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**Neural Basis of Motor Planning for Object-Oriented  
Actions: the Role of Kinematics and Cognitive Aspects**

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## **Abstract**

The project I have carried out in these three years as PhD student pursued the aim of describing the motor preparation activity related to the object oriented actions actually performed. The importance of these studies comes from the lack of literature on EEG and complex movements actually executed and not just mimed or pantomimed. Using the term 'complex' here we refer to actions that are oriented to an object with the intent to interact with it.

In order to provide a broader idea about the aim of the project, I have illustrated the complexity of the movements and cortical networks involved in their processing and execution. Several cortical areas concur to the plan and execution of a movement, and the contribution of these different areas changes according to the complexity, in terms of kinematics, of the action. The object-oriented action seems to be a circuit apart: besides motor structures, it also involves a temporo-parietal network that takes part to both planning and performing actions like reaching and grasping. Such findings have been pointed out starting from studies on the Mirror neuron system discovered in monkeys at the beginning of the '90s and subsequently extended to humans. Apart from all the speculations this discovery has opened to, many different researchers have started investigating different aspects related to reaching and grasping movements, describing different areas involved, all belonging to the posterior parietal cortex (PPC), and their connections with anterior motor cortices through different paradigms and techniques.

Most of the studies investigating movement execution and preparation are studies on monkey or fMRI studies on humans. Limits of this technique come from its low temporal resolution and the impossibility to use self-paced movement, that is, movement performed in more ecological conditions when the subject decides freely to move. On the few studies investigating motor preparation using EEG, only pantomime of action has been used, more than real interactions with objects. Because all of these factors, we decided to get through the description of the motor preparation activity for goal oriented actions pursuing two aims: in the first instance, to describe this activity for grasping and reaching actions actually performed toward a cup (a very ecological object);

secondly, we wanted to verify which parameters in these kind of movements are taken into account during their planning and preparation: because of all the variables involved in grasping and reaching movements, like the position of the objects, its features, the goal of the action and its meaning, we tried to verify how these variables could affect motor preparation creating two different experiments. In the first one, subjects were requested to perform a grasping and a reaching action toward a cup and in a third condition we tied up their hands as fist in order to verify what it could happen when people are in the condition of turning an ordinary and easy action into a new one to accomplish the final task requested. In the second experiment, we better accounted for the cognitive aspects beyond the motor preparation of an action. Here, indeed, we tested a very simple action like a key press in two different conditions. In the first one the button press was not related to any kind of consequence, whereas in the second case the same action triggered a video on a screen showing a hand moving toward a cup and grasping it (giving like a video-game effect).

Both the experiments have shown results straightening the role cognitive processes have in motor planning. In particular, it seemed that the goal of the action, along with the object we are going to interact with, could create a particular response and activity starting very early in the posterior parietal cortex.

Finally, because of the actions used in these experiments, it was important testing the hypothesis that our findings could be generalized even to the observation of those same actions. As I mentioned before, object-oriented actions have received great attention starting from the discovery of the mirror neuron system which showed a correspondence between the cortical activity of the person performing the action with the one produced in the observer. Such a finding allowed to describe our brain as a social brain, able to create a mental representation of what the other person is doing which allows us to understand others gesture and intentions. What we wanted to test in this project was the possibility that such a correspondence between the observer and the actor would had been extended even to the motor preparation period of an upcoming action, giving credit to the hypothesis of considering the human brain as able to

even predict others actions and intentions besides understanding them. In the last experiment I carried out in my project, thus, I used the same actions involved in the first experiment but asking this time to observe them passively instead of performing them.

The results provided in this study confirmed the cognitive, rather than motor, role the PPC plays in action planning. Indeed, even when no movements are involved, the same structure are active reflecting the activity found in the execution experiment.

The main result I have reported in this dissertation is related to the suggestion of a new model to understand the role the PPC has in object-oriented movements. Unlike previous hypothesis and models suggesting the contribution of PPC in extracting affordances from the objects or monitoring and transforming coordinates between us and the object into intention for acting, we suggest here that the role of the parietal areas is more to make a judge about the appropriate match of the action goal with the affordances provided by the object. When actually the action we are going to perform fits well with the object features, the PPC starts its activity, elaborating all those coordinates representation and monitoring the execution and programming phases of movement. This model is well supported by results from both our experiments and well combines the two previous models, but putting more emphasis on the 'goal-object matching' function of the PPC and the Superior parietal lobe (SPL) in particular.

# Chapter 1

## General introduction

### 1.1 Motor behavior, development and representation

The motor behavior represents the link between our thoughts and actions. All the interactions with the surrounding world occur through the agency of the motor system. Motor processing begins with an internal representation of the world or the body state we want to obtain. The infrastructures of the motor control are determined evolutionarily: there are pre-established circuits delegated to a basic movement repertoire (i.e. posture, breathing, etc), and others that underlie reaching, finger and hand movements and sound production. These latter circuits are available after maturation of the nervous system.

Since our birth, we are able to perform different motor behaviors due to innate motor programs, and by the growth, the motor system continues to develop by learning through different motor activities, like playing. During the first year, newborn matures progressively, learning or developing complex motor tasks such as the control of different types of posture, an activity involving hundreds of different muscles that collaborate coordinated. In addition to the basic motor skills, as standing or walking, humans also develop skilled motor coordination, allowing delicate hand and fingers actions used in writing, playing an instrument or using tools. The neural substrate allowing learning and execution of these complex motor sequences are expressed genetically and characterize our species. Our ability in using tools, along with the language development, makes our species to be different from other primates.

Motor skills are partly innate and partly learned. Thanks to the practice of new experiences it is possible to produce a permanent change in the way we respond to the environment. Functional imaging and physiological studies have provided evidences of changes in the anatomical location of representation of motor programs as a motor behavior progresses from novel to automatic (Halsband, 2006). The muscle combination that produces a sequence of motor

pattern is stored in the nervous system and is performed with a very little awareness and, therefore, motor learning is principally referred to as an “implicit”, procedural learning. Motor learning represents a relatively permanent modification in motor behavior or improvement of motor skill occurring after experience or practice conditions. It is an internal phenomenon, not directly observable but that can be inferred from observable behaviors or changes in performance. The presence of feedback is one of the most important factors in motor learning and is considered a critical variable in skill acquisition. It represents any kind of sensory information related to a response or movement. A feedback can be intrinsic (response that occurs when a movement is performed and the sources may be internal or external to the body, i.e. vision, proprioception and audition), or external (the augmented information provided by an external source and indicated as *knowledge of performance* or *knowledge of results*).

The *knowledge of performance* (Schmidt and Wrisberg, 2004) represents a kinematic feedback related to information provided to a performer. It indicates the quality of the movement executed based on parameters as displacement, velocity or joint motion. The *knowledge of performance* is useful in ecological tasks and is frequently assessed in sports and rehabilitation training.

The *knowledge of results*, instead, is the extrinsic information provided to the performer after a response and indicating the success of his actions with regards to a goal (Salmoni et al., 1984). The *knowledge of results* is necessary to learning: both internal and external sources of feedback work together in the performance of a motor task. The performers are informed of their own errors in the task performance and can use the discrepancy to improve their performance in next trials. Learning is more effective when both environmental and movement conditions are included in practice sessions. The benefit of practice occurs because motor learning is specific for the feedback available during the process. In particular, for more complex tasks the learning process lays on the creation of a representation of the task and all the information related to it is integrated. That determines the importance of feedback.



Usually the first stage of motor learning is imitation. Imitation has been studied from two different points of view: the first one concerns the ability to reproduce a motor behavior already belonging to our own skills. The second concerns the ability of learn a new motor pattern observing someone else performing it. The imitation process involves different processes starting with a sensory input to be turned into a motor output. Despite of the anatomical differences between these systems, a model has been proposed that assumes that both the observation of an action and its execution share the same neural substrate (Prinz, 2002). Several studies (Howard et al., 1992; Heyes and Foster, 2002) showed that the mere observation of someone else performing a motor sequence could generate a learning process in the observer. Such a process is possible thanks to a mental representation of the movement we are observing (Heyes and Foster, 2002; Bird and Heyes, 2005; Iacoboni, 2009) and that makes the imitation be the principal and higher expression of motor learning.

For several years the motor system has been considered only from its executive point of view: the behavioral schema was thought as hierarchical, starting with the perception of a stimulus in the environment, followed by the integration of this stimulus with an inner mental representation and, in the end, the implementation of movement kinematics and mechanical parameters. The schema was thus sharply divided into perception-cognition-movement processes. Recently, the motor system function has been adjusted giving it a more important role: the connections between frontal and parietal areas, along with connections to visual, auditory and somatosensory areas, have shown a more complex structure and functionality starting from the '80s. Since the discovery of the 'Mirror Neuron System', the study and concept of the motor system have been totally changed. The Mirror Neuron System (MNS) represents an amount of multimodal neurons spread over different cortical areas activated by both execution of specific motor acts and observation of both tools we usually interact with and the same specific motor act performed by someone else (Gallese et al., 1996). The MNS seems to be activated only by this particular class of movements rather than simple movements, showing how in our species, as like as other primates, gestures and object-oriented actions are the most important movements that we perform to interact with the surrounding

environment. The finding of the MNS has smoothed out the fixed boundaries between perception, cognition and movement, turning the motor behavior into a more complex and sophisticated system in which any action is modulated and related to the comprehension of others' intentions. The description of the Mirror Neuron System well matches with the idea of a common neural representational scheme for both observation and execution suggested by Prinz as core of imitation. However, the role of the MNS in the imitative learning process is still not clear. Indeed, several studies have provided evidences that this system would be more active during the imitation of motor programs already belonging to the subject's motor knowledge in respect to the acquisition of new skills (Iacoboni, 1999; 2001; Heiser et al., 2003).

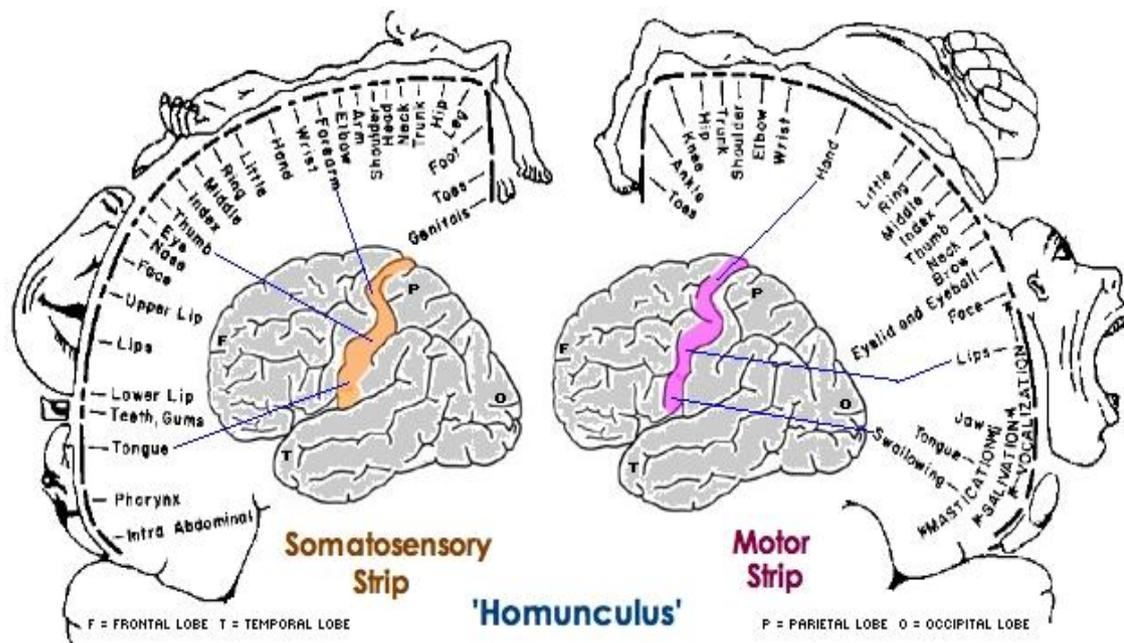
Another important aspect of the motor behavior that differentiates human beings from other species is the ability to carry out skilled movements still performing cognitive tasks, like speaking while walking. Once trained, the motor system is able to execute motor programs for each skill almost automatically and effortlessly: despite our awareness of the intent to plan a sequence of actions and to move at a particular moment, our movements mainly occur automatically. This ability depends on a continuous flow of visual, somatosensory and postural information that reaches the motor system. Indeed, deprivation of one of this sensory information can impair its effortless quality, making it be more inaccurate and unstable (Martin et al., 1999).

## **1.2 Motor cortex, connections and movement implementation**

The generation and control of movement are principally located in the frontal lobe. The primary motor cortex (M1) represents the principal motor area working in association with the premotor cortex, the supplementary motor area (SMA), the posterior parietal cortex and other subcortical regions for the planning and the execution of movements. The primary motor cortex is located in the anterior wall of the central sulcus, posteriorly the frontal lobe, and it extends onto the precentral gyrus. In its anterior part it is bordered by the lateral premotor cortex, whereas, posteriorly, by the primary somatosensory cortex.

All the portions of the body are represented in the cortex somatotopically. Penfield and Boldrey stimulated the surface of the somatic sensor cortex of a patient undergoing brain surgery and found out that sensation from the lower limbs is mediated by neurons near the midline of the brain, whereas sensation from the upper body, like hands and fingers, face and mouth are mediated by neurons more laterally (Penfield and Boldrey, 1937). This somatotopic representation is not proportion to the body mass but to its degree of innervations.

As like as the somatosensory cortex, also the primary motor cortex shows a peculiar organization in which different parts of the body are represented in a somatotopic fashion called *motor homunculus*. Even here, legs and feet are represented more medially, the face more laterally and the upper extremity is in between. These areas are not represented proportionally to their size in the body, as for the somatosensory cortex (see Fig. 1); on the contrary, two areas are represented with a disproportionately large region: the hands with fingers and the mouth. Such a difference is due to the fine control required in speech and fine manipulation of objects with the fingers (Penfield and Rasmussen, 1950).



**Figure 1.** Somatosensory and motor *homunculus*. Somatotopic representation of the different parts of the body on the motor and somatosensory areas.

The strong connection and similarity between somatosensory and motor cortices has a functional meaning: the main function of the perceptual system is to provide the motor system with the sensory information necessary for the action. Any motor pattern is coordinated by specific neuronal network that encloses a motor program. This motor program can be activated by will or be triggered by sensory stimuli. Most of the motor behaviors are characterized by sensory feedback that closes the motor control circuit determining its duration.

The way in which the information coming from different cortical levels and structures turns into an integrated representation has been explained through the description of association areas. These are higher-order areas that associate sensory inputs to motor responses and perform the mental processes between sensory inputs and motor outputs (Jackson, 1870). It has been experimentally proved that information from one sensory modality is projected from separate pathways to the association cortex that integrates all these information. The unimodal association areas project to the multimodal sensory association areas rostral to the primary motor cortex in the frontal lobe. This sensory information are then transformed from higher-order motor areas into planned movements that set their program that conveys to the premotor and primary motor cortex M1 for the implementation. Therefore, M1 represents the final site for the processing of motor commands. The motor commands originate from M1 and it has been shown that lesions in this area are associated with the complete absence of voluntary movements, although some stereotyped involuntary movements may persist. Lesions in the premotor cortex (a set of interconnected areas including areas 6, 8 and SMA) result in the inability to use the contralateral limb, as if the motor programs for that moving had been lost. The use of different techniques has enabled to describe the contribution of other motor areas to the production and control of movement, as like the use of microelectrodes, functional imaging or surface potentials recording.

According to the movement we are performing, different areas can be involved, including the primary sensorimotor area (for the representation of the body segment we are moving), the SMA and the premotor cortex, in both its ventrolateral (PMv) and dorsolateral (PMd) parts. All these areas concur

differently to the execution of a movement. M1 activity is principally related to the mechanical parameters of the movement. Kinematics and dynamic parameters of movement also activate the SMA and the PMd along with the parietal area projecting to the SMA and PMd; all these areas, indeed, can be modulated by the movement direction and force.

Previously, different areas in the frontal lobe have been associated to the motor system, whereas, thanks to the recent imaging data, it has been possible to better distinguish their anatomical and functional organization, which appears not only related to motor aspects but also to providing cognitive inputs to the motor areas. On the medial wall, the SMA has been divided into two parts: the proper SMA and the pre-SMA, originally considered involved in learning sequential movements. Connectivity studies have related these areas to the more prefrontal areas than to the motor one and thus to a more cognitive and motivational aspects of the movement. Only the SMA indeed is directly connected to M1, whereas pre-SMA is connected to the prefrontal cortex and activated by visuo-motor associations (Picard and Strick 2001). A similar differentiation has been also found for the PMd area; it is divided into a rostral and caudal subdivisions and only this latter portion seems to be more involved in motor tasks, whereas the rostral part appears like more connected to the prefrontal cortex and so more involved in cognitive rather than motor processes, not having any direct connection with M1. PMv is also divided in two portions, largely connected to M1. The caudal part is partly related to the transformation of object locations into the appropriate movement toward them (Rizzolatti et al., 1981); neurons here are responsive to tactile stimuli and active for protecting body from surrounding objects (Graziano et al., 1999; 2006). The other portion, PMv rostral, contains two different types of neurons: canonical and mirror neurons. Canonical neurons respond to the visual presentation of 3D objects and their motor response is limited to specific goal oriented actions. Mirror neurons, instead, are activated by presentation of visual stimuli denoting a goal-oriented action and also during the execution of the same type of action (Rizzolatti et al., 1988; Murata et al., 1997).

