dimming detection. The subject had to detect, and verbally signal, as fast as possible, the dimming of a light stimulus appearing on a computer screen. TMS was administered during the final phase of grasping in experimental condition 1 and arm movements in experimental condition 4, after about 2 seconds in experimental condition 2, and during dimming detection in experimental condition 3. Subjects were subdivided into two groups. The difference between the two groups was the way in which subjects were induced to pay attention to visual stimuli. In the first group, this was achieved by asking the subjects, in some trials, to imitate the last observed action (movement-observation conditions) or to grasp the last observed object (object-observation condition). In the second group, the subjects were informed that, at the end of the experimental session, they would be presented with some grasping and arm movements as well objects, and they would have to tell the experimenters which one among these stimuli they had seen during the experimental session. They were not asked to perform any movement. Results are shown in Fig. 5.

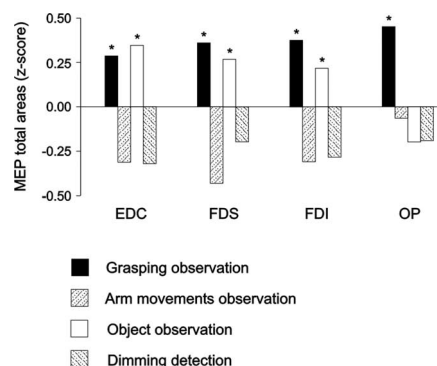


FIGURE 5. Mean values (\pm standard errors of the mean) of standardized motor-evoked potentials (MEPs) recorded in all subjects in the four experimental conditions. Ordinates: z-score of MEP total areas. Asterisks indicate the presence of statistical significance ($P < 0.05$) between action observation and control conditions. EDC, extensor digitorum communis muscle; FDS, flexor digitorum superficialis muscle; FDI, first dorsal interosseus muscle; OP, opponens pollicis muscle.

For both groups of subjects, during “grasping observation” the MEP amplitude of the recorded muscles increased with respect to the conditions in which visual stimuli were not related to actions. However, whereas during grasping observation the largest increase was observed in the OP muscle (the main agonist for opposition of thumb to other fingers), during “arm movement observation” the increase was present in all muscles except OP. Does this differential activation relate to what is happening during real execution? How can be explained the activation of FDI during arm movements, which apparently require no distal involvement? To answer these questions, the same four muscles were recorded during rest, execution of object grasping, and execution of arm lifting movements. Results showed that whereas during grasping all the recorded muscles became significantly more active than during rest, during arm elevation the OP muscle remained virtually silent and the largest increase of activity was shown by the FDI. This muscle could indeed participate to wrist stabilization during arm lifting.

These results strongly demonstrate that the pattern of corticospinal facilitation revealed by TMS during action observation strictly resembles that which occurs during actual execution of the observed movements. Furthermore, the lack of statistical significance between the two groups of subjects (those sometimes imitating the last observed action and those asked to attentively observe the presented stimuli) indicates that the facilitatory effect depended on the mere observation of the actions and not on a possible “mental practice” induced by the instruction to perform occasionally those actions.

Further experiments confirmed our observations and demonstrated the cortical origin of this facilitation (Baldissera et al., 2001; Patuzzo et al., 2003; Strafella and Paus

2000). Strafella and Paus (2000), by using the double-stimulus TMS technique, showed that the interstimulus interval between two close stimulations that evoked the larger motor facilitation during action viewing was compatible with cortico-cortical facilitating connections. A similar technical approach was recently used by Patuzzo et al. (2003). These authors confirmed the specific motor facilitation during action observation, and showed that no differences are present when subjects observe actions performed by themselves or by others.

Baldissera et al. (2001) investigated the spinal excitability of hand motoneurons in normal volunteers while observing a video-clip showing different kinds of goal-directed hand actions. Spinal cord excitability was tested by eliciting the H-reflex in a finger flexor muscle (FDS). Constant current pulses were used to evoke the monosynaptic H-reflex. Subjects were presented with a randomized sequence of three videos representing (1) right-hand closing on a sphere with a whole-hand prehension (FDS muscle acts as an agonist); (2) right-hand enlarging a rubber band with all fingertips (FDS muscle acts as an antagonist); and (3) right hand at rest. The test H-reflex was elicited after 25% (early stimulation) or 75% (late stimulation) of the total video movement time. During observation of finger extension, the FDS H-reflex was consistently greater than the mean reflex size. Facilitation was larger in the early phase than in the late phase. During observation of finger closing, the H-reflex size was smaller than the mean reflex size. The maximum effect occurred in the late closing phase. In a second experiment, subjects were presented with videos showing the repetition of a reaching-grasping movement performed on a sphere. During each video presentation, an H-reflex was elicited after a certain delay from video onset. The possible delays were selected to cover the relevant period of the observed movement (the start of the reaching movement, hand opening, hand closing, and object lift). The time course of the changes in H-reflex excitability during the different phases of the movement is illustrated in Fig. 6.

The FDS H-reflex undergoes in the observer a complex modulation. H-reflex increased during observation of the finger opening, preceding grasping; it was progressively depressed during observation of finger closure on the object, and the depression reached a maximum just after the finger contact with the sphere. During observation of object lifting, the reflex depression was quickly reverted to a second phase of facilitation. In conclusion, the results showed that, in the absence of any detectable muscle activity, the mere observation of hand action modulates the excitability of the observer's spinal circuitry involved in hand movement execution. The changes in the H-reflex size showed a very specific temporal correlation with the different phases of the observed movement. These data, however, indicate that the excitability modulation observed during spinal H-reflex testing contrasts

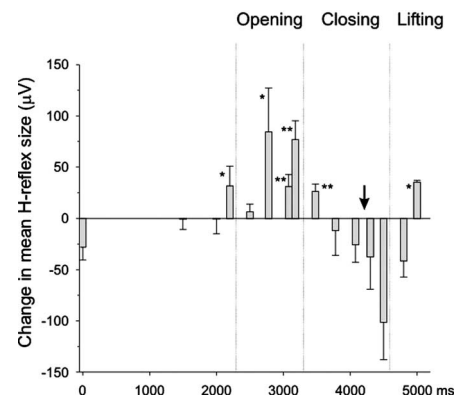


FIGURE 6. Changes in excitability of the right flexor digitorum superficialis muscle (FDS) H-reflex during observation of a video showing a human hand reaching, grasping, and lifting a sphere. Abscissae: time from video onset. The observed movement started 1500 milliseconds after video onset and lasted 3500 milliseconds. Different phases of the observed movement are indicated. The vertical arrow marks the contact of the fingers with the sphere. Each column indicates the mean value (\pm standard error of the mean). A significant difference from the value measured at time 0 is indicated by a single ($P < 0.05$) or a double ($P < 0.01$) asterisk.

with the results obtained by Fadiga et al. (1995). Although modulation of cortical excitability strictly mimics the seen movements as if they were performed by the observer (FDS MEP enhancement during observation of hand closing), the behavior of the spinal cord appears to be the opposite, being spinal motoneurons of finger flexors facilitated during observation of hand opening (finger extension) and inhibited during observation of hand closure (finger flexion). These experiments, taken together, indicate that during action observation there is both an activation of cortical areas connected (directly and/or indirectly) with M1 and the generation, in the spinal cord, of a signal opposite in sign that determines the reciprocal behavior observed by Baldissera et al. (2001). This inhibitory mechanism, which prevents the execution of observed actions, might leave free the cortical motor system to “react” the observed action without the risk of overt movement generation.