### 1.2.1 The “object-oriented action” circuit

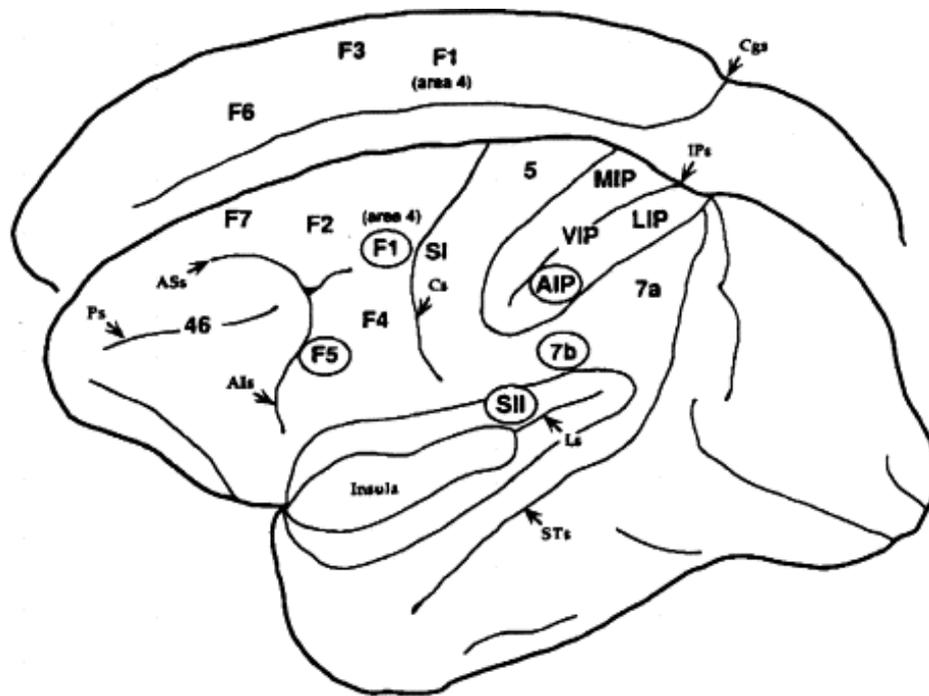
The action execution is the motor process most studied in literature. Thanks to researches on this topic it was possible to delineate the involvement and the role of other cortical areas, besides the motor cortex, in motor execution. Most of our movements, indeed, can be labeled as actions defined by goals and expectancy. Studies on the monkey brain using single cell recording, have shown the connection between the frontal and parietal areas in object-oriented actions and the control of distal hand (Rizzolatti et al., 1996). The area called F5, located in the ventral premotor cortex (PMv), receives input from different areas, like the prefrontal gyrus, the anterior part of the Intraparietal area (AIP) and the secondary somatosensory area (SII), and it is directly connected to M1 (Muakkassa and Stick, 1979; Matelli et al., 1986).

Goal-oriented actions are a complex type of actions requiring the translation of the location of a target into a set of muscle activation patterns. In order to do that, coordinates frames (internal and external) are transformed by the central nervous system to create movement representation (Kakei et al., 2003).

Many studies have proved that neurons in area F5 were very specific for the kind of action monkeys were going to perform and were related to different steps of the mental representation and understanding of that movement (Jeannerod, 1995). This area appeared to be likely involved in more cognitive aspects of the action rather than to the movement *per se* as it is active even during the observation of action or particular tools (Rizzolatti and Craighero, 2004). The activation of the premotor area is under control of different systems as the mesial cortical area and the prefrontal area; only when these areas allow action execution, the activated action representation becomes actual action (Rizzolatti and Luppino, 2001).

The ‘object-oriented movement’ circuit is one of the most studied networks for actions. The AIP-F5 circuit is involved in visuo-motor transformations for grasping. Such a circuit seems to start in the AIP area where visual dominant neurons receive information about object-properties and features from neurons located in another portion of the IPL, the LIP. AIP

visuo/motor neurons transform these visual objects into motor affordances and the best movement to perform is selected in the AIP according to these affordances. This information is then sent to the area F5 where it remains a potential action until an appropriate go-signal is sent from premotor areas (pre-SMA) (Figure 2) (Fagg and Arbib, 1998). Different studies have also suggested the possibility that such a translation of visual features of an object into a potential motor action could actually take place in the PMv area. It would be responsible for transforming a target location into the direction of action needed to acquire the target, that is from a visual frame of reference to a motor one (Murata et al., 1997; Kakei et al., 2001; 2003).



**Figure 2:** Cortical areas belonging to the object-oriented action network in monkeys. AIP receive input from PPC about the parameters of the object (location, shape, size) and projects them to anterior area F5.

After the description of this parieto-frontal circuit in monkeys, researches have been more focused on investigating the presence of a corresponding network even in humans. Several experiments showed an object-oriented hand action representation anatomically corresponding to the one described in monkeys. Such a circuit is represented by the pars opercularis in the Inferior

Frontal Gyrus, the posterior parietal cortex (PPC) and area SII (Binkofski et al., 1999). The PPC has a crucial role in sensory control (Andersen et al., 1987). It includes the superior parietal lobule, including the parietal reach region (PRR), and the inferior parietal lobule, more related to execution and observation of actions respectively, and divided by the intraparietal sulcus. Neuroimaging studies have pointed out the strong anatomical overlapping and functional equivalence of different areas included in the PPC between monkeys and humans, in particular of areas laid on the intraparietal sulcus (Grafkes et al., 2004).

Most of the findings about the role and involvement of the PPC in reaching and grasping actions comes from studies on patients affected by optic ataxia. These patients show inaccurate reaching movements towards peripheral target following a lesion in the parietal lobule always including the intraparietal sulcus along with the medial occipito-parietal junction (mOPJ) (Karnath and Perenin, 2005; Prado et al., 2005). Studies that have investigated grasping movements are fewer compared to those related to reaching actions; however, several evidences have suggested that a region in the human anterior intraparietal sulcus (aIPS) is involved in visually-guided grasping. Indeed, the application of the TMS (a technique that produces a virtual and temporary lesion effect) in this area and the superior parietal lobule disrupts the hand-preshaping adjustments to changes in object orientation. Moreover, studies on patients having lesions in the aIPS have revealed an inability of these subjects in object grasping performance but not for reaching (see Culham and Valyear, 2006).

Another important action-related function of these occipito-parietal areas seems to be related to the perception and representation of some object's features, such as orientation, depth and motion, that can be considered "action-related attributes of the object". Among these objects, tools have received particular attention. For this category, investigations have reported a left-lateralized network of areas including the PPC involved in the representation of knowledge about familiar tools. Tools parietal areas are supposed to be related to the motor representation for that object and its specific use rather than its semantic meaning, more related to the ventral, parieto-frontal stream (Chao and



Martin, 2000). Anatomically, this grasping area appears as posterior to aIPS, as defined by grasping versus reaching movements (Culham and Valyear, 2006).

Finally, it has been demonstrated that activity in PPC can precede the actual arm movement by several seconds, thus relating this area even to the planning of the action, in particular in the left hemisphere (Shenoy et al., 2003; Wheaton et al., 2005). Such activation has been described as more posterior compared to that associated to the execution of that gesture (Fridman et al 2005; Johnson-Frey et al., 2005).

### **1.2.2 The Mirror Neuron System**

The mirror neurons have been originally described in the portion of the ventral premotor areas of monkeys called F5. These neurons presented the property of discharging in association with movements having a specific goal (motor acts), but not for simple movements (Rizzolatti et al., 1988). The most interesting property of these neurons have been described after experiment showing their activity in concomitance to the observation of someone else (another monkey or the experimenter) performing a particular motor act, not just for its execution (di Pellegrino et al., 1992; Rizzolatti et al., 1996). Neurons presenting the same properties have been subsequently discovered in the inferior parietal lobule (IPL) giving rise to a network responsible for actions organization (Rizzolatti et al., 2006).

It has been assumed that the main function of this parietofrontal circuit is to understand motor acts performed by others matching them to the motor repertoire already belonging to the monkey. Such interpretation comes from studies showing that these neurons are actually active even when the movement is not visible but just inferred, but the final goal of the action is understood, or again when the only sound produced by the action is perceived (Umiltà' et al., 2001; Kohler et al., 2002; Keyser et al., 2003). These studies have pointed out on the cognitive aspect related to the premotor area that appears activated by the internal representation of the motor act. Moreover, among these neurons, a particular differentiation according to the motor act actually executed has been

found; neurons, in particular belonging to IPL, shown a different discharge for the same motor act related to different actions (i.e. grasp to eat or grasp to throw) proving that these mirror neurons are more related to the aim of the observed action more than the observation of the motor act (Fogassi et al., 2005; Hamilton and Grafton, 2006).

Studies on humans through different neurophysiological techniques have indicated a corresponding network in humans overlapped with the areas found in monkeys (ventral premotor cortex and IPL). First studies have used the frequency domain analysis to investigate the Mu rhythm modulation associated to the execution and observation of motor acts. The Mu rhythm presents a frequency between 8-12 Hz, like the occipital alpha rhythm, and is localized in the anterior motor areas. This activity is present as long as the motor system is at rest and desynchronizes in concomitance to movement or sensory stimulation (Gestaut et al., 1954). Thanks to this property, studies on the human mirror system have investigated the relation between the Mu rhythm and the MNS during observation of object-oriented movements (Cochin et al., 1998).

Neuroimaging and psychophysiological studies have subsequently allowed to describing the neural circuit subtending the human Mirror activity, showing the similarities between the areas activated in monkeys and humans (Buccino et al., 2001) and the functional similarities between the two species: also for humans it has been described a system active for both execution and observation of particular motor acts (Buccino et al., 2004) and even hearing of the sound produced by particular motor actions (Galati et al., 2008; Giusti et al., 2010). Anyway, several evidences have proved that only motor acts already belonging to the motor repertoire of the observer are effective in activating the mirror system (Buccino et al., 2004), or to the observer motor experience of a given action, like observing a dancing performance (Calvo-Merino et al., 2005; Cross et al., 2006).

### **1.3 Motor control theories**

The question about how the body moves to carry out the desired movement has addressed to the degree of freedom question, that is, to figure out

how it is possible to control the body and produce the desired movement within any situation. Studies on motor control account for how the central nervous system (CNS) solves the degrees of freedom problem (Schmidt and Lee, 2005) and are mainly focused on coordination, representing the best way we can make body move. Most of the researches focus on representing and exploring how the CNS produces coordinated movements that allow the body to interact with the environment, pursuing the aim of producing a comprehensive description of physical and physiological processes undergoing movements (Latash et al., 2011). These researches assume that the body works as a system able to be programmed for doing anything you want.

The two main questions characterizing motor control are related to:

1. the nature of physiological variables used by the brain to control muscles;
2. how the brain selects a solution among infinite sets by the redundant design of neuromotor system (Bernstein et al., 1967).

The first question has opened up to investigating if the motor program already contains all the information needed to carry out the action from its start to the end or if there are continuous adjustments by a response-based feedback mechanisms. This fundamental question has given rise to two main theories on motor control: the open and the close loop theories.

### **1.3.1 Open/close loop movement control**

Among the earliest hypotheses of movement control, an important one was proposed by William James (1890) who suggested an *open-loop* hypothesis postulating that movements require attention only for the initiation of the first action and the subsequent movements are automatically triggered by afferent information provided by muscles. This theory is also called “non-feedback control”, which assumes that feedback provided by the new status achieved or by the environment are not taken into account to adjust or modify movement already planned and started. Thus, according to this theory, movements cannot be changed once started even when unexpected changes occur in the environment. The statement underneath the open-loop theory is that decisions

are made in the brain that sends all the information for performing one movement in a single message to muscles that control and perform it; thus motor program contains all the information needed to carry out the action. This theory accounts well for fast and continuous movements but not for those slower that involve reactions. On the other hand, the *close-loop* motor control theory assumes that if during the performance the accuracy of the movement is actually recorded and evaluated then the movement is controlled by a closed loop-control mechanism.

The closed-loop control theory was proposed by Adams (1971) and is based on motor learning researches on slow positioning tasks involving error detection and correction to reach the final goal. The strong point of this theory is the role memory plays in learning; in particular, this theory starts from the observation that in order to learn a movement, a motor program consisting of two states of memory is required. The first one is the memory trace, which initiates the movement choosing the initial direction and determining its initial part. Strengthening of this memory trace comes from practice and feedback about movement outcomes. The second stage is the perceptual trace involved in guiding the limb to the correct position. This aim is achieved by comparing incoming feedback to this perceptual trace formed from the sensory information of the limb and its position in comparison to the past experience. As soon as we make an error, the limb is adjusted to obtain the movement appropriate to the goal of the action.

The closed-loop control, therefore, uses feedback and the motor program only contains initial movement instructions (Adams, 1971). This theory is able to account for slow movement execution but not for fast movements. Moreover, part of its weakness is related to the strict correspondence between the motor program stored in the brain and the movement to be performed and thus cannot account for new movements or the extent of possible movements we can perform due to the limited storage capacity of the central nervous system, that is, it does not represent an economic approach.

### 1.3.2 Schema theory

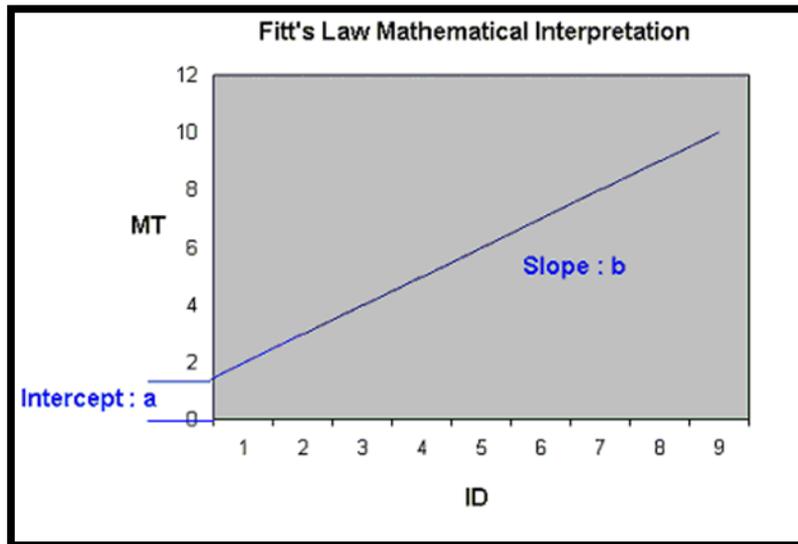
Although the closed-loop theory considered feedback as factor to control and generate movements, previous theories didn't really account for evidences illustrating the influence of feedback for the modification of ongoing movements. Therefore, in 2005, the Generalized Motor Program (GMP) theory was developed, which contains an abstract representation of movement with invariant features belonging to the order, the timing and the force of the different movements (Schmidt and Lee, 2005). The notion of GMP starts from the schema theory proposed by Schmidt in 1975 in opposition to the closed loop-control, suggesting that a motor program having general rules can be applied to different context, thus putting together the open-loop control process and the GMP. The schema contains the generalized rules that generate the muscular pattern to produce movement. Therefore, when a novel movement has to be learned the individual can generate a new GMP based on the selection of parameters or refine existing GMP. The theory suggested that motor programs can be clustered and are changeable to respond to the situation (Schmidt, 1975). Four processes are stored in memory after having generated a movement: 1. The initial/proprioceptive information of the body. 2. The response specification for the motor program. 3. The sensory consequences of the response. 4. The outcome of that movement. All this information is stored in the motor response schema as a long-term memory trace that is divided in two components: the recall schema and the recognition schema. They are connected but different: the recall schema is used to select a specific response with the use of response specification, it occurs before a movement is initiated and includes information about the current status and the goal to be achieved. The recognition schema is used *in fieri* to correct or alter the response according to the expected sensory information and the ongoing movement. The schema theory shows that motor learning consists of processes able to continuously update the recall and the recognition schemas.

### 1.3.3 Fitts's law and speed-accuracy trade off

Another model of human psychomotor behavior is represented by the Fitts's Law, which describes motor output from a mechanical point of view. It predicts that the time required to move to a target is a function of the distance and the size of the target itself. It describes a relationship between movement duration, movement amplitude and target demands. Fitts's law basically used to model the act of pointing and reaching, thus those movements involving an interaction with an object and it was proposed by Paul Fitts in 1954. It represents a mathematical model of movements applied in particular in human-computer interaction (HCI), ergonomics and computational human motor control. The most popular mathematical formulation of it was suggested by MacKenzie (1992):

$$T = a + b \log_2(1 + D/W)$$

Where  $T$  represents the movement time (often referred to as  $MT$ );  $a$  and  $b$  are two constants representing the start/stop of the device and the speed of the device;  $D$  is the distance from the starting point to the target and  $W$  is the width of the target. The term  $\log_2(1+D/W)$  is even known as index of difficulty (ID) and describes the difficulty of the motor task. This equation shows the speed-accuracy trade-off indicating that targets that are smaller and/or further require more time to be reached. As in many human tasks, the more precisely the task is to be accomplished, the slower the movement is and, conversely, the faster the task is completed the less precisely it tends to be accomplished. The key aspect of this formulation is that movement time depends in the ratio of movement amplitude and movement precision. Mathematically interpreted, Fitts' Law is a linear regression model with  $a$  as intercept and  $b$  as slope ( $1/b =$  index of performance [IP] describing the difficulty of the motor task (see Figure 3).



**Figure 3:** Fitts' s Law as linear regression model.

Physically interpreted, Fitts's Law states the following: 1. Big targets at close distance are acquired faster than small targets at long range 2. ID provides a single combined measure of two main physical properties of movement tasks 3. Positive intercept indicates additive factors unrelated to ID.

Fitts's law has been largely studied and applied in human-computer interaction studies (Card et al., 1978) and psycho-movement literature. It can be used in several conditions with movements performed with different limbs like hands, feet and eye gaze. It is an effective quantitative method for modeling user performance in rapid aimed movements and can be used to assist in the design of user interfaces and to predict the performance if operators in a user-adaptive system. Practically the principles developed y the Fitts' Law in the interface design are that things done more often should be assigned a larger button and should be closer to the average position of the users cursor. To date, the Fitts's law is one of the few reliable human-computer interaction predictive models, allowing new understanding and application in HCI research (Mottet et al., 2001; Accot and Zhai, 2003; Zhai et al., 2003), although it appears as valid but limited model. It doesn't address other factors besides width and amplitude that can affect user input performance; moreover it doesn't consider the effect of parallel strategies used but separate limbs and the effect of human body asymmetry on

performance (Kabbash et al., 1993). Finally it results to be a valid prediction model for rapid aimed movement but not for other input activities such as drawing and writing (Viviani and Terzuolo, 1982; Accot and Zhai, 1997).

Kelso studies on the coordination of two-handed movements lay on the Fitts' Law formulation. First studies from Kelso and coll. pursued the aim of investigating what happens when a subject is asked to move the upper limbs to targets each of which varies in amplitude and precision requirement (Kelso et al., 1979). According to Fitts' law, considering a hand movement condition in which the target size is large and the movement amplitude is short (easy condition) and a condition in which the target size is small and the movement amplitude long (difficult condition) the movement in the easy condition will result obviously shorter. The new aspect investigated by Kelso was the combination of these conditions with both hands. Results demonstrated that the movement time of the hand performing the easy task under combined conditions was almost doubled compared to single hand task or double hands both performing the easy task. This finding allowed to describing that the hand moving to the easy target seemed to wait for the hand moving to the difficult one in order to reach the target together. Such a finding indicated that despite differences in target position and dimension, response duration is a constant function and duration can be therefore interpreted as a major parameter in the program for two-handed movement (Kelso et al., 1979). Hands appear to perform asymmetrical and differently demanding tasks in a unitary manner shading lights on the interlimbs coordination motor control. In particular, Kelso suggested that when the motor system is faced with controlling multiple degrees of freedom, as it happens in two-handed task, it solves the problem by constraining the limb to act as a single unit.

#### **1.3.4 Motor control as action representation function**

All these theories well account for explaining and modeling the basis of movement and motor control from a kinematic point of view. What actually they don't account for is the cognitive aspect related to the execution and selection of the appropriate action. Even the close-loop theory, although uses feedback as



important factors in adjusting action execution, only considers them from a sensory and proprioceptive point of view rather than from their cognitive aspects that are actually those guiding and making the action start.

A fundamental problem and question in neuroscience is to understand complex, praxic and goal-directed behaviors that actually represent the majority of movement humans perform most. Such an issue has been addressed principally in terms of investigation of the cognitive structures underneath goal-directed action and their link to neural implementation. As yet, a comprehensive model able to account for action representation is still not present because of the motor system ability to create always new motor combinations, thanks to its redundancy, its flexibility and the possibility to adapt an action representation in response to a changing environment. Action representation, indeed, may vary as function of context, construct and means. However, three cognitive models for action representation have allowed to giving rise to an overall perspective: the context-guided, the ideomotor and the process models.

*Context-guided model:* according to this model, action representation is linked to external stimuli. This approach has been extensively described in the past, starting from Descartes who suggested action formation as a reaction to an external cause defining it in terms of perceptual events (Descartes, 1664). This approach has been then extended thanks to the experimental method by Donders who studying reaction time paradigms explained the action in terms of the physical properties of stimuli (Donders, 1862). Starting from these hypotheses, the stimulus-response pairing has then been considered more than a fixed relationship between inputs and outputs and the context started being thought creating what is considered an action representation. The importance of the context lays on the use of arbitrary symbols to drive an action following the learning of visuomotor association.

Different formulations of the action-perception relationship have been suggested and the context-guided representation represents an important variable, although the direction of this relationship is still unknown. The context-guided model allows to consider how actions are selected when simultaneous inputs provide competition for the selection of actions, suggesting a need for

some form of control, in particular when in a novel context or when the habitual behavior cannot be performed (Shallice et al., 1989).

*Ideomotor model:* according to this model the representation of action bases on internal, volitional causes of action. The main difference with the context-guided model is the irrelevant role of sensory causes. The action comes from an internal operation rather than external outputs and the goal is the causal determinant. The goal is indeed defined initially, followed by the implementation of the correct action in order to achieving it. This model lays mainly on studies on patients affected by ideomotor apraxia, a disease that affects goal-directed motor behavior because of an inability to perform the correct action in the absence of perceptual and sensory deficits (Danes and Pizzamiglio, 1996). Such a disease appears frequently following left hemisphere lesions showing a specialization of it for action representation.

The ideomotor model has led recently to the simulation theory (Jeannerod, 2001) suggesting that the mental state of actions involves simulations of the process associated with the execution of the action. Several neuroimaging studies have indeed shown how execution and cognition overlap (Sirigu et al., 1995; Decety, 1996; Grafton et al., 1996). Patients and imaging studies have provided evidences for a distinction between representations of the goal and action in terms of implementation leading to the goal.

*Process model:* in comparison to the previous models, the process model focuses more on how the mental representations are transformed and can influence the performance more than the representation itself. Actions present invariant properties associated with invariant features, in particular space and time. Two process models have been particularly studied: reach and grasp model and bimanual movements. According to process models the motor output can be modified in real time according to the task goal change. In order to be able to do that there must be an internal model able to estimate the current state of the motor system in real time.

#### **1.4 Movement phases: preparation and execution**

Many brain areas collaborate to movement execution but one of the questions more recently debated was whether and how these areas were also

involved in the movement preparation. As already mentioned, any high level task can be achieved in multiple ways. An important aspect in studying motor behavior is, therefore, to figure out how the brain prepares the correct, and most convenient, action for that task.

Motor planning and motor preparation represent pre-movement processes strictly related to, and led by, sensorimotor transformations and cognitive aspects of the action we are going to perform. In these phases the selection of the action takes place. Motor preparation is the generic term we refer to for talking about the period preceding the physical and kinematical onset of a movement. It is actually not a unitary process, but divided, at the least, in two phases. Thanks to clinical studies on patients affected by apraxia, it was possible indeed to distinguish between two separate steps of motor preparation: motor planning and motor programming. Apraxia represents a disease following lesions in the left temporo-parietal regions characterized by the inability to execute movements without presenting deficits of the motor system (Wilson, 1909). Depending on the region of lesion, it is possible to distinguish between different kinds of apraxia among whom the principal are *ideative apraxia*, represented by the inability to plan motor actions: although still able to explain it, subjects cannot create a mental representation of it. A second type is the *ideomotor apraxia*, representing a deficit in transforming the gesture in its appropriate motor programming. Clinical studies have now shed light on the complexity of those processes preceding the actual execution of the action.

First studies on motor preparation started around 1965 when electrophysiological findings described an activity preceding movements as a slow potential (Kornhuber and Deecke, 1965) and subsequently investigated through the fMRI technique (Cunnington et al., 2003; 2005). Two main paradigms have been used for studying activities preceding movements: self-paced/voluntary movements and externally triggered movements as reaction to an external go-signal, selected based on the technique of investigation to be used. However, in both cases movements performed by subjects were simple actions, like finger contraction, or complex sequence of fingers movement (Shibasaki and Hallett, 2006). Mostly, these studies have pointed to the role played by different motor areas as involved in the kinematics of these movements.

In particular, Kornhuber and Deecke claimed the role of the Supplementary Motor Cortex (SMA) in starting movements (Deecke and Kornhuber, 1978). Kornhuber (1989) hypothesized three main questions the brain has to give an answer before making a movement start: 1. What to do. 2. How to do. 3. When to do; and it was suggested then how all of those actually took place in the frontal lobe (Eccles, 1982). Three different areas appeared being responsible for these three questions: the fronto orbital cortex as involved in deciding what to do; the fronto lateral cortex as involved in the ‘How to do’ question thanks to its strong connection with sensory association areas of the parietal lobes; the fronto mesial cortex and SMA representing the phase actually recorded through the EEG technique as the *Bereitschaftspotential*. Deecke and colleagues indeed, claim about the fact that the first two questions could be actually just be inferred and not really measured experimentally.

The fact that the activity related to the SMA and then M1 was more related to the kinematics aspects of motor preparation, that is its programming phase, was reported also by other studies showing modulation of activity in these areas related to force, speed, precision, complexity and the amount of muscles involved in the movement (Shibasaki and Hallett, 2006). Other studies, instead, have claimed the involvement of pre-SMA and PMd area in the motor planning more than programming: the activity in these areas indeed, starts well before that one in SMA and M1 showing how they could be better involved in the representation stage of motor preparation (Cunnington et al., 2005).

Because of the clear role of parietal areas in the apraxia disease, it appeared evident the role of this area in those activities actually preceding the execution of a movement. Even studies on the mirror neuron system presented evidences about the involvement of the parietal areas, in particular, the inferior parietal lobule (IPL) in movement planning (Johnson et al., 2002) and studies investigating more complex motor acts like reaching and grasping movements, showed an anticipatory activity in parietal areas preceding those in motor areas (Wheaton et al., 2005). The planning of the action is the phase more related to the motor representation and the selection of the more convenient action among different possible solutions. Because of that, the involvement of the parietal areas seems fundamental in providing frontal structures with information

related to the surrounding environment coming from other senses. Previous studies have shown the involvement of these regions in representing kinematics parameters like the shape of hands (Jacobs and Jeannerod, 2005). However, further researches have also revealed the importance of parietal areas in representing the final goal of an action and its involvement in higher order intentions and, thus, their role in the initial part of the motor planning stage. These information are then forwarded to the PMd and the pre-SMA, responsible for planning the kinematic aspects of movement and finally to the SMA and M1 responsible for its programming and final execution (Hemilton and Grafton, 2006). The parietal areas in these actions seems also be involved in a monitoring activity of the action and their activity is indeed sustained throughout the motor preparation process (Hemilton and Grafton, 2008).

It seems, thus, that depending on the complexity of the movement to be performed, different structures take part in the representation and planning process making it more elaborate and hierarchical complex.

### **1.5 The movement related cortical potentials**

The movement related cortical potentials (MRCP) represent a particular kind of event-related potentials (ERP) recorded in concomitance with a movement. The ERP are a variation of the cerebral electrical activity following the presentation of an external sensory stimulus or event. The output produced by the brain is represented by specific waveforms with positive and negative polarities spreading all over the scalp in areas involved in elaborating that particular information. Such a response can be transient or steady-state depending on the stimulation rate that activate the brain at two different level: the exogenous (automatic) and the endogenous, more cognitive level (Hillyard et al., 1983; Picton et al., 1988).

For transient ERP, the first, earlier, components following a particular stimulus represent the first response level related to the perception of the stimulus and its physical features, and therefore are recorded in the sensory areas of the brain. The second part of the activity is instead related to the elaboration of the stimulus, involving its recognition; it starts later around 200

ms after stimulus presentation and it is recorded in associative and anterior areas.

As like other ERPs, the MRCP amplitude is very low and can be detected only by averaging the signal synchronized to the event. This method allows to extrapolating these low-amplitude potentials from the ongoing spontaneous EEG and environmental noise through the repetition of the event and the systematic recording of the activity in concomitance with it (Baillet et al., 2001). In the MRCP situation, it is possible to time-lock the signal to the movement onset recorded using the electromyography (EMG) located on the limb of interest or by a trigger sent by a button press.

### **1.5.1 MRCP components and their modulation**

The MRCPs were described in 1964 by Kornhuber and Deecke, who investigated for the first time volitional acts and voluntary movements instead of passive perception (Kornhuber and Deecke, 1964). The first experiment involved the recording of a self-initiated finger flexion movement detected through the use of EMG and the analysis of the activity preceding it. This activity was referred to as *Bereitschafts Potentiale* (Bereitschaftspotential or BP), or Readiness Potential, and physiologically it represents the cortical involvement in the pre-motor planning of volitional movements.

The readiness potential appeared as a slow negative component (BP) preceding volitional movements and followed by a positivity, the re-afferent potential (RAP) (Kornhuber and Deecke, 1964). Following studies allowed the two authors to describe two more components appearing just before movement onset: the pre-motion positivity (PMP) and the motor potential (MP) occurring in concomitance with the movement start and represented by the maximum peak of the shift (Deecke et al., 1969).

Because of the complexity of this waveform that doesn't appear to be a unitary component, the readiness potential is referred to as MRCPs due to the different components subsequently described. In 1979, Deecke and coll. distinguished two parts of the BP, the early BP (from -1.5 to -0.5 s before

movement onset) and the late BP (from -0.5 to movement onset). MEG studies carried out by Weinberg (1982) allowed to localizing better these two components, early and late BP, in the supplementary motor area (SMA) and the primary motor cortex (M1) respectively.

Other researchers have kept investigating the MRCP trying to describe and segregate different components related to it. In 1980 Shibasaki and coll. identified up to eight different components belonging to MRCP, four in the preparation period and 4 after the MP, among which the most important one was represented by the Negative Slope (NS'), a steep negative increase appearing just before the motor potential and previously described by Kornhuber and Deecke as the late BP (Shibasaki et al., 1980). The description Shibasaki made of these components involved also a more accurate scalp topography description that was followed, recently, by the source localization of such components thanks to new dipole source technique and MEG studies. Altogether these researches described the BP as a component starting around 2000 ms before movement onset, peaking at the midline centro-parietal area, symmetrically and widely distributed over the scalp regardless of the site of movement. This component has been principally localized in the supplementary motor area (SMA) shifting then on the lateral premotor cortices and peaking contralaterally in the primary motor cortex M1 where the NS' and MP components come from (Ikeda et al., 1992; Praamstra et al., 1996; Cui and Deecke, 1999; Erdler et al., 2000). The NS' was indeed distinguished from the BP based on the difference in scalp distribution; this component appears as peaking over the contralateral central area according to the site of movement, anatomically corresponding to the lateral premotor and primary motor cortices (Di Russo et al., 2005). Due to this asymmetric distribution, the MRCP have been studied subsequently as lateralized readiness potential (LRP) derived by subtracting the potential recorded at two corresponding electrodes in the two hemispheres for both left and right movements separately (Coles et al., 1988).

The pre-motor positivity (PMP), already described even by Kornhuber and Deecke in 1969, was described as predominant over the hemisphere ipsilateral to the site of movement, but it is still a component which role is still

unclear and debated. Finally, the main component occurring after the motor potential (MP) is the RAP, a positive deflection recorded around 300 ms after movement onset and peaking on the somatosensory cortex contralateral to the site of movement.

After having described how the motor related cortical potentials look like and having differentiated and localized its different components, researches started moving to investigate the stability of such a potential throughout different paradigms and movements. This allowed to describe that MRCPs can be modulated in both magnitude and time course according to the movement to be performed. In particular, it seems that level of intention, movement selection as fixed or freely selected, pace of movement, repetition, praxic movement, speed and accuracy, are all features that can affect the motor preparation period (Benecke et al 1985; Simonetta et al 1991; Kitamura et al., 1993; Masaki et al., 1998). The BP component seems to be the one more affected by them in both its amplitude and onset latency. Compared to mean amplitude, the onset latency seems to be the parameter modulated more by cognitive aspect rather than physical and mechanical aspects (such as effort and precision).

Most of the studies have so far investigated simple motor tasks like finger flexion, extension or tapping (Lang, 2003), but recently more complex movements, in terms of praxis, have started being investigated. The first attempt was made by Wheaton and coll. (2005), who studied pantomime of praxic movements. The complexity associated to those kinds of actions is not related to the amount of muscle districts involved in the performance, but to the meaning of the action, that can be considered a gesture in this case. Wheaton studies (2005a,b) showed for the first time a modulation of the BP component even in terms of latency and not only amplitude. Moreover, these studies reported such an early activation as originating from the parietal areas and not from the supplementary motor area (SMA) as previous literature described.

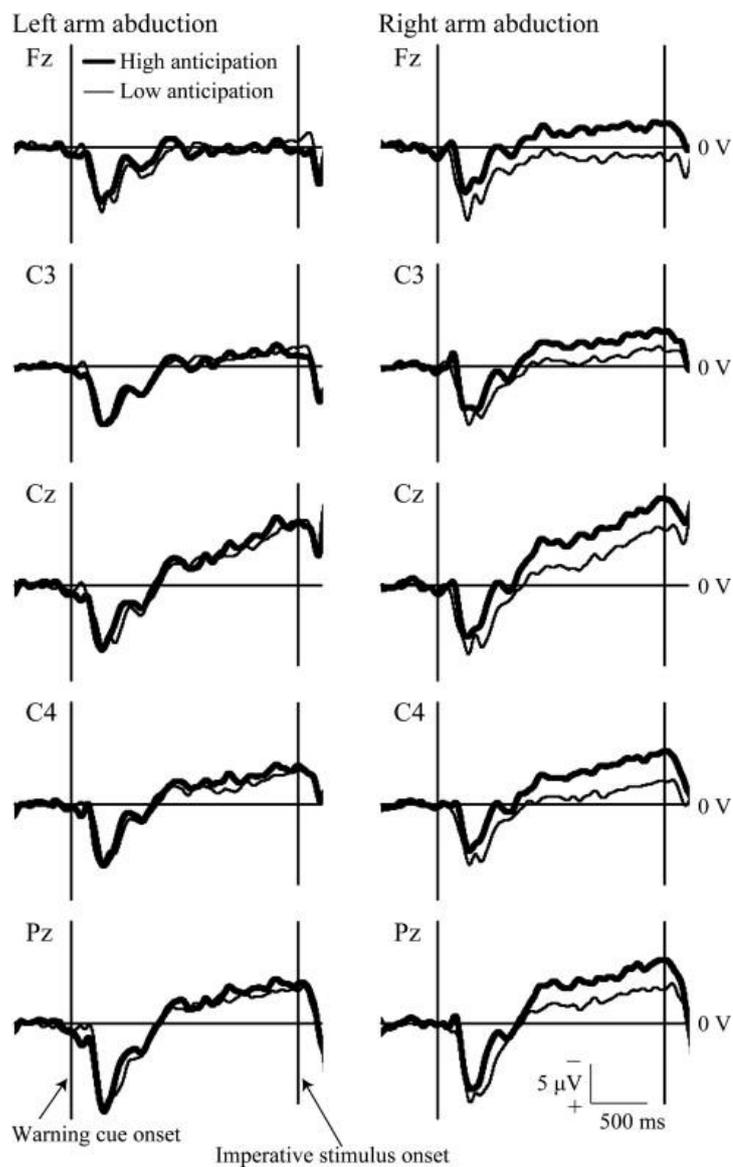


### **1.5.2 MRCPs and CNV**

The readiness potential is not the only potential that has been studied with regards to motor preparation. Contemporaneously to the first description of the MRCPs by Kornhuber and Deecke, a new potential was discovered and described by Walter and coll. (1964). The paradigm that allowed such a finding laid on the use of two stimuli presented in sequence: the first one, called warning, has to prepare subjects to the second one, the imperative stimulus, that is the one subjects are supposed to respond to behaviorally. The delay period between the warning and the imperative stimulus represents the time used to study the preparation period, represented by a waveform called Contingent Negative Variation (CNV). This potential appears as a long latency negative potential varying with the contingency between the two stimuli; thus, it is elicited only when two linked stimuli are presented.

The negative peak rises around 250-450 ms after the warning stimulus, rising more gradually according to the confidence of the subject with stimuli presentation timing, and spreads centrally and bilaterally in a symmetric way (Tecce, 1972) (Figure 4). CNV shows both motor and cognitive components, representing an arousal during orienting, as like attention and expectancy, interstimulus interval and intensity, all aspects that can modulate it (Tecce, 1972; Walter et al., 1964).

Many have debated about the correspondence between CNV and MRCP, considering them as overlapped. Although both associated to a motor preparation, CNV and MRCP appear as very different from each other for several aspects. In the first instance, the appearance of the CNV is strictly related to the association process between two subsequent stimuli; for being detected it requires, therefore, to be triggered to a warning stimulus, since it appears as a stimulus-related activity. On the contrary, the MRCP may be elicited in concomitance with a self-paced motion, that is, not constrained by temporal restriction and triggered by action onset. Other differences between the two conditions are also related to their scalp distribution that appears more lateralized on the contralateral site of the movement in the MRCP, whereas more bilateral in the CNV.



**Figure 4:** Waveforms showing the CNV component.

Another interesting aspect of the CNV is related to its 'not only motor' property: some studies have shown how it would be possible to elicit a CNV response even in absence of a motor response task (Ruchkin et al., 1986; Frost et al., 1988). It seems, thus, that this negativity is not just related to the preparation

to react, but also to an expectancy, anticipation and mental preparation for the coming stimulus, process.