Further evidence that cortical motor areas are activated during movement observation comes from MEG experiments. Hari et al. (1998) recorded neuromagnetic oscillatory activity of the human precentral cortex elicited by median nerve stimulation in healthy volunteers during rest, during manipulation of a small object kept in their right hand, and while observing of another individual performing the same task. The cortical 15- to 25-Hz rhythmical activity was measured. In agreement with previous data (Salmelin and Hari, 1994), this activity was suppressed during movement execution. Most interestingly, the rhythm was also signifi-

cantly diminished during movement observation. Control experiments confirmed the specificity of the suppression effect. Because the recorded 15- to 25-Hz activity originates mostly in the anterior bank of the central sulcus, it appears that the human primary motor cortex desynchronizes (and therefore becomes more active) during movement observation in the absence of any active movement. Cochin et al. (1998) obtained similar results. They recorded EEG from subjects observing video movies in which human movements were displayed. As a control, moving objects, moving animals, and still objects were presented. The data showed that the observation of human movements, but not that of objects or animals, desynchronizes the EEG pattern of the precentral cortex.

Recently, a series of reaction-time experiments investigated the possibility that the activation of the premotor cortex induced by hand action preparation facilitates the discrimination of hand poses visually presented (Craighero et al., 2002). Normal participants were instructed to prepare a hand-grasping movement toward one of two bars that differed in orientation (clockwise or counterclockwise). They then had to execute the prepared grasping movement at the presentation of a picture representing a given hand pose (go signal) on the computer screen. Two were the possible pictures presented to subjects, and both of them were images of the right hand as seen in a mirror. One represented the posture of the hand when it reached the bar clockwise oriented, and the other represented the posture of the hand when it reached the bar counterclockwise oriented. At the presentation of the go signal, the subject had to respond by grasping the bar. The combination of picture and actual grasping gave origin to congruent and incongruent conditions. Results showed that the reaction times were faster when there was congruency between the hand depicted in the visual stimulus and the subsequent grip. A possible interpretation of this finding is the presence of a specific visuomotor link between the visual stimulus and the subsequent action.

Which brain areas are involved in the action-observation/execution resonant system? A series of brain-imaging experiments were made to assess which cortical area could be the homologue of the monkey F5 mirror system. Hand-grasping movements (Grafton et al., 1996; Rizzolatti et al., 1996b) as well more complex hand/arm movements were used as visual stimuli (Décety et al., 1997; Grèzes et al., 1998). The results of the first experiments showed that during the observation of hand grasping there was an activation of the left inferior frontal cortex corresponding to Broca's region. In addition, activations were found in the left superior temporal sulcus, the rostral part of the left inferior parietal lobule (area 40), the left opercular parietal region, and the rostral part of the supplementary motor area proper (Grafton et al., 1996; Rizzolatti et al., 1996b). The first three regions most likely correspond to the monkey cortical areas where there are neurons that discharge when the monkey

observes biologic actions; namely, area F5 (Gallese et al., 1996), the superior temporal sulcus region (Carey et al., 1997; Perrett et al., 1989), and the rostral part of the inferior parietal lobule (Fogassi et al., 1998). In studies performed by the Lyon group (Grèzes et al., 1998; Décety et al., 1997), the involvement of Broca's area during observation of hand/arm actions was further confirmed. The authors instructed subjects to observe meaningful (with a goal) and meaningless movements. The main results of the condition in which subjects observed meaningless arm movements were an activation of the parietal lobe bilaterally, in the left precentral gyrus and the cerebellum on the right side (Grèzes et al., 1998). On the contrary, the observation of meaningful hand actions, in addition to the already mentioned frontal and parietal areas, activates the left inferior frontal gyrus (Broca's region). Note that the activation of Broca's region during observation of action suggests for this area the putative role of human homologue of area F5. In this direction point also some comparative cytoarchitectonical data (see Petrides and Pandya, 1994) that draw a morphologic parallel between monkey premotor area F5 (a disgranular frontal cortex) and Broca's area (pars opercularis and pars triangularis of inferior frontal gyrus), and recent fMRI data from Binkofsky et al. (1999) demonstrating that Broca's region becomes active also during manipulation of complex objects. In an fMRI study from our group (Buccino et al., 2001), we aimed to assess whether the observation of actions made with different effectors would activate specific parts of the premotor cortex in accord with the somatotopic organization of the region. While being scanned, normal participants were asked to carefully observe different videotaped object-related and non-object-related actions performed by another individual with different effectors (mouth, arm/hand, and foot). Results showed that observation of both object-related and non-object-related actions determined a somatotopically organized activation of premotor cortex. The somatotopic pattern was similar to that of the classical motor cortex homunculus. In addition, during the observation of object-related actions, an activation, also somatotopically organized, was found in the posterior parietal lobe. Thus, when individuals observe an action, an internal replica of that action is automatically generated in their premotor cortex. In the case of object-related actions, a further object-related analysis is performed in the parietal lobe, as if the subjects were indeed using those objects. These results bring the previous concept of an action-observation/execution matching system (mirror system) into a broader perspective: this system is not restricted to the ventral premotor cortex, but involves several somatotopically organized motor circuits.