## **1.6 General aim of this dissertation**

So far, I have described the human motion control as a complex neural process involving many different cortical and sub-cortical areas, active during both the execution phase and the period before it. The period preceding movement onset, that is the motor preparation, has been studied by several research groups, especially using the EEG technique. Through the use of ERP and frequency domain analyses, it was possible to describe the motor potentials related to movement (MRCP or *Bereitschafts Potential* or Readiness Potential), reporting timing and localization of the activity (Cochin et al., 1998; Shibasaki and Hallett, 2006). All these studies have shown how the activity in the motor areas starts well before the execution of a movement, recorded and triggered through the EMG signal; in particular, more than one second before movement onset it is possible to record a negative variation, or Mu rhythm desynchronization, in the premotor and motor cortices.

What the most of these first studies has been more focused on, though, was the study of simple movements, like finger extension or key press performed at a self-paced rate. Only starting from 2005 more complex actions, in terms of praxis, have been investigated (Wheaton et al., 2005). Wheaton's studies for the first time described the MRCP related to praxic actions, although not actually executed but just pantomimed. However, he showed a more complex motor related activity in terms of latency and scalp distribution: it seemed indeed this activity started in the parietal areas shifting afterward more anteriorly, as previously described in other studies. Apart from that, most of the studies investigating object-oriented actions used neuroimaging techniques, confirming this fronto-parietal network involved in both action planning and execution. However, limits of these studies are represented by the low temporal resolution of these techniques, a very important issue if you want to investigate motor preparation, and moreover the need to use movement triggered by external cue-signals instead of self-paced.

The questions I wanted to address to in the project I have carried out for my PhD were multiple and I tried to give a first answer to them through these first experiments. First of all I wanted to shed more light on the description of motor preparation for object-oriented actions, i.e. grasping and reaching, actually executed and not just mimed. I wanted to create a more 'ecological' setting in order to investigate how the brain works when we perform ordinary actions. Secondly, I was interested into distinguishing what kinds of processes are involved in the preparation of an action. Is it related principally and simply to the mechanics and kinematics aspects of the movement or even more cognitive processes, as like sensorimotor transformation of the object we are going to interact with, our goal and final outgoing, are fundamental issues taken into account during action preparation? Such a question came up to me getting through the literature just reported: several MRCPs components seem to be modulated and affected by the complexity of the action (Shibasaki and Hallett, 2006), that is, performing a movement that involves more fingers, or sequential finger movements or still praxic actions, the motor preparation activity, especially in its earlier part, increases its amplitude, starts earlier and, in the case of praxic movements, changes its scalp distribution. At the first instance, it seems that such a modulation could be referred to the kinematics complexity and the increased amount of muscles involved in that action; but what I was interested into was what happens if we perform that action with a particular reason or to pursue a particular goal. Does the activity change if we perform that sequence of fingers movement to play a piano or write a document on a computer? And what, instead, if the action we are performing was, for some reason, meaningless?

I decided to try to give an answer to these questions creating two experiments. The aim of the first study was to describe the MRCP related to a grasping action really performed, thus producing a gesture very common and familiar in our daily life: hold a cup lifting it up and drink. To this first condition I added another one, in order to investigate what it would happen if such a familiar and simple action was prevented somehow making subjects unable to perform it correctly and, thus, making the action lose its meaning. I tried to induce a feeling of frustration closing subjects' hands as fists with a band and asking them to perform the same action as before, that is, grasp the cup and

drink. It was physically impossible and subjects were forced to find and try different strategies or give up after having realized the impossibility and pointlessness of that action. Because of the difference in the mechanical aspects of the second action, in which all the grasping factors were absent, I added a third condition as control, a reaching movement, in which subjects were simply requested to reach to the cup with their fist.

The second study better addressed for the cognitive aspects of motor preparation. In this study I decided to test a simple movement already investigated in other researches, a key press action. Although very simple kinematically speaking, this action can actually hold several meanings according to the context we are performing it: we can switch the light on/off pressing a button, ring a bell, switch channels on the television or activate a bomb, or still not having any kind of consequence. Because of that I created a set up in which subjects were in front of a screen showing a picture of two hands and a cup and I tested two conditions: in one condition, according to the cup handle orientation, subjects had to press the right or left button without producing any consequence; in the other condition, the pressure of the button triggered a video showing the corresponding hand moving towards the cup and grasping it. This created a virtual condition, very similar to what we experience playing video games. Both these conditions were even compared with the motor preparation related to the real execution of a grasping movement.

Since the principal interest of the project was to better highlight the motor preparation activity, the best way for achieving it was using a self-paced paradigm: subjects didn't have to be constrained by any external signal but were free to execute and start the action whenever they wanted and felt ready to go.

Finally, I carried out a third study considering a passive observation task. Object-oriented actions, indeed, have been extensively studied in the last decades heading to different theories on motor resonance and mirror neuron system (MNS). Meaningful actions have been shown to be able to activate in the spectator an activity and network very similar to the one activated in the executor and such an ability has been thought to allow people to understand each other intentions and give a sense to what the other is doing (di Pellegrino et al., 1992; Buccino et al., 2001; Uithol et al., 2011). All the studies that have

brought to these theories have been carried out during the execution of a grasping or other meaningful actions, highlighting the overlap between the areas activated in the person that was performing the action and in the one who was just observing, as like he was imaging himself performing the same action. In 2004, Kilner showed a motor preparation-like activity during the observation of two stationary hands about to move of which subjects could predict the starting movement. Such a study opened up to the possibility of considering the motor resonance as involved well before the observation of the action execution, but including even the motor preparation phase (Kilner et al., 2004) and accounting for the understanding and prediction of other's intentions. What Kilner did was to compare the motor preparation activity, the readiness potential, during the execution of a grasping movement with the observation of a hand waiting to move toward an object. The timing before the hand started moving was fixed and, therefore, subjects were able to predict the starting movement. This study was the first one showing that the mental representation of the action we are observing starts even before the real movement, and such a correspondence between the executor and the observer is extended even to what precedes the movement. Kilner rightly attributed this finding to the ability of understanding other's intentions, aspect that actually is more related to the comprehension of the action well before it is executed.

Here I wanted to make a step forward in order to investigate in what degree the observation of a "motor preparation" could actually reflect the motor preparation activity for that specific kind of action. That is, whether the observation and the execution of different actions are modulated in the same way. I considered the best way to address to this issue was to use the same actions subjects were requested to perform in the first experiment, but this time asking them to observe videos showing an actor performing those two actions, the one in which the grasping was accomplished and the one in which it was hindered. Videos were presented in order to create expectancy about the upcoming movement, generated by a fixed image of the two hands lasting 3s. After this period, one of the two hands started moving toward the cup accomplishing or not the final goal. I used this same paradigm because the fact of

having already run these movements previously could give me a baseline to check out if and how we actually mentally represent what we actually see.

## Chapter 2

### Awareness Affects Motor Planning for Goal-Oriented Actions

#### Summary

The MRCP (motor related cortical potential) are electrophysiological signal related to the activity before and just after voluntary movements. MRCPs have been studied using simple movements and are composed of three main different components: two negativities preceding the movement (BP and NS') peaking in medial centro frontal areas, and one negative peak just after the movement (MP) in the contralateral central areas. Using complex movements (pantomimed), few studies described an activity in the parietal and prefrontal cortices starting up to 2 sec before the movement onset. Our aim is to describe the MRCPs for goal-oriented actions (grasping and reaching) in natural (free-hands) and handicapped (tied-hands, grasp is hindered) conditions in order to study activities in the prefrontal and parietal areas. Subjects performed three actions: a real grasp an impossible grasp and a reach separately. For the first time we have described the motor preparation activity for object oriented action really performed finding that the grasp has a more complex activity appears, starting posteriorly in the parietal areas (*posterior* BP) and spreading then frontally. This parietal activity was not detected in the reaching condition though, probably because of the task and the object included. Finally, the pre-frontal positivity is ascribable to the awareness of the impossibility of the action and the meaningless of the action, and therefore, to the inhibition to open the fingers.



## Chapter 3

### How Virtual Becomes Reality: Similar Motor Plans for Real and Virtual Actions

#### Summary

The spread of technological instruments has simplified our life allowing us to accomplish many complex actions. A simple movement such as pressing a button can hold different meanings and produce different consequences. So far, literature has shown that the complexity of the action we are going to perform can modulate the motor preparation activity. The question we addressed here was if motor preparation could be affected not only by the mechanical complexity of the action, but also by cognitive aspects such as its aim and meaning. Motor related cortical potentials were compared in three conditions: two key-press actions having different consequences and a grasping execution. Results showed that the early part of motor preparation for *virtual grasp* (a key press triggering a video of a grasping) was different from that in *key-press* (a simple key press) and similar to the *real grasp* preparation (both starting 3 s before movement onset), as if subjects had to grasp the cup in person. In particular, a posterior parietal negativity preceding activities in motor and pre-motor areas was associated with *virtual* and *real grasp*.



## Awareness affects motor planning for goal-oriented actions

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### ABSTRACT

We studied pre-movement cortical activity related to praxic actions performed at self-paced rate and having ecological meanings and functions. Motor-related cortical potentials were recorded using 64-channels EEG in two experiments. Experiment 1 included 15 subjects performing in separate blocks two object-oriented actions: *grasping* a tea-cup and *impossible grasping* of a tea-cup (same goal but the grasp was mechanically hindered). Experiment 2 included a subset of 7 subjects from Exp. 1 and the action was *reaching* a tea-cup; this control condition had a different goal but was kinematically similar to *impossible grasping*. Different activity patterns in terms of onset, amplitude, duration and, at least in part, sources were recorded in the preparation phase (BP component) according to the specific action and to the possibility of accomplishing it. The main result is that parietal areas were involved in *grasping* preparation (called "posterior" BP) and not in *reaching* and *impossible grasping* preparation. The anterior frontal-central activity (called "anterior" BP) during preparation for *grasping* started earlier than the other two conditions. The cortical activity during preparation for *reaching* was similar to that for *impossible grasping*, except for a frontal activity only detected in the latter condition. It is concluded that the action preparation, even in its early phase, is affected by action meaning and by the awareness of being able to perform the requested action.

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### 1. Introduction

In humans, the cerebral activity preceding movements has been extensively studied with electroencephalography (EEG) starting from the sixties. In 1965, for the first time, the Bereitschaftspotential (BP) was described as a negative cortical potential beginning ca. 1.5 s prior to the onset of self-paced movements underlying the preparation for action (Kornhuber and Deecke, 1965) and 15 years later, by Shibasaki et al. (1980), it was divided into different components as the early BP, the negative slope (NS'), the motor potential (MP), and the re-afferent potential (RAP), a positive component appearing after the onset of the movement related to the somatosensory cortex activation.

Several studies on the motor-related cortical potentials (MRCPs), have investigated simple motor tasks, i.e. finger flexion or extension, foot extension or tongue protrusion, and indicated that the sources of MRCPs components are located in the frontal cortical areas during motor-planning of simple self-paced movements

(Shibasaki and Hallett, 2006). In contrast, few MRCPs studies have investigated motor preparation for praxic movements, i.e. pantomime of tool-use and intransitive actions as to say goodbye (Wheaton et al., 2005a,b). These studies showed for the first time the involvement of parietal activity preceding that of the frontal areas. However, MRCPs studies have never investigated self-paced complex actions (not-pantomimed) such as goal-oriented reaching and grasping, having ecological meanings and functions. In particular, the response timing of the parietal regions in these complex actions is still unknown.

On the other hand, there is considerable neuroimaging literature on motor preparation related to complex actions, such as object-oriented grasping and reaching (Prado et al., 2005; Cavina-Pratesi et al., 2010), showing a parieto-frontal cortical network activated in action-planning and action-execution for reaching, grasping (Connolly et al., 2003; Filimon et al., 2009; Galati et al., 2011), pantomime (Johnson-Frey et al., 2005) and as well as for simple movements, such as moving fingers with eyes closed (Filimon et al., 2007). However, none of the fMRI studies previously cited have investigated motor preparation preceding *spontaneous self-paced complex* movements, such as reaching and grasping; indeed, only a few fMRI studies have examined cortical activations for self-initiated movements, but only considered simple movements such as key-press (Cunnington et al., 2005). Additionally, due to fMRI's

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poor temporal resolution, the activation timing within the parieto-frontal network remains unknown: the activation of parietal and frontal areas is well documented, but it remains unclear if the activation is simultaneous or in sequence, and – if so – what the sequence is.

The MRCPs are particularly suitable to discriminate the brain activity associated with the preparation and execution phases. Here we used MRCPs to investigate motor preparation related to grasping and reaching movements, i.e. complex actions which require more computations than simple finger movements, such as those used in most previous MRCP studies (Shibasaki and Hallett, 2006). Indeed, finger tasks lack the transport component of the arm, which is fundamental in real-world reach-to-grasp movements. Thus, the spatial coding and the motor programming during the preparatory delay is likely not the same for simple finger and complex arm movements as reaching and grasping.

Thus, in the present study we referred to complex movements toward a real object, i.e. grasping a tea-cup, performed at self-paced rate. The aim of the present research was twofold. First, we sought to analyze the activation timing of the cortical areas involved in the praxic movements verifying the involvement of the parietal areas in this kind of actions. Second, we sought to verify whether motor preparation was modulated by the awareness of the possibility/impossibility of correctly performing the requested action.

To address this latter issue, we implemented a second condition (*impossible grasping*), in which grasping was hindered by closing the fingers with a band. The presence of the object and the interaction elicited by the instruction (“try to grasp the cup”), made this condition somewhat similar to the real grasping, distinguishing it from a pantomimed action (where the object is absent; e.g. Wheaton et al., 2005a,b). However, in the *impossible grasping*, the final goal could not be accomplished, changing the meaning of the action performed with respect to *grasping*.

Comparison between *grasping* and *impossible grasping* enables us to evaluate any modulation of motor preparation activities induced by the awareness of being able/unable to accomplish the action. Since the two conditions were kinematically different in the execution phase (*impossible grasping* movement was actually turned into reaching the cup), we set a third condition (*reaching*) to verify whether cortical activities recorded for *impossible grasping* were simply related to the action’s kinematics, i.e. to evaluate if the brain activity underlying *impossible grasping* was actually equal to that for *reaching*, or was affected by the awareness of the impossibility of accomplishing the action’s goal.

Summarizing we performed this study to find out whether the planning of complex actions (*grasping* and *reaching*) involves activity at parietal level (as expected given the neuroimaging literature on this issue) and is modulated by the awareness of being able to perform the requested action. If the possibility of accomplishing the action was irrelevant, brain activity preparing the *impossible grasping* should be similar to that preparing reaching of the same object.

## 2. Materials and methods

### 2.1. Subjects

Fifteen volunteers university students (mean age 24.7 years; SD 6.2; 8 females) with no neurological or psychiatric disease, participated in the study. All subjects were right-handed, and the manual preference was evaluated with the use of the Edinburgh Handedness Inventory (Oldfield, 1971) ( $LI > 60$ ; mean score 85). After a full explanation of the procedures, all subjects provided written informed consent. The study was approved by the local ethical committee.

### 2.2. Tasks

Participants were required to perform two tasks in separated blocks. The first task was to extend the limb to grasp a tea-cup, located in front of the subject at a convenient distance, lifting it up, as for drinking, then put it back on the table and

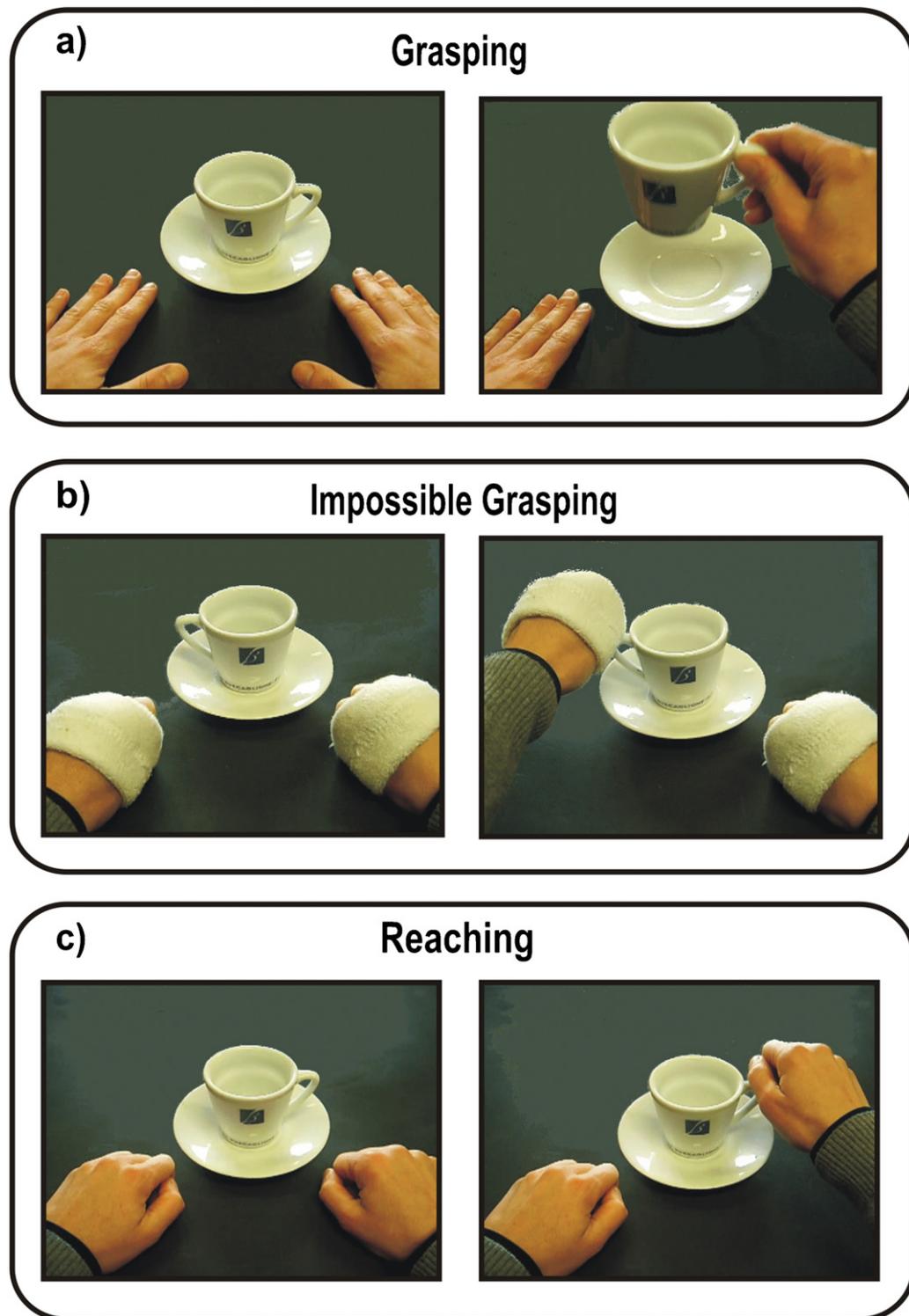
return to the resting position. The task was accomplished with the right and the left hand alternately, according to the left/right position of the cup handle. This condition is called hereafter “*grasping*”. In the second task, in order to hinder the grasping, the hands of the subjects were tied-up as fists with a band. Thus, the task was to grasp the cup but the action was actually hindered, and subjects were told they could not open their fingers. They reached, touched with the fist the cup’s handle, and felt the failure to grasp (this condition is called hereafter “*impossible grasping*”). Though the subjects were aware to be unable to cope the requested action, they were requested to perform the action as in the first condition, trying to grasp the cup, but never opening their hands (as represented in Fig. 1a and b).

### 2.3. Procedure

Subjects comfortably seated on a chair in front of a table with an empty tea-cup on top (35 cm distance from the body). Their hands were placed on the table in a resting/starting position. Subjects were instructed to maintain, during the task, stable posture and fixation. They were instructed to choose a point over the tea cup and to fix it for the trial duration. The action was self-paced and had to be performed slowly. The action ended when the hand returned to the resting position. The action duration was ca 4 s and 1 s was the time subjects spent to arrive touching the cup in every condition. After each trial, the experimenter (seated behind the subject) turned the cup on the table switching the handle to left or right, alternating the side on each trial. The interval between each action was ca 10 s. Subjects repeated each action 240 times (120 with left hand, 120 with right hand) for each condition. Tasks were executed in separated blocks, alternating different conditions (*grasping* and *impossible grasping*); each block included 60 actions. In both conditions, the movement initiation was spontaneous and self-paced, and subjects were trained to not count or synchronize their start with the researcher cup handle switch.

### 2.4. Electrophysiological recording and data processing

Electrical brain activity was recorded during the tasks using a BrainVision™ 64-channel system (Brain Products GmbH, Munich, Germany) connected to an active sensor system (ActiCap™ by Brain Products GmbH, Munich, Germany), adopting the standard 10–10 system montage. The system included four electromyography (EMG) channels with bipolar recording located on the left and right deltoids. Eye movements were recorded. Left mastoid (M1) was used as initial reference electrode for all scalp channels. Signal was digitized at 250 Hz, with an amplifier band-pass from 0.001 to 60 Hz with 50 Hz notch filter. To further reduce high frequency noise, the time-averaged MRCPs were filtered at 8 Hz. The EMG signal was rectified and visually inspected to identify and manually mark the movement onset. EMG onset was considered as the first increased of the signal on the beneath noise. Data were segmented in epochs from 3500 ms prior to movement onset to 1000 ms after it. Only the activity related to pre-movements phase was analyzed. Semi-automatic computerized artifacts rejection was performed prior to signal averaging, in order to discard epochs contaminated with gross ocular movement or muscular contractions from further analysis; trials with amplitude exceeding  $\pm 100 \mu\text{V}$  were individually inspected and discarded if contained the aforementioned artifacts. Around 20% of the trials were rejected. Blinks were found to be the most frequent cause for rejection. The baseline was calculated from 3500 to 3000 ms before onset and used for onset and amplitude measurement. The onset of the MRCPs was calculated as the first time sample where potential exceeded the 95% confidence interval of the baseline absolute value. The period used for statistical analysis started 3000 ms prior to movement onset up to the peak of the MP. All the MRCPs components were identified on visual inspection carried out by the first author and independently confirmed by the last author. Statistical differences in the MRCPs amplitudes between *grasping* and *impossible grasping* were initially assessed with sample *t*-test in all electrodes to select the locations and time windows where the differences were consistently significant. This preliminary analysis allowed us to select 10 electrodes (F7, F8, FCz, FC1, FC2, C1, C2, Pz, P3 and P4) and four time windows (–2000/1000 ms, –1000/–500 ms, –500/0 and 0/50, which also represent the main MRCP components) for further statistical analysis. On each contralateral electrode and time window, a  $2 \times 2$  repeated-measure ANOVA was carried out with task (*grasping* vs. *impossible grasping*) and hand (left vs. right) as within-subjects factors. For the MRCP onset latency and the MP peak latency a similar  $2 \times 2$  ANOVA was carried out on the electrode with the earliest activity. The LSD test was used for main effects comparisons. The overall alpha level was set at 0.05. Lateralized readiness potential (LRP) was also calculated considering the pairs of symmetrical electrodes selected by the *t*-test analysis (see above), in order to verify the lateralization of the motor preparation activity (De Jong et al., 1988; Coles, 1989). To visualize the voltage topography of the MRCPs components, spline-interpolated 3D maps were constructed using the Brain Electrical Source Analysis system (BESA, 2000 version 5.18, MEGIS Software GmbH, Gräfelfing, Germany). Given that changes in electric field indicate changes of the underlying generator configuration (Lehmann and Skrandies, 1980); we measured the statistical differences among scalp topographies using a non-parametric randomization test as the topographic analysis of variance (TANOVA) at each time-point between the two conditions. For more details on TANOVA, see Murray et al. (2008). Prior to TANOVA, the MRCPs were average referenced and transformed to a global field power (GFP) of 1, which ensured that the dissimilarity was not influenced



**Fig. 1.** The left side of the figure a–c represent the starting position of the hands in the three experimental conditions (*grasping* and *impossible grasping* (a and b, Experiment 1) and *reaching* (c, control experiment)). On the right side a video-frame presenting the interaction of the hand with the object is shown.

by higher activity across the scalp in any of the conditions. Thus, this analysis provides a statistical method to determine if the brain networks underlying *grasping* differ from networks underlying *impossible grasping* and its timing.

#### 2.5. Source analysis

The intracranial sources were determined using the BESA, 2000, which calculated the cerebral areas involved in the tasks and tested for possible differences in the temporal evolution of the active areas across the studied conditions. The noise-normalized minimum-norm method was employed to estimate the current

density dipoles on the cortical scalp. The minimum-norm approach is a method that is used regularly to estimate the distributed electrical current in a brain image at each time a sample; it is able to resolve the inverse problem without a priori constraints and is also able to reveal the unique constellation of current elements that models the recorded electric field distribution with the smallest amount of overall current (Hämäläinen and Ilmoniemi, 1984; Ilmoniemi, 1993). The algorithm employed minimizes the source vector current derivative from 1426 evenly distributed dipoles that are located 10% and 30% below the surface of the brain by using the approach adopted by Dale and Sereno (1993), where the correlation between  $p_i$  of the lead field for regional source  $i$  and the inverse of the data covariance matrix is computed together

with the largest singular value  $\lambda_{\max}$  of the data covariance matrix. The weighting matrix  $R$  is comprised of a diagonal matrix with weights. The equation consists of the following:  $1/(1 + \lambda_{\max} (1 - p_i))$ . To improve the minimum norm estimate (MNE), we also included depth weighting parameters across the entire source space because, as demonstrated by Lin et al. (2006), depth-weighted MNEs can improve the spatial accuracy by allowing displacement errors within 12 mm.

### 3. Results

#### 3.1. Waveform analysis

Both conditions (*grasping* and *impossible grasping*) presented the typical MRCPs components, including the slow negative potential BP (hereafter called anterior BP) slightly peaking on the contralateral fronto-central sites (FC1 and FC2), the NS' and the MP peaking more posteriorly on the contralateral central sites (C1 and C2) as shown in Fig. 2. Statistical analysis showed differences between the two conditions either in onset latency and amplitudes of these components.

LRP analysis in the  $-3000/-500$  ms time window did not show marked lateralization, but widespread distributions for both *grasping* and *impossible grasping* conditions which didn't differ each other ( $t(14) = 1.77, p = 0.1$ ).

The anterior BP component initiated about 800 ms earlier in the *grasping* (at  $-1910$  ms) than in the *impossible grasping* (at  $-1097$  ms) condition ( $F(1,14) = 4.62, p = 0.049$ ). The amplitude of this component ( $-1000/-500$  ms on FCz) was affected by the task and it was larger in the *grasping* ( $-2.0 \mu\text{V}$ ) than in the *impossible grasping* ( $-1.1 \mu\text{V}$ ) condition ( $F(1,14) = 4.86, p = 0.044$ ). Similar to BP, also the NS' component ( $-500/0$  ms on C1/2) was affected by the task, and it was larger for the *grasping* ( $-4.8 \mu\text{V}$ ) than the *impossible grasping* ( $-3.0 \mu\text{V}$ ) condition ( $F(1,14) = 6.60, p = 0.022$ ).

Since the EMG signal always precedes movement onset, the MP component was delayed with respect to the time 0, defined by EMG (see Fig. 2). The task effect was significant for the MP component which was larger in the *grasping* ( $-7.8 \mu\text{V}$ ) than the *impossible grasping* ( $-5.1 \mu\text{V}$ ) condition ( $F(1,14) = 7.04, p = 0.019$ ). ANOVA on the MP latency was not significant ( $F(1,14) = 0.08$  ns). LRP analysis showed that both NS' and MP were strongly lateralized in both conditions, which did not differ each other ( $t(14) = 1.47, p = 0.16$ ). In all the ANOVAs neither hand effect nor interaction effect were significant.

Note that in the *grasping* condition, partially overlapping to the anterior BP, it was possible to distinguish a large negative activity peaking on contralateral parietal sites P4 and P3 for left and right hand, respectively. This parietal activity, hereafter called posterior BP, started at  $-2835$  ms for left hand and at  $-2490$  for right hand lasting up to about  $-500$  ms from movement onset. Comparing the latency onset for the anterior and posterior BP in the *grasping* condition, the analysis showed such a difference as significant ( $t(1,14) = 14.73, p = 0.001$ ). Notably, the posterior BP was absent in the *impossible grasping*, as shown on the bottom panels of Fig. 2. Statistical analysis on the posterior BP amplitude ( $-2000/-1000$  ms on Pz) showed a significant effect of task ( $F(1,14) = 7.53, p = 0.015$ ), and interaction ( $F(1,14) = 4.84, p = 0.045$ ). Main effect analysis showed larger amplitude of the component ( $p < 0.02$ ) in the *grasping* ( $-3.0 \mu\text{V}$ ) than in the *impossible grasping* ( $-1.9 \mu\text{V}$ ). Further, in the *grasping* only, the left hand showed larger amplitudes ( $-3.3 \mu\text{V}$ ) than right hand movements ( $-2.7 \mu\text{V}$ ), though it was not significant.

Finally, the *impossible grasping* condition showed a contralateral pre-frontal positivity, starting from  $-2600$  ms to  $-480$  ms and peaking at  $-1450$  ms on F8 and F7 sensors (for left and right hand, respectively). This activity was not present in the *grasping* condition (top panels of Fig. 2) as revealed by statistical comparisons ( $-2000/-1000$  ms on F7/8) which showed a significant effect of

task ( $F(1,14) = 6.25, p = 0.022$ ). The hand effect and the interaction effect were not significant.

#### 3.2. Scalp topography and source localization

The topography of the BP component (Fig. 3) showed in all conditions the typical anterior (slightly contralateral) fronto-central negative focus ( $-1000$  ms maps). However, limited to the *grasping* condition, a posterior bilateral parietal focus was present. This activity was slightly more intense on contralateral hemisphere and more widespread for the left hand action, including also medial parietal sites 1–2 s before movement onset.

Voltage distributions of the NS' and the MP components were quite similar between conditions; the NS' focused on contralateral fronto-central scalp at  $-500$  ms and the MP more posterior on contralateral central sites ( $+50$  ms maps). The positivity, present in the *impossible grasping* condition, was strongly lateralized, focused on contralateral pre-frontal scalp and extended to anterior temporal sites ( $-1500$  ms maps).

Looking at the maps, it seems that the larger anterior BP amplitude recorded in the *grasping* condition may be explained by the volume conductance from the posterior BP. Furthermore, the presence of the prefrontal positivity in the *impossible grasping* condition (being partially overlapped in time to the anterior BP) might have additionally reduced the anterior BP.

Source localization obtained by minimum-norm analysis showed that the posterior BP (*grasping* condition) might originate in the superior parietal lobe, where the peak activity was detected. The pre-frontal positivity (*impossible grasping* condition) was localized within the contralateral middle frontal gyrus (Fig. 4a).

TANOVA comparison of motor preparation for *grasping* and *impossible grasping* showed that the two topographies were statistically different ( $p < 0.021$ ) mainly between  $-2000$  and  $-1000$  ms (Fig. 4b).

### 4. Control experiment

The *grasping* and the *impossible grasping* conditions mainly differed in terms of parietal activity (only present in the *grasping* action) and in terms of prefrontal activity (only present in the *impossible grasping* condition). An interpretation of these results is that the *impossible grasping* actually reflects preparation processes underlying a reaching movement, because at a kinematic level the two actions were similar. To test this interpretation, a control experiment employing a standard *reaching* condition was set. Note that the *reaching* condition is also interesting per se, since there are not MRCPs data for spontaneous self-paced reaching.

#### 4.1. Materials and methods

##### 4.1.1. Subjects

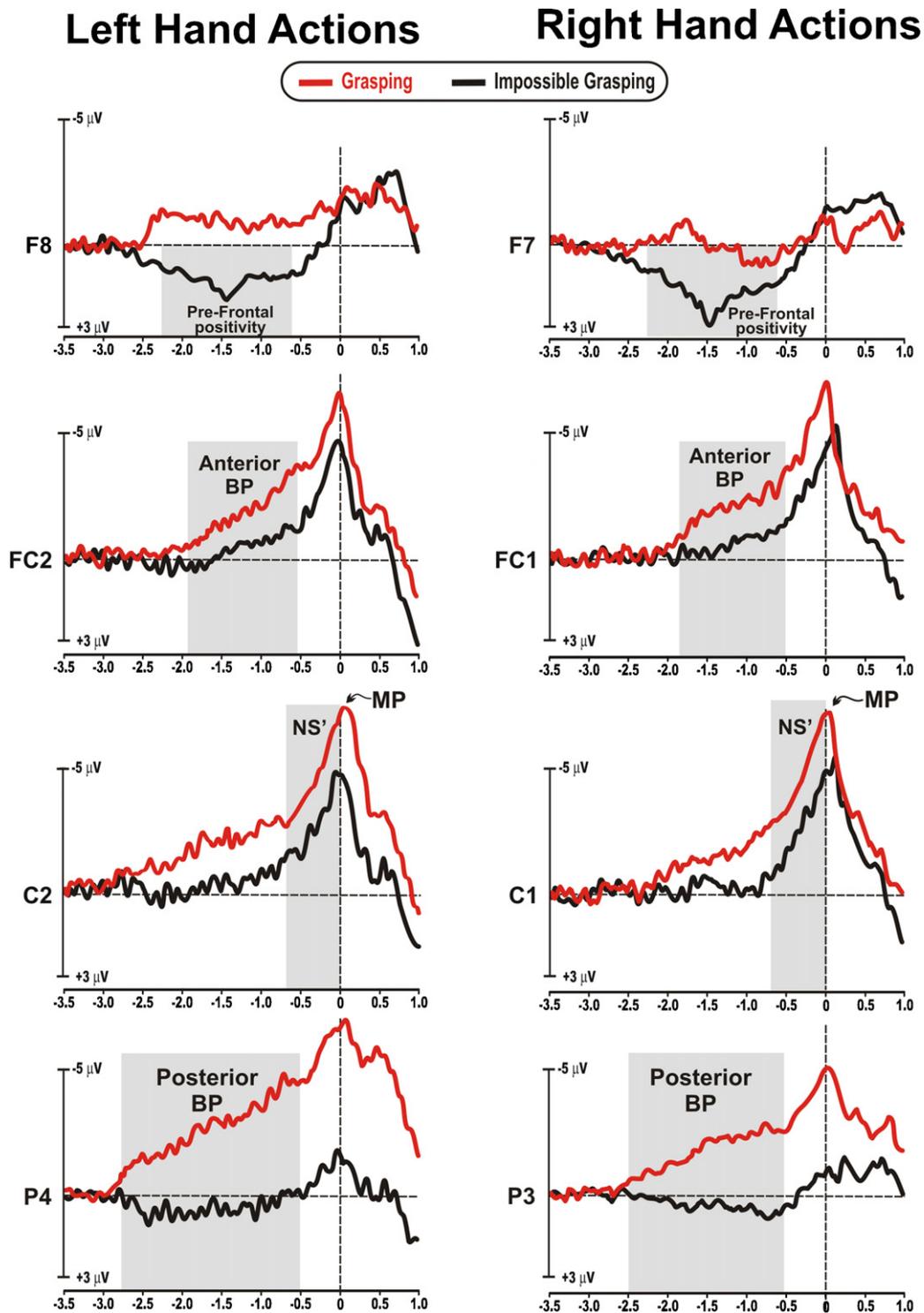
A subgroup from the previous sample (seven right-handed subjects, mean age 24.3 years, 5 females) participated to the control experiment. All subjects provided written informed consent after full explanation of the procedures.

##### 4.1.2. Task

Subjects were required to perform reaching-to-touch task with the right and the left hand alternately. The task was performed with the hand closed (in fist position), but without hand bands to replicate the position of the hand in the *impossible grasping* condition of the main experiment (see Fig. 1c).

##### 4.1.3. Procedure

Procedure was very similar to that of the main experiment, except for the task: subjects executed reaching movement toward



**Fig. 2.** Experiment 1. MRCPs activities averaged across 15 subjects for both right and left hand in *grasping* (red line) and *impossible grasping* (black line) at representative contralateral electrodes. The shaded areas represent the time window with significant differences between the two conditions. The main MRCPs components are labeled (anterior BP, posterior BP, NS' and MP). In the first row, the pre-frontal positivity is shown and it was limited to the *impossible grasping*. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

the cup with the left or right hand, according to the cup handle position. They touched the cup and then returned to the resting position. As in the main experiment, at the end of each trial the experimenter changed the side of the handle (left/right). Movements were repeated 240 times (120 with the right hand, 120 with the left hand) for each condition. Tasks were executed in separated blocks including 60 movements.

#### 4.1.4. MRCPs recording and data analysis

The brain activity recording and the data analyses were the same as in the main experiment. Statistical analyses included three tasks (*grasping*, *impossible grasping* and *reaching*) and were carried out on the data of the seven subjects who underwent also to the control experiment. A  $3 \times 2$  repeated measures ANOVA was used considering task and hand as factors.