Acoustic-Motor Responses: A Mechanism for Speech Perception?

Both object observation and action observation (mirror) F5 visuomotor neurons discharge in response to visual stimuli. They address a common reservoir of action representation that, in our view, might be used to categorize action-related

visual percepts for imitation and identification purposes. Thus, in the case of object observation neurons, vision of graspable objects activates the motor representations more appropriate to interact with those objects; in the case of mirror neurons, objects alone are no more sufficient to evoke a premotor discharge—what is necessary is a visual stimulus describing a goal-directed hand action in which both an acting hand and a target must be present. Others' actions, however, do not generate only visually perceivable signals. Action-generated sounds and noises are also very common in nature. One could expect, therefore, that also this sensory information, related to a particular action, can determine a motor activation specific for that same action.

A very recent neurophysiologic experiment addressed this point. Kohler and colleagues (2002) investigated whether there are neurons in area F5 that discharge when the monkey makes a specific hand action and also when it *hears* the corresponding action-related sounds, starting from the observation that a large number of object-related actions (e.g., breaking a peanut) can be recognized by a particular sound. The authors found that 13% of the investigated neurons discharge both when the monkey performed a hand action and when it heard the action-related sound. Moreover, most of these neurons discharge also when the monkey observed the same action, demonstrating that these “audiovisual mirror neurons” represent actions independently of whether they are *performed, heard, or seen*.

These results have been extended to humans by a TMS experiment (Fadiga et al., 2002) during speech listening. In agreement with the idea originally proposed by Liberman and colleagues (Liberman et al., 1967; Liberman and Mattingly, 1985; Liberman and Wahlen, 2000), the authors started from the perspective that sounds conveying verbal communication could be a vehicle of motor representations (articulatory gestures) shared by both the speaker and the listener, on which speech perception could be based. In other terms, the listener understands the speaker when his/her articulatory gestures representations are activated by verbal sounds (motor theory of speech perception). To test this hypothesis, normal subjects were requested to attend to an acoustically presented randomized sequence of disyllabic words, disyllabic pseudowords, and bitonal sounds of equivalent intensity and duration. Words and pseudowords were selected according to a consonant-vowel-consonant-consonant-vowel scheme. The embedded consonants in the middle of words and of pseudowords were either a double “f” (labiodental fricative consonant that, when pronounced, requires slight tongue tip mobilization) or a double “r” (linguapalatal fricative consonant that, when pronounced, requires strong tongue tip mobilization). Bitonal sounds, lasting about the same time as verbal stimuli and replicating their intonation pattern, were used as a control. The excitability of motor cortex in correspondence of tongue movements representation was assessed

by using single pulse TMS and by recording MEPs from the anterior tongue muscles. The TMS stimuli were applied synchronously with the double consonant of presented verbal stimuli (words and pseudowords) and in the middle of the bitonal sounds. Results (see Fig. 7) showed that during speech listening there is an increase of motor evoked potentials recorded from the listeners' tongue muscles when the listened word strongly involves tongue movements, indicating that when an individual listens to verbal stimuli, his/her speech-related motor centers are specifically activated. Moreover, words-related facilitation was significantly larger than pseudowords-related facilitation.