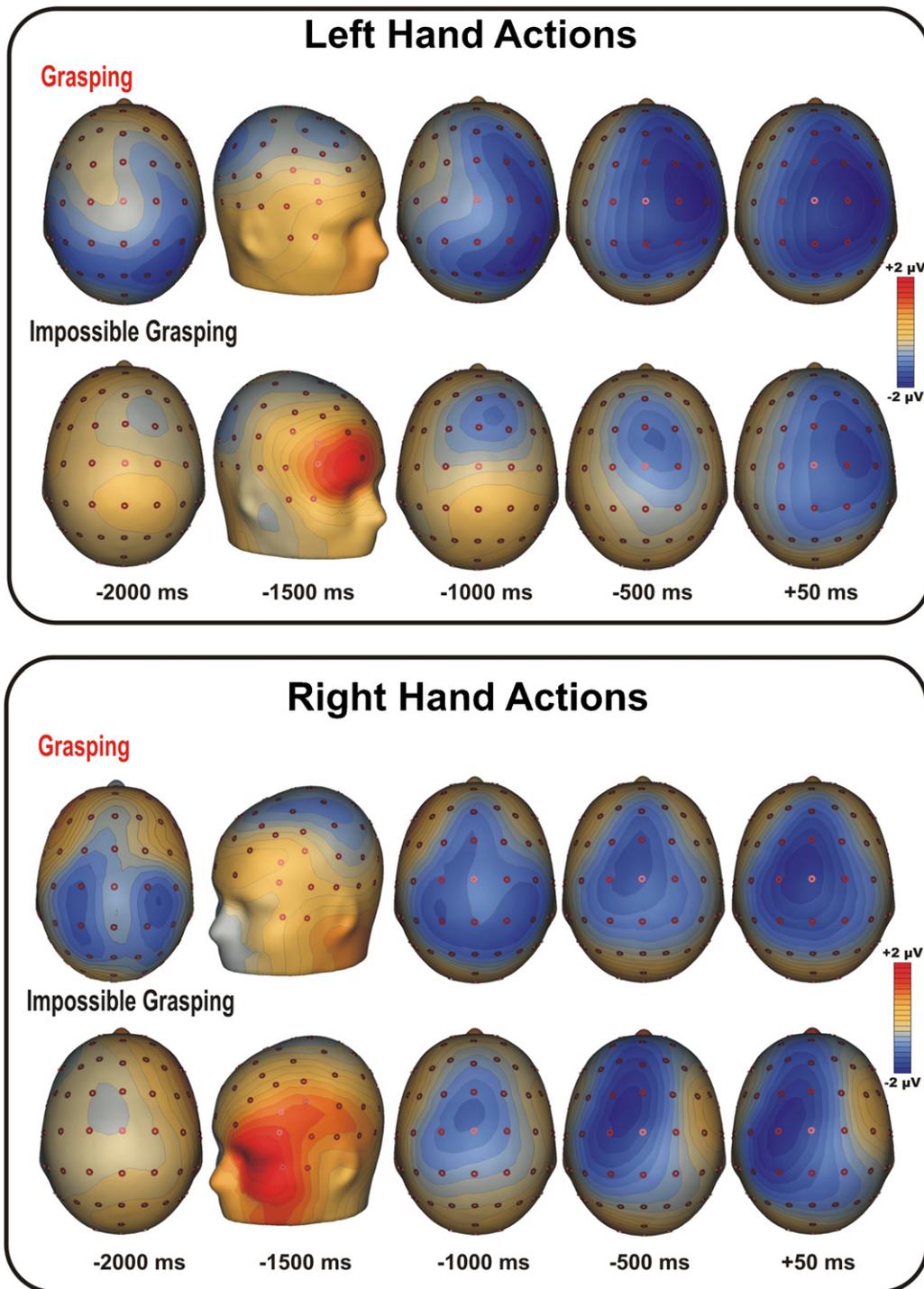


Fig. 3. Topographic 3-D maps for both left and right hand in *grasping* and *impossible grasping* conditions (in appropriate time windows) for each MRCPs component detected.

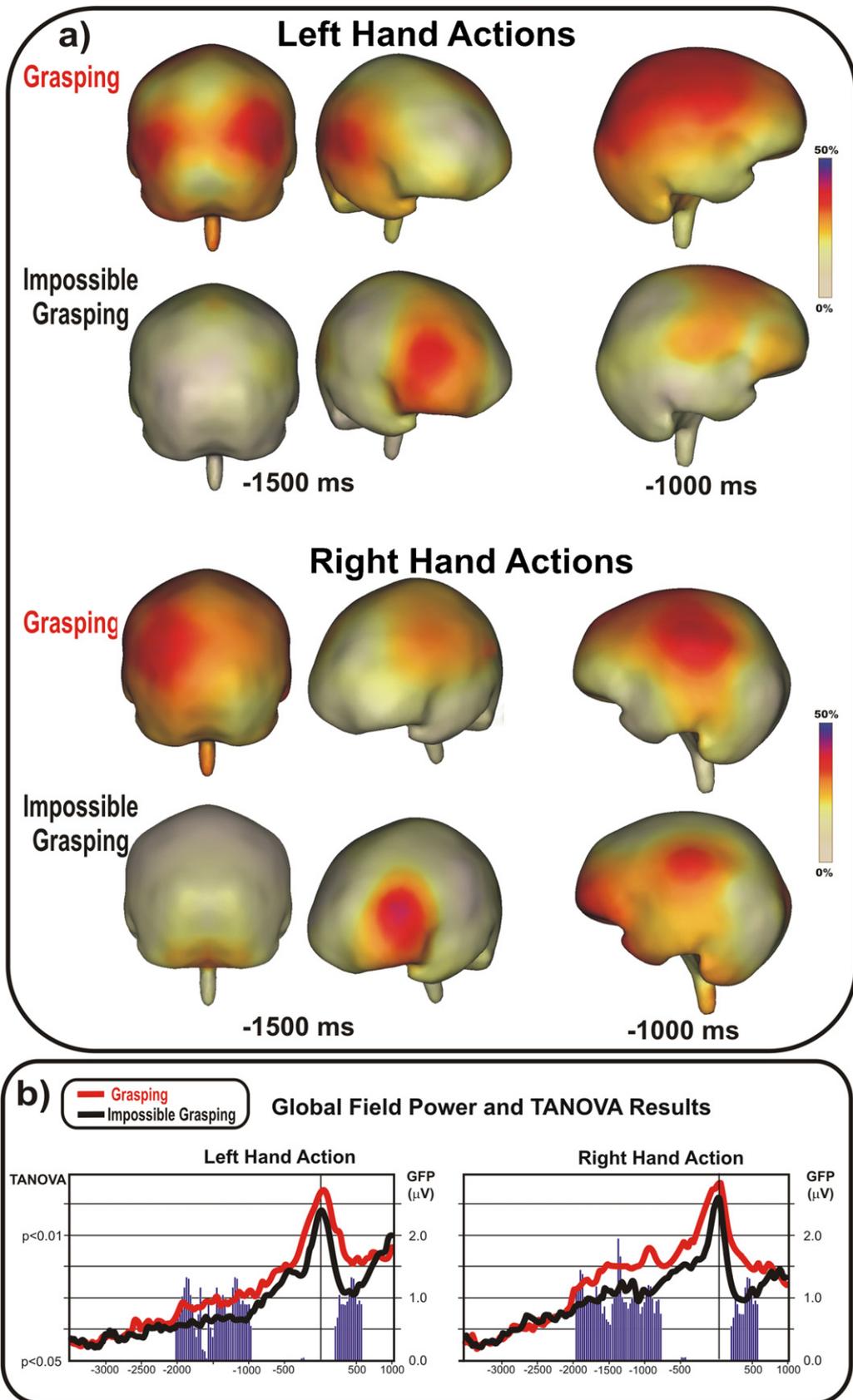
## 5. Results

### 5.1. Waveform analysis

The BP component of *reaching* started at 1450 ms before movement onset in the fronto-central areas, followed by the NS'; the MP peaked at about 70 ms after movement onset on contralateral central sites. No other activities were detected related to motor preparation. Differences between right and left hand were observed, mainly related to the components latencies: left hand components were delayed by about 40 ms. LRP analysis of the

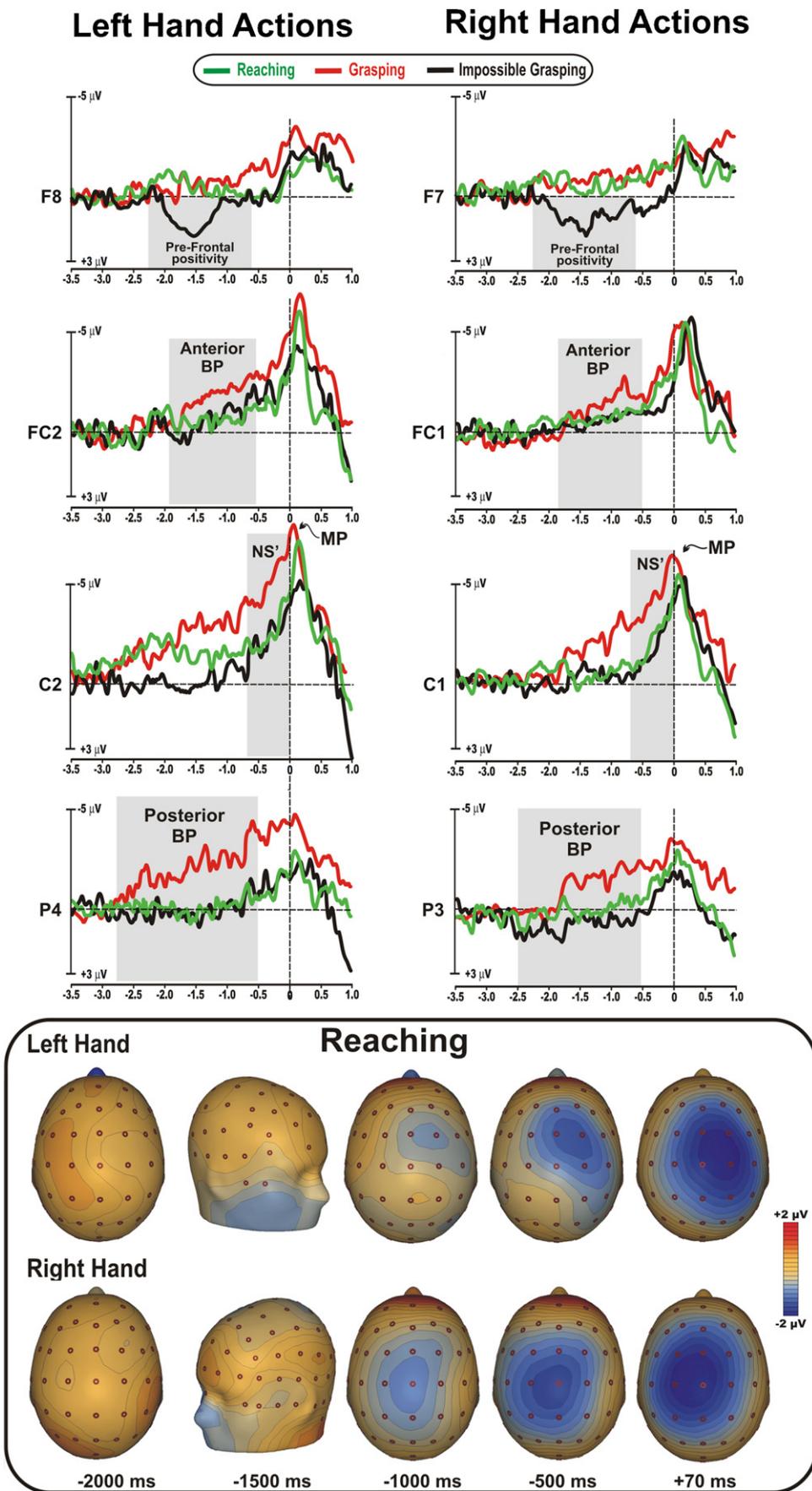
early BP component did not show a strong lateralization over the fronto-central electrodes for *reaching*, as well as in the other two conditions ( $F(2,12)=2.66$ ,  $p=0.11$ ,  $FC1/2$ ).

Comparing the MRCPs waveforms for the *reaching* with the *grasping* and *impossible grasping* conditions, significant differences were found for latency onset ( $F(2,12)=7.69$ ,  $p=0.007$ ), showing an earlier activity for *grasping* (2440 ms,  $p<0.001$ ) condition but no difference between *reaching* and *impossible grasping* onset (1200 and 1450 ms, respectively). Also amplitudes of the anterior ( $F(2,12)=4.29$ ,  $p=0.039$  on  $FC1/2$ ) and posterior ( $F(2,12)=9.91$ ,  $p=0.002$  on  $Pz$ ) BP, the NS' ( $F(2,12)=7.44$ ,  $p=0.008$  on  $C1/2$ ) and



**Fig. 4.** (a) Noise-normalized minimum norm source estimation at relevant latencies in *grasping* and *impossible grasping* condition for left and right hand action; (b) global field power time course and TANOVA results (vertical bars) for *grasping* and *impossible grasping* for left and right hand action.





**Fig. 5.** Control experiment: Top: MRCPs activities averaged across seven subjects for both right and left hand in the three studied conditions. The same electrodes as in Fig. 2 are shown. The gray area highlights the time windows with the differences between cortical activities in the three conditions tested with ANOVA on the seven subjects (see text for details). Bottom: topographic 3D maps for both left and right hand in reaching at relevant latencies for each MRCPs component considered.

the MP components ( $F(2,12) = 4.19, p = 0.042$ ) showed a main effect of the task were the *grasping* condition was larger than the other two conditions, which did not differ each other (Fig. 5). LRP analysis showed that both the NS' and MP were markedly lateralized in all the three conditions, but did not differ between conditions ( $F(2,12) = 0.58, p = 0.57$  C1/2). No differences were detected between *reaching* and *impossible grasping* except for the contralateral frontal positivity ( $-2000/-1000$  on F7/8) only present in the *impossible grasping* ( $F(2,12) = 4.19, p = 0.041$ ) (top panels of Fig. 5). In all the previous analysis, either hand and interaction effects were not significant.

## 5.2. Scalp topography

Fig. 5 shows the scalp topography of motor preparation for *reaching*. The BP component started 1 s before the movement onset, and showed, for both right and left movements, the anterior fronto-central negativity, slightly contralateral. Approximately 500 ms before movement the NS' topography focused on the contralateral central sites. The MP peaked around 70 ms after movement onset on contralateral central sites. No other activities were recorded before  $-1$  s, either on the parietal or frontal areas.

## 6. Discussion

In the present study, we described the time sequence of cortical activities underlying motor preparation for three complex actions: *grasping*, *impossible grasping* and *reaching*, with particular focus on the grasping action in an ecologically valid context (grasping a tea cup on the table at reaching distance).

### 6.1. Spatiotemporal pattern of grasping

The first aim of the study was to analyze the cortical activity underlying grasping programming, and its response timing, verifying in particular the involvement of the parietal areas. Results showed that motor preparation for *grasping* started earlier (about 2.5 s before movement onset), and presented a wider and more complex range of components than those previously described in other MRCPs studies (see Shibasaki and Hallett, 2006). The earliest activity in the parietal cortex, posterior BP, was followed by classic MRCPs frontal components. The parietal activity detected, was present only for *grasping* condition and was localized in the superior parietal lobe (SPL) as indicated by the Minimum-Norm analysis. This activity was bilateral, even though it was more evident in the hemisphere contralateral to the hand used. These results are consistent with previous fMRI (see Castiello, 2005) and single-cells studies (Matelli and Luppino, 2001; Andersen and Buneo, 2002) which showed SPL involvement in grasping movements.

About one second after the onset of the parietal activity (1.5 s before the grasping), the classical anterior BP was recorded. Then, one second later (and lasting until action onset) the NS' was present. The anterior BP is supposed to be generated in the supplementary-motor area (SMA) and in the pre-SMA, while the NS' is generated in the pre-motor cortex (Shibasaki and Hallett, 2006); this sequence of activation is consistent also with previous fMRI studies using time-resolved event-related paradigms (Cunnington et al., 2005).

Comparing *grasping* performed with left and right hands, motor preparation differed in terms of amplitude and latency. The onset of left hand movement was faster and its amplitude was larger than the right hand, though such a difference was not significant. Anyway, in MRCPs literature, longer motor preparation and more intense activity is generally interpreted as a sign of less economic or higher metabolic (or mental) costs in action planning, and thus reflects a more complex task to be performed (Di Russo et al., 2005).

This difference supports the view that for right-handers, programming an action with the left hand is more demanding than for the right-hand (Begliomini et al., 2008).

The timing of activities of the different cortical areas here described, converges on the view that the superior parietal areas provide the frontal pre-motor areas with grasp-related information by parallel channels for sensory-motor integrations (Milner et al., 1999; Rizzolatti and Luppino, 2001). In fact, posterior BP starting ca. 2500 ms before action was too early to be considered an activity of monitoring the execution of plans generated in the premotor areas (Haggard, 2011) and would indicate an interaction between parietal and premotor areas, with the starting activity rising in the parietal area. Parietal activity was also present in the temporal window closer to the action, even though encompassed by the anterior motor areas' activities; this later parietal activity would be consistent with a monitoring function.

The view that the superior parietal areas provide the frontal pre-motor areas with grasp-related information is supported by a vast body of literature mostly based on single-cells (see Rizzolatti and Matelli, 2003), fMRI and TMS experiments (Tunik et al., 2005; Davare et al., 2010), describing parallel parieto-frontal circuits underlying visually guided grasping movements (see Castiello, 2005). Several areas along the intra-parietal sulcus in SPL are also critical for processing context and grasp-dependent information, enabling the pre-motor areas to prepare hand shaping (Davare et al., 2010) and update visually guided grasp (Tunik et al., 2005). Indeed, grasping actions require moving the arm and the hand toward an object, and also involve the processing of object shape, size and orientation to pre-shape the hand. These features of the object are mainly processed in the anterior intraparietal sulcus, in correspondence with the anterior intraparietal area (AIP), a critical node for visually guided grasping execution and planning (Culham et al., 2003, 2004; Shmuelof and Zohary, 2005). Present results are also supported by fMRI literature investigating the interaction with graspable-objects, especially tools (Creem-Regher and Proffitt, 2001, Creem-Regher and Lee, 2005).

The parietal activity observed here for grasping resembles that observed in previous MRCP studies investigating motor preparation for pantomimes of hand praxic actions (Wheaton et al., 2005b,c). However, the parietal activity for pantomimes observed by Wheaton was considerably more posterior than that observed in the present study. Likely, this might be due to differences between pantomime and grasping actions in terms of visual, motor and somatosensory aspects related to a real interaction with the object. The more anterior activity observed here for grasping, possibly related to area AIP, would be explained by a visuo-motor gradient along the posterior parietal cortex (PPC) in the posterior-anterior direction (Stark and Zohary, 2008; Beurze et al., 2009; Filimon et al., 2009; Filimon, 2010; Galati et al., 2011). According to this gradient, spatial specificity decreases and action specificity increases when gradually moving from posterior to anterior regions. This smooth gradient of selectivity, which may reflect different stages of transformation of visual signals into motor commands, might justify the more anterior grasping-related activity observed here. Moreover, Wheaton et al. found an activity mainly contralateral to the hand used whereas the results here described showed a bilateral involvement. This is likely due to the difference between the task employed here (movements toward the body midline) and that used by Wheaton and coworkers (movements confined on the left ipsilateral side).

### 6.2. Action planning and awareness

The second aim of the study was to investigate whether cortical activities underlying action planning were modulated by the possibility of accomplishing the action. Results support this view:

*impossible grasping* was planned in a different way compared to *grasping*. The posterior BP was absent, the anterior BP and NS<sup>+</sup> were reduced and a peculiar prefrontal activity was observed. To control for kinematic aspects we tested a pure reaching condition. Brain activity underlying the *impossible grasping* was very similar to that recorded for *reaching*, except for prefrontal activity only being present in the *impossible grasping* condition. This difference in activity between *impossible grasping* and *reaching* is a key result with respect to the second aim of this study. Indeed, since the two actions were similar at a kinematic level, a lack of difference between planning *impossible grasping* and *reaching* could be explained by the fact that the same motor plan was planned and executed in both cases. The different activity found at the prefrontal level between these two actions was remarkable and likely reflects a correlate of the possibility/impossibility of accomplishing the action. Source analysis roughly localized the prefrontal activity in the middle frontal gyrus, an area known to be involved in spatial working memory processes (Leung et al., 2006) and inhibitory control (de Zubizaray et al., 2000). This prefrontal activity, only present in *impossible grasping*, could be explained as an inhibition of the goal of grasping action due to the hand handicap, or as a marker of the awareness of the impossibility of performing the requested action. In any case, we can deduce that motor preparation was affected by the awareness of the impossibility of accomplishing the action.

These data opens up the possibility of considering the so-called “unconscious period” in the decision to act expressed by the BP component (Libet et al., 1983), as not entirely unconscious. Libet and many other authors investigating the volition to move have isolated the time window during which the intention to move becomes conscious (around 300 ms before movement); before this time, the medial frontal activity grows systematically, without any consciousness of “urge to move” (Libet, 1985; Haggard, 2008, 2011; Fried et al., 2011). Unlike these studies, what we refer to for awareness is not related to the volitional control of movement itself, but to the type and meaning of the movement to be performed. The awareness of not being able to accomplish the action affected the brain activity associated with the early phase of action preparation, i.e. the unconscious period.

The absence of early activity in parietal cortex (the parietal BP) in the *impossible grasping* deserves some comments. We previously interpreted the posterior BP as an activity to provide the frontal premotor cortex with grasp-related information; the lack of posterior BP in *impossible grasping* and *reaching* would be consistent with a non-grasping action: in the first case grasping was hindered, in the second case the task was only to reach. Results suggest that this early SPL activity is related to the type of interaction to be performed with the object itself. Indeed, the kinematic of the *grasping* condition is more complex than that in the *impossible grasping* and pure *reaching* conditions. Grasping an object requires a sequence of movement to be prepared/executed (grasp, lift, lowering the cup). Sequential movement is well known to elicit stronger cortical activations as compared to a single movement. Thus the parietal activation, present only in the multi-step grasping movement, might be related to planning a movement with multiple steps. Additionally, long-range grasping requires fingers pre-shaping, recruiting a large number of muscles and joints; the execution lasts longer and involves more somatosensory feedback than *reaching* and *impossible grasping*. Thus, it is likely that the general higher complexity of the *grasping* affected the type of spatial and motor coding during the preparatory delay and revealed the posterior BP at parietal level.

Interestingly, the cup with its handle was present in all cases; thus the three conditions were comparable from the point of view of the object’s affordances. The graspable object should automatically activate the reach-to-grasp network (e.g. Chao and Martin, 2000; Grezes and Decety, 2002; Grezes et al., 2003a,b) in the three

conditions; in contrast, the parietal activity was modulated by the goal of the action, being posterior BP a specific feature of the *grasping* condition. In this respect note that our subjects were instructed to attempt to achieve the goal of grasping the cup also with the bound hands. Thus, in theory, the goal in the *grasping* and *impossible grasping* conditions were the same, nevertheless we observed the posterior BP only in the grasping condition. Observing the subjects in the *impossible grasping*, we noted that they did not simply extended the arm and touched the cup, as in *reaching*; their movement was more controlled and a hesitation was present when the handicapped hand was close to the cup, as if they tried, as requested, to grasp the cup. However, we cannot rule out the hypothesis that binding the hands itself did actually alter the goal of the movement, regardless of instruction.

One might contend that another possible interpretation for the lack of the posterior BP in the *impossible grasping* condition is that, in the latter case, a part of the hand was occluded from vision. It is well known that viewing the hand elicits activation in parietal areas (such as V6A, MIP and AIP), especially as related to the presence of graspable objects in the peripersonal space (e.g. Filimon et al., 2009). However note that the hand, though covered by a band, was still visible: fingers knuckle as well as part of the back of the hand appeared from the band (though this is not easily appreciable from Fig. 1c). Thus, the lack of parietal activity cannot be easily explained in terms of invisible vs. visible hand. In support of this view, note that in the *reaching* condition (where the hand was completely visible) we did not record any posterior parietal activity. Thus, we feel to exclude the possibility that results have been influenced by hand vision (or absence of vision) rather than the type of task.

### 6.3. Lack of parietal activity in reaching

The absence of parietal activity during *reaching* was unexpected; in fact previous studies reported the parietal involvement in reaching movements, both in monkeys (Fattori et al., 2001; Calton et al., 2002; Gail and Andersen, 2006; Ferraina et al., 2009) and in humans (Astafiev et al., 2003; Connolly et al., 2003; Prado et al., 2005; Hinkley et al., 2011; Galati et al., 2011). The present result may be due to various reasons. First, the technique used involved “back averaging” neural activity time-locked to a motor response (see Haggard, 2011); it is possible that parietal activity preceding reaching actions (unlike grasping) might not be strictly time synchronized to the movement onset (movement-related) and so hardly detectable by the MRCPs technique, whereas the aforementioned fMRI, and single-cells studies measured visual (go-signal) stimulus-related brain activity. Support for this view comes from description of a visuo-motor gradient along the PPC in the posterior–anterior direction, with posterior-reaching regions dominated by visual/attentional signals, and anterior-grasping ones under the control of the effectors that will be used in the following action (Beurze et al., 2009; Filimon et al., 2009; Galati et al., 2011). Second, in all three conditions the target was located in a central position respect to the subject. It is known that the parietal reach-circuit is constituted by cortical areas greatly dominated by contralateral responses (e.g. Astafiev et al., 2003; Hagler et al., 2007; Konen and Kastner, 2008; Galati et al., 2011). Due to the presence of the aforementioned visuo-motor gradient along the PPC, the posterior reaching-related areas, more dominated by visual signals, are likely sensitive to the lateralized position of the target. Thus, it is possible that, unlike for *grasping*, the central position of the target was not ideal to trigger the activity of parietal reach-regions. Third, we know from the neuroimaging literature that the human cortical regions underlying reaching movements are located medially in the POS (Beurze et al., 2009; Filimon et al., 2009) where monkey area V6A is located (Galletti et al., 1996) and in the IPS (Connolly et al., 2003) where monkey area MIP is located (Snyder et al., 1997). The

surface technique used in the present study might not allow the recording of such deep activities as in fMRI and single-cells recordings. Fourth, according to previous fMRI studies (Culham et al., 2003; Kròliczak et al., 2007) grasping execution produces greater activation than reaching in several regions, including the parietal areas. This smaller parietal activation for *reaching* might also occur in the preparation phase, thus giving a parietal contribution too small to be detected with EEG.

Alternatively, it is possible that this lack of parietal activity for *reaching* reflects a genuine effect related to the type of paradigm and task used here. In this respect, it is noteworthy that present results on *movement-related* brain activity preceding *self-paced complex-actions* have not a direct counterpart in the literature to be compared to. The fMRI studies investigating motor preparation in self-paced paradigms used only very simple tasks such as a key-press (Cunnington et al., 2002). To date, there are no other MRCPs or fMRI studies investigating the neural network underlying motor preparation by combining both complex task and self-paced paradigms. Indeed, previous EEG studies comparing simple versus 'complex' movements (e.g. Cui et al., 2000a,b; Lang et al., 1989; Mizelle et al., 2010) considered complexity differently than the current work. They used bimanual sequential movements (i.e. finger abduction/extension and knee movement), which are not comparable to grasping in kinematic terms. Future studies using the same combination self-paced paradigm and complex action could shed new light on the role of the parietal cortex.

## 7. Conclusions

The present study extends literature on the neural basis of action planning and contributes to the analysis of the interaction between parietal and premotor cortex. We showed the presence of parietal activity, well before the action begins, for goal-oriented actions such as grasping an object. This activity starts about two seconds prior to the action and is maximal about one second later in the areas contralateral to the used hand. Moreover, the type of action to be performed also modulates motor preparation in terms of timing and intensity of the different brain activity. Finally, the prefrontal activity in the impossible condition might be related to the awareness of being unable to perform the requested action, which is another aspect affecting action planning.

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## **Chapter 4**

### **I know what you do before you do it: different cortical activity for the observation of meaningful and meaningless object-oriented actions**

#### **Summary**

It has been shown that the observation of an action generates a motor activity occurring before the action producing a pre-movement activity, which anticipates other's actions. We demonstrate that such an anticipation well reflects the pre-movement activity for the execution of that same actions and different actions elicit different motor preparation-like activities in the observer, providing evidences that what we do and see lay on the same networks.

# Similar Cerebral Motor Plans for Real and Virtual Actions

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## Abstract

A simple movement, such as pressing a button, can acquire different meanings by producing different consequences, such as starting an elevator or switching a TV channel. We evaluated whether the brain activity preceding a simple action is modulated by the expected consequences of the action itself. To further this aim, the motor-related cortical potentials were compared during two key-press actions that were identical from the kinematics point of view but different in both meaning and consequences. In one case (*virtual grasp*), the key-press started a video clip showing a hand moving toward a cup and grasping it; in the other case, the key-press did not produce any consequence (*key-press*). A third condition (*real grasp*) was also compared, in which subjects actually grasped the cup, producing the same action presented in the video clip. Data were collected from fifteen subjects. The results showed that motor preparation for *virtual grasp* (starting 3 s before the movement onset) was different from that of the *key-press* and similar to the *real grasp* preparation—as if subjects had to grasp the cup in person. In particular, both *virtual* and *real grasp* presented a posterior parietal negativity preceding activity in motor and pre-motor areas. In summary, this finding supports the hypothesis that motor preparation is affected by the meaning of the action, even when the action is only virtual.

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## Introduction

The spread of technological instruments has simplified our lives, allowing us to easily accomplish many complex actions; thus, people are used to interacting with technological instruments and controlling them with simple movements. For instance, in our daily lives, we frequently press a button to switch channels on the TV, to call an elevator, to send e-mails on a computer, or to perform an "out and out" action, i.e., while playing video games. Thus, a very simple movement, such as a key-press, can have multiple meanings and different outcomes.

So far, it is not clear whether the motor preparation of an action, such as a key-press, could vary with the additional meaning of that action, i.e., when the key-press produces a specific consequence. Alternatively, the preparation might be entirely defined by the kinematics of the movement, which, obviously, does not change with the specific result of the action.

The neural bases of action motor preparation have been widely studied using the motor related cortical potentials (MRCPs). The MRCPs are characterized by two pre-movement components: the Bereitschaft Potential (BP) and the Negative Slope (NS<sup>+</sup>). The BP is thought to be related to readiness for the forthcoming action [1,2], as it begins well before the movement (from 1 to 3 s) and reflects early motor preparation in the supplementary motor area (SMA) and, according to more recent studies, in the superior and inferior parietal lobe [3,4]. The NS<sup>+</sup> has been associated with the urge to

act; it starts about 500 ms before the movement and reflects activity in the pre-motor area (PMA) [5,6].

The MRCPs literature shows that several factors related to movement are able to modulate the motor preparation. Among these factors, the complexity of the movement plays an important role. For instance, praxic movements (i.e., movements implying interaction with an object) or sequences of finger movements compared to a single finger abduction (or flexion), or the speed and precision of execution and the free movement (self-paced movement) instead of externally triggered movement, affect the onset and the amplitude of both the BP and NS<sup>+</sup> components [3,4,5,7,8,9,10].

The aim of the present study was to investigate whether identical simple movements producing different consequences were supported by identical motor preparation. Our hypothesis was that the specific cognitive value of a movement (related to its consequences and its goal) was able to affect the motor preparation of the movement itself.

Support for this hypothesis comes from a previous study from our group [4] that showed how the awareness of the possibility/impossibility of achieving a specific goal affected the action preparation. In fact, when the grasping action was hindered by closing the subject's fingers with a band, the awareness of being unable to accomplish the action modulated the BP component with respect to the real grasp condition. In addition, studies on monkeys and humans have provided evidence that during either the execution phase or observation of the execution of a movement

producing different outcomes (i.e. finger flexion for grasping vs. scratching; pulling vs. pushing), regions belonging to the inferior parietal lobe (IPL) and inferior frontal gyrus (IFG) encoded for the outcome of the action rather than for its kinematic aspect [11,12].

In the present study, we tested a very simple action by producing different effects: in one condition, the key-press had no consequences (called “*key-press*”); in another condition, the key-press triggered a video clip showing a hand grasping a cup from an egocentric point of view (called “*virtual grasp*”). As a control condition, we considered a *real grasp* of a cup, a complex movement associated with a complex motor preparation activity [4] but that shares similar cognitive aspects with the “*virtual grasp*” condition, in particular the (real or virtual) interaction between hand and object. Comparing the MRCs associated with these three actions, we would be able to verify to what extent the goal of the action and the kinematics of the action modulated the motor planning.

It is worth noting that the present investigation expresses a different point of view with respect to virtual reality studies. In those studies, a particular brain-computer interface allows people to interact with a computer-generated environment in a naturalistic fashion (see [13]) and requires performing specific actions (such as grasping, throwing, or reaching for an object) within a simulated environment [14,15,16]. In the present study, we investigated a simple motor behavior (key-press), which had the power of producing a complex, simulated, and virtual action.

## Materials and Methods

### Subjects

Fifteen volunteer university students (mean age 24.7 years; SD 6.2; 9 females) participated in the study. None of the participants had a history of neurological or psychiatric illness, and all the participants were right-hand dominant, according to the Edinburgh handedness inventory [17] ( $LI > 60$ ; mean score 85). All subjects previously participated in our study investigating MRCs for grasping actions [4], and they were all called back to perform the two key-press experiment investigated here.

### Ethics Statement

After a full explanation of the procedures, all subjects provided their written informed consent prior the experiment. The study and all procedures were approved by the independent the IRCCS Santa Lucia Foundation of Rome ethics committee.

### Tasks

Participants were comfortably seated on a chair in front of a table with a monitor on top and were required to perform three tasks in three separate blocks. In two blocks, subjects were required to press a key on the keyboard located on their legs (subjects were prevented from seeing their own hands). A 24-inch monitor, located in front of the subject at a distance of 35 cm, showed the static image of two hands laid on the table (the same table that was in front of the subjects) in a resting position presented from an egocentric point of view: the hands were in the bottom of the screen, the fingers pointed away from the subject, and a tea cup was located in the middle-upper part of the screen (figure 1A). The hands wore yellow gloves and a white coat, which made distinguishing whether the hands belonged to males or females impossible. Moreover, in order to facilitate identification with the character in the image, subjects were requested to wear the same yellow gloves and a white coat.

In the first task (hereafter called *key-press* task), the subjects were instructed to press the left or right button of the keyboard with the left or right index finger, according to the left or right orientation

of the tea cup handle. After the key press, the image remained steady for 2 s, followed by a new image displayed with the opposite cup handle position. In a second task (hereafter called *virtual grasp* task), the setting was identical to the former, except for the fact that the key-press triggered a video showing one of the hands (according to the left/right key press, which was in turn indicated by the handle position) moving toward the tea cup, grasping and lifting it up as for drinking (see figure 1B). The duration of the video was 2 s. In both the conditions the orientation of the cup was randomized. In a third task (hereafter called *real grasp* task), the monitor was removed, and the subjects had to grasp a real tea cup located on the table at a convenient distance (35 cm from the body). Starting from a resting position with their hands laid on the table (as shown in figure 1A), the subjects extended their arms, grasped the tea cup, lifted it up as to drink from it (as in figure 1B), and then put it back on the table while returning their hand to its resting position. The action was performed with the right and the left hand alternately according to the cup handle orientation (which was switched for each new trial by the experimenter), and its duration was approximately 2 s. This third condition has already been thoroughly described in a previous study [4].

### Stimuli

The authors filmed the video clips. In the *virtual grasp* condition, in order to match the stimuli for left and right hand movements, video clips were also mirrored using video editing software (Ulead VideoStudio 9.0), and the stimuli were counterbalanced so that 50% of the videos of one hand's movements were actually mirror movements of the other hand. We selected the first frame of the clip to create the static image of the hands in the resting position with the tea cup in the middle (figure 1A). This static image was used both in the *virtual grasp* and in the *key-press* conditions. Stimulus timing was controlled with the Presentation software (Neurobehavioral Systems, Davis, CA), triggered by the keyboard used by the subjects. The size of the hands and the cup in the static images and the video simulated the real size of the objects.

### Procedure

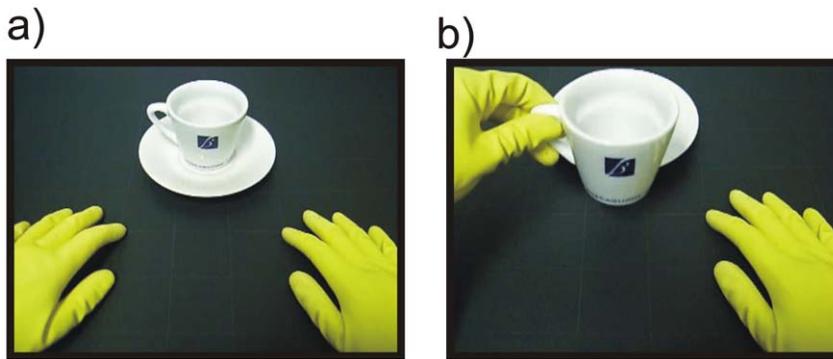
The tasks were executed in separate blocks. Each block included 10 runs; each run was composed of 24 trials (12 *per hand*). The *virtual grasp* condition was always performed after the *key-press* task, in order to ensure that the subjects performed the simple key-press without bias. The three conditions were performed in a block design paradigm. In particular, in order to elicit a better response, even the two key press conditions were not randomized: it was important subjects knew in advance what to expect from the key press in order to prepare the appropriate action. In this way, we could measure, if present, differences between motor preparations in the two cases.