These results indicate that the passive listening to words that involve tongue mobilization induces an automatic facilitation of the listener's motor cortex. Furthermore, the effect is stronger in the case of words than in the case of pseudowords, suggesting a possible unspecific facilitation of the motor speech center due to recognition that the presented material belongs to an extant word. The presence of “audiovisual mirror neurons” in the monkey and the presence of speech-related acoustic motor “resonance” in humans indicate that, independently from the sensory nature of the perceived stimulus, the mirror resonant system retrieves from action vocabulary (stored in the frontal cortex) the stimulus-related motor representations. The immediate translation of different sensory information into motor representations could be the key to a congruent, unique representation of the environment, always crowded of acting individuals, allowing an automatic understanding of others' different occupations.

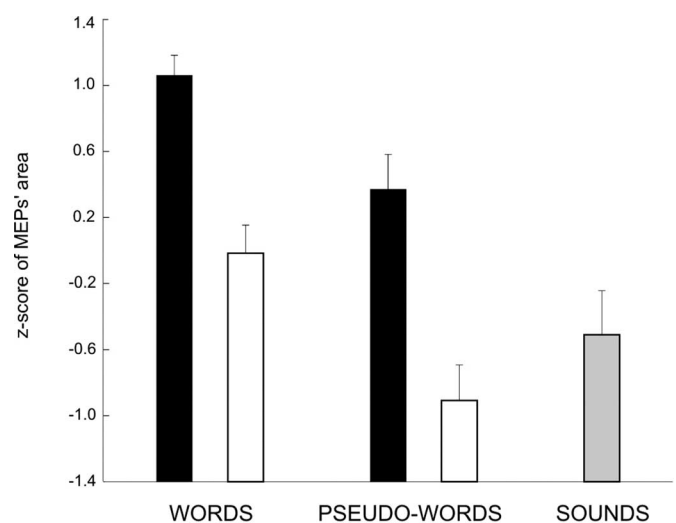


FIGURE 7. Mean standardized values (\pm standard error of the mean) of tongue motor-evoked potentials (MEPs) recorded in each experimental condition from all subjects (see text for details). *BLACK*, verbal stimuli containing the double “r” consonant; *white bars*, verbal stimuli containing the double “f” consonant; *gray bar*, control.

CONCLUSIONS

In this article, we present evidence showing that, in primates, actions are represented in the brain not only for motor execution, but also during imagination of actions, observation of graspable objects, and while perceiving the sensory consequences (visual or acoustic) of actions performed by others. The presence of such a “vocabulary” of actions has important functional implications. Firstly, the execution of motor commands is strongly facilitated. The existence of preformed motor schemata, which are anatomically linked (hard-wired) with cortical (primary motor cortex) and subcortical motor centers, facilitates the selection of the most appropriate combination of movements simply by addressing the general idea of an action. Thus, the number of variables that the motor system (at the premotor level) has to control to achieve the action goal is reduced. Secondly, it simplifies the association between a given stimulus (i.e., a visually presented object) and the appropriate motor response toward it. This is the case of “object observation”-related visuomotor responses in monkeys and humans. Thirdly, it gives the brain a storage of “ideas of action” that could be used also for non-strictly motor purposes. The specific involvement of the motor system during motor imagery demonstrates this proposition. It remains an open question whether primates’ mirror neurons play a role only in action “understanding”, or if they may also be involved in imitation/learning processes. If, on one side, the finding that in monkeys only already known actions are represented seems to exclude this possibility, on the other side TMS experiments in humans show that also simple movements, apparently devoid of explicit goal, are capable of activating the motor system in a specific way. This evidence suggests the possibility that, as suggested by Rizzolatti et al. (1999), two levels of motor resonance may exist. A first, goal-related, is similar to what we described in the monkey, and a second, movement-related, is responsible for motor facilitation during observation/listening of meaningless movements (i.e., arm movements observation and pseudowords listening). This movement-related resonant system has been found only in humans by TMS experiments. However, it is possible that a similar mechanism exists also in monkeys. Further experiments are required to elucidate this possibility. (Rizzolatti et al., 1998) (Umilata et al., 2001)

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