Every action needed to be performed at a self-paced rate because we were interested in voluntary, not externally triggered, movements. The subjects were instructed to take their time before performing the task, and the interval between each action was approximately 10 s. The subjects were also trained not to count or synchronize their start either with the image onset or with the cup switching (in *grasp* condition). The subjects received online feedback when they were too fast in starting the movement and were trained to maintain, during all tasks, a stable posture and fixation on the small logo depicted in the center of the tea cup.

### ERPs Recording and Data Processing

Electrical brain activity was recorded during the tasks using a BrainVision™ 64-channels system (Brain Products GmbH, Munich, Germany) connected to an active sensor system





**Figure 1. Representation of hands position at different stages.** A) Starting position: the figure represents the starting image shown in both the *key-press* and *virtual grasp* conditions. B) In the *virtual grasp* condition, after the key press, the starting image was followed by a video clip representing the hand moving toward the cup, grasping and lifting it up (final frame). This image is also representative of the actual action performed by the participant in the *real grasp* condition.  
doi:10.1371/journal.pone.0047783.g001

(ActiCap™ by Brain Products GmbH, Munich, Germany), adopting the standard 10–10 system montage. The system included four electromyographic (EMG) channels with bipolar recording located at the left and right deltoids, and two channels for electrooculogram (EOG). A vertical EOG was recorded from above the left eye and a horizontal EOG from the left and right outer canthi. The left mastoid (M1) was used as initial reference electrode for all scalp channels. The signal was digitized at 250 Hz, with an amplifier band-pass from 0.001 to 60 Hz with a 50 Hz notch filter. To further reduce high frequency noise, the time-averaged MRCPs were filtered at 8 Hz. For the key-press conditions, the movement onset was triggered through the keyboard used by the subjects. In the *real grasp* condition, the EMG signal was rectified and used to identify and manually mark the first activity of the muscle (movement onset). Data analysis was conducted using BrainVision™ Analyzer 1.5 (Brain Products GmbH, Munich, Germany). Data were segmented in epochs from 3500 ms prior to movement onset to 1000 ms after it. Semi-automatic computerized artifact rejection was performed prior to signal averaging in order to discard epochs with ocular or muscular contraction artifacts from further analysis. The trial recorded for each condition were 150, but on average 20% of trials were rejected. Blinks were the most frequent cause for rejection. The baseline was calculated from  $-3500$  to  $-3000$  ms. The time period used for statistical analysis started 3000 ms prior to movement onset and lasted until 1000 ms after movement onset.

For the statistical analysis, the mean amplitudes and onset times of the BP and NS' and the peak of the motor potential (MP) were obtained from the MRCPs analysis on the electrodes showing an intense activity in all the three conditions and chosen because more representative. The BP onset was calculated as the first deflection that was larger than twice the absolute value of the baseline mean. Onset timing for the NS' components were established by a visual inspection carried out by the first author and independently carried out again by the last author. The BP amplitude was calculated as the mean amplitude of the BP component (from the BP onset to the NS' onset). Similarly, the NS' amplitude was calculated as the mean amplitude from its onset to the MP peak latency. The MP was measured at peak amplitude, roughly corresponding to the onset of the movement. Statistical comparisons were carried out to verify significant differences between conditions of the MRCP components latency and amplitude using a  $3 \times 2$  repeated-measure ANOVA with task

and hand as within-subjects factors. The Bonferroni post-hoc correction was used to interpret the main effects, while the Tukey HSD post-hoc was used to interpret interaction effects. All significant effects were reported at an alpha value of 0.05. To visualize the voltage topography of the MRCPs components, spline-interpolated 3D maps were constructed using the Brain Electrical Source Analysis system (BESA 2000 version 5.18, MEGIS Software GmbH, Gräfelfing, Germany).

We also compared scalp topographies of different conditions by measuring statistical differences with a non-parametric randomization test as the topographic analysis of variance (TANOVA). In order to assess the TANOVA, data were average referenced and transformed to a global field power (GFP) of 1, which prevents any influence from higher activity across the scalp topographies (for more details, see [18]). Significant topographical differences were considered to occur if they were consistently present for at least 150 ms (5% of the whole epoch). This analysis provides a statistical method to determine differences between the brain networks and activation timing underlying the studied conditions.

To produce a model of the intracranial sources of the MRCP components, the Brain Electrical Source Analysis system (BESA 2000 version 5.18, MEGIS Software GmbH, Gräfelfing, Germany) was used. The spatio-temporal dipole analysis of BESA was used to estimate the orientation and time course of multiple equivalent dipolar sources seeded in known locations by calculating the scalp distribution, which was obtained for any given dipole model (forward solution). This distribution was then compared with the actual MRCPs. Interactive changes in the orientation of dipole sources led to the minimization of residual variance (RV) between the model and the observed spatio-temporal distribution of MRCPs. The position of the electrodes was digitized and averaged across subjects. The 3-D coordinates for each dipole of the BESA model were determined according to the Talairach axes and scaled according to the brain size. In these calculations, BESA used a realistic approximation of the head (which was based on the MRI of 24 subjects), and the radius was obtained from the group average (85 mm). The possibility that dipoles would interact was reduced by selecting solutions with relatively low dipole moments with the aid of an “energy” constraint (which was weighted 20% in the compound cost function as opposed to 80% for the RV). The optimal set of parameters was identified in an iterative manner by searching for a minimum in the compound cost function. Dipoles were fitted sequentially. Latency ranges for fitting were chosen (see results) to minimize overlap among

successive, topographically distinct components. To minimize cross-talk and interactions between sources, dipoles that accounted for earlier portions of the waveform were left in place as additional dipoles were added. The fit of the dipole model was evaluated by measuring its RV as a percentage of the signal variance, as described by the model, and by applying residual orthogonality tests (ROT; e.g., [19]). The resulting individual time series for the dipole moments (the source waves) can also be subjected to an orthogonality test, which will be referred to as a source wave orthogonality test (SOT; [19]). All t-statistics were evaluated for significance at the 5% level.

## Results

### Waveform Analysis

Figure 2 shows the MRCP waveforms recorded at the most relevant locations (FC1/2, C1/2 and P1/2) in the three conditions (*key-press*, *virtual grasp* and *real grasp*).

The earliest cortical activity (the BP component) started at about 2.8 s before the movement in the *real grasp*,  $-2.7$  s in the *virtual grasp* (both on contralateral parietal electrodes) and  $-1.7$  s in the *key-press* (on FC1/2). The task effect on the BP latency was significant ( $F_{(2,28)} = 10.23$ ,  $p < 0.0005$ ) and post-hoc comparisons showed that the *key-press* preparation started later ( $p < 0.02$ ) than that of the other two conditions, which did not differ from each other. Additionally, the hand effect was significant ( $F_{(1,14)} = 4.63$ ,  $p < 0.05$ ), indicating that the BP onset was about 200 ms earlier for left- than right-hand movements. The interaction between factors was not significant.

In the *key-press* condition, the BP peaked on the contralateral fronto-central sites (anterior BP), whereas in the *virtual grasp*, it peaked more posteriorly on contralateral centro-parietal sites (posterior BP). For the *real grasp* condition, the BP peaked on contralateral parietal sites (posterior BP). Statistical analysis showed that the BP amplitude was affected by task ( $F_{(2,28)} = 10.28$ ,  $p < 0.0005$ ) and hand ( $F_{(1,14)} = 4.76$ ,  $p < 0.05$ ); the interaction was also significant ( $F_{(2,28)} = 3.55$ ,  $p < 0.05$ ). Post-hoc comparisons showed that the BP amplitude for both hands was smaller ( $p < 0.005$ ) in the *key-press* condition than the other conditions, which did not differ. The BP amplitude for the *real grasp* condition was larger ( $p < 0.002$ ) for left- than right-hand movements; in contrast, this difference was not significant in *virtual grasp* and *key-press* conditions.

The NS' onset ranged from 450 ms to 730 ms before the movement according to the task. An ANOVA showed significant task effects on the latency of the NS' onset ( $F_{(2,28)} = 20.45$ ,  $p < 0.00001$ ). Post-hoc comparisons showed that the NS' for *key-press* was later ( $p < 0.001$ ) than that for the other two conditions. For *real* and *virtual grasp* conditions, the onset of the NS' did not differ. Neither the hand factor ( $p = 0.81$ ) nor the interaction ( $p = 0.17$ ) was significant. The NS' peaked in all conditions on contralateral central sites, and its amplitude was affected by task ( $F_{(2,28)} = 25.48$ ,  $p < 0.00001$ ), but the hand factor ( $p = 0.07$ ) and the interaction ( $p = 0.2$ ) were not significant. Post-hoc comparisons showed that the NS' was larger in the *real grasp* condition ( $p < 0.0003$ ) than in the other conditions.

The MP peaked 30–80 ms after the *key-press* or the *real grasp* onset, and the latency was not affected by either task or hand. Similar to the NS', the MP was prominent in all conditions on contralateral central sites, and its amplitude was affected by task ( $F_{(2,28)} = 10.35$ ,  $p = 0.0004$ ). Post-hoc comparisons showed that the MP was larger in the *real grasp* condition ( $p < 0.01$ ) than in the other conditions, which did not differ. The effects of hand and the interaction were not significant.

After the movement, the re-afferent potential (RAP) was present in *key-press* and *virtual grasp* conditions, peaking at 160–200 ms after movement on contralateral central electrodes. This activity is strictly related to the somatosensory afferents elicited by the finger press on the key, and thus, it is very different from the activity elicited in the *real grasp* condition, wherein the movement onset was followed by the transport phase of the arm toward the cup, which was reached and touched on average 1.5 s after the movement onset. However, because the study of post-movement activities was outside the scope of the present study, which focuses on motor planning, the RAP was not further analyzed.

### Scalp Topography, TANOVA and Source Analysis

Figures 3 and 4 show the spatial distribution of the MRCP activity in the three conditions for the left and right hand, respectively.

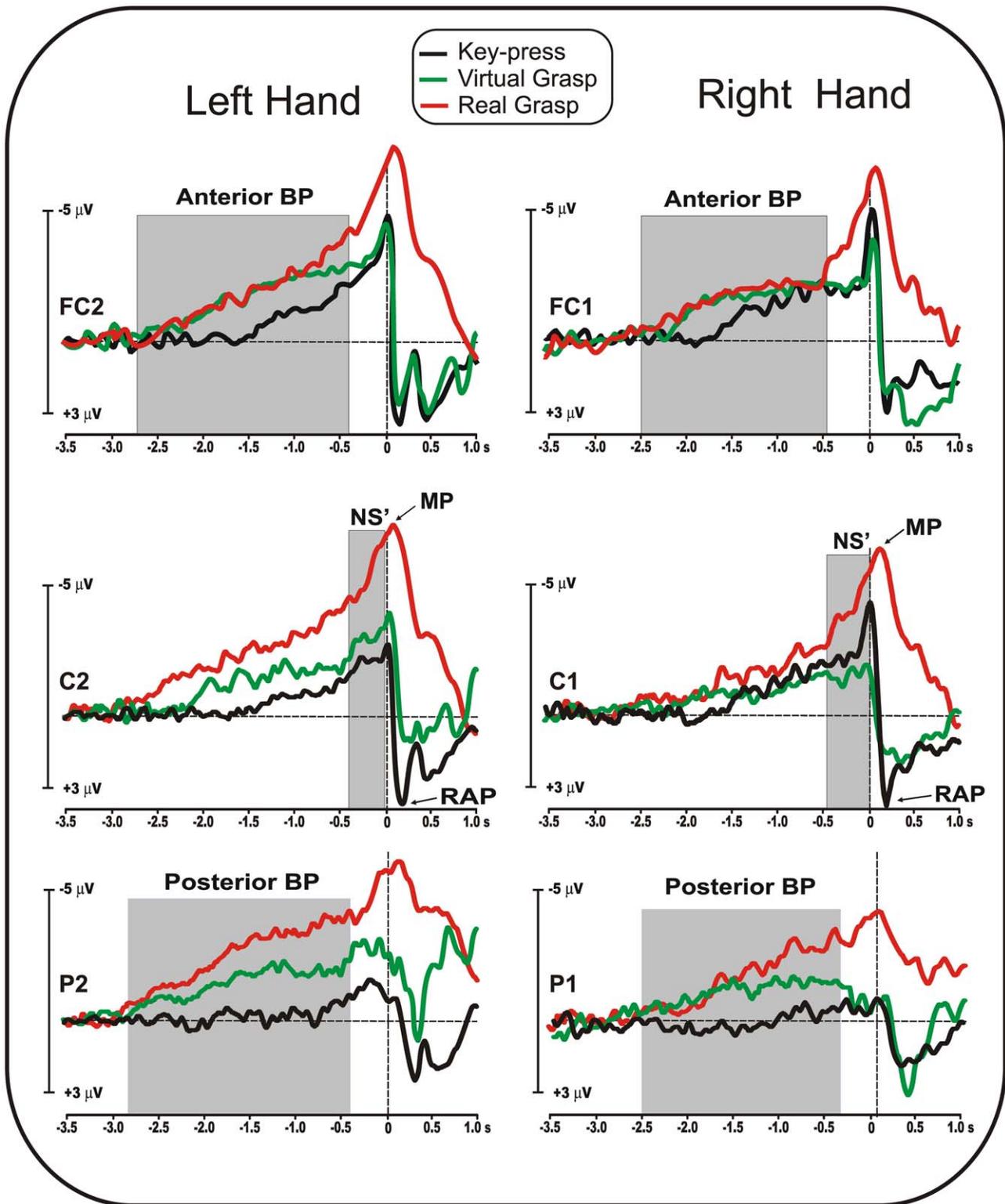
**Key-press condition.** The BP topography focused on the contralateral frontal areas, starting from  $-1.5$  s; this activity was followed by the broader and larger distribution of the NS' component that focused on contralateral fronto-central scalp from  $-0.7$  s. The MP was more lateralized, focusing more posteriorly than previous components on contralateral central sites. Notably, in this condition, we did not see activity in the parietal lobes during the preparation phase.

**Virtual grasp condition.** The BP showed a parietal distribution (slightly contralateral) starting approximately 2.5 s before the movement. From  $-1500$  s, the activity became wider and more anterior: the NS' and the MP scalp topographies were similar to the *key-press* condition described above.

**Real grasp condition.** The BP scalp topography showed early activity on posterior bilateral parietal areas, more intense activity on the contralateral site and more widespread and earlier activity for the left hand movements. This negativity shifted anteriorly on the central sites, slightly contralateral to the hand used. The distribution of the NS' was prominent on the contralateral fronto-central area of about 0.7 s before the MP, which focused more posteriorly on a contralateral central site.

The TANOVA was carried out between *virtual grasp* and *key-press* and between *virtual* and *real grasp* (figure 5) in order to evaluate the differences and similarities of the brain networks underlying those conditions. The comparison between *virtual grasp* and *key-press* revealed that the topographies were statistically different in the interval between  $-2500$  and  $-500$  ms ( $p < 0.05$ ) for both left and right movements. The *virtual* and the *real grasp* conditions did not differ at a topographical level during the motor preparation period.

Figure 6 shows the source model of the MRCPs for the three studied conditions. The scalp topography (figures 3 and 4) shows a sequence of at least three distinctive patterns in the parietal, mid-frontal and central scalp that likely correspond to the cortical areas involved in the grasping action [20;21;22]. Thus, according to the aforementioned literature [6;20;21;22;23], we seeded the source model location to the areas corresponding to the anterior intraparietal area (AIP, Talairach coordinates  $-40, -50, 45$ ), the SMA (Talairach coordinates  $-2, -10, 60$ ), the PMA and M (Talairach coordinates  $-40, -7, 50$ ) and the SMA (Talairach coordinates  $-2, -10, 60$ ). Because of their vicinity and the low resolution of MRCPs source localization, PMA and M1 were considered as a single source (Talairach coordinates  $-40, 7, 50$ ). After fixing these locations (figure 6A), we were able to calculate the



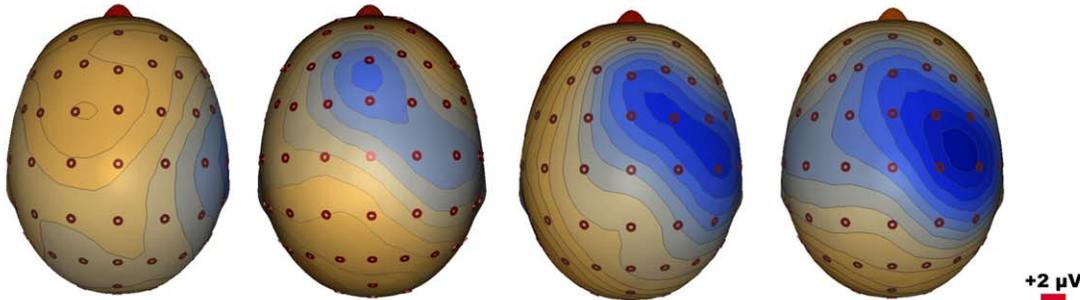
**Figure 2. MRCPs activity from relevant electrodes for both the left and right hands in the *key-press* (black line), *virtual grasp* (green line) and *real grasp* (red line) conditions. Major MRCPs components are labeled.**  
doi:10.1371/journal.pone.0047783.g002

time course of the activity of these areas in the three conditions. To increase the signal to noise ratio (typically low in this kind of potential), waveforms were collapsed across the left and right

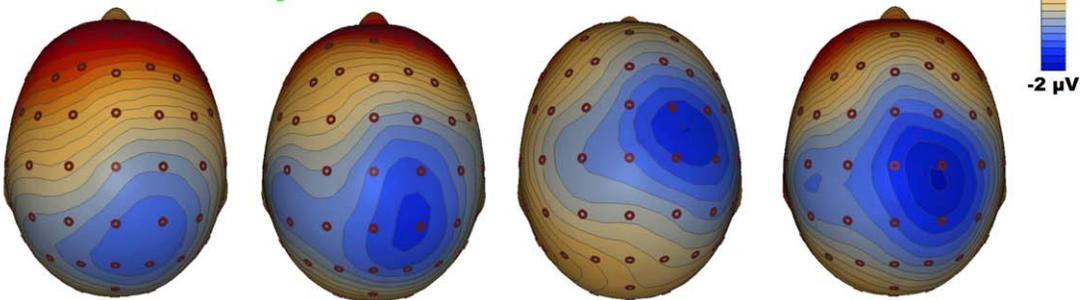
movements. The AIP source was fit into the interval between  $-2.5$  and  $-1.5$  s to account for the posterior BP. The SMA source was fit into the interval between  $-1.5$  and  $-1.0$  s to

## Left Hand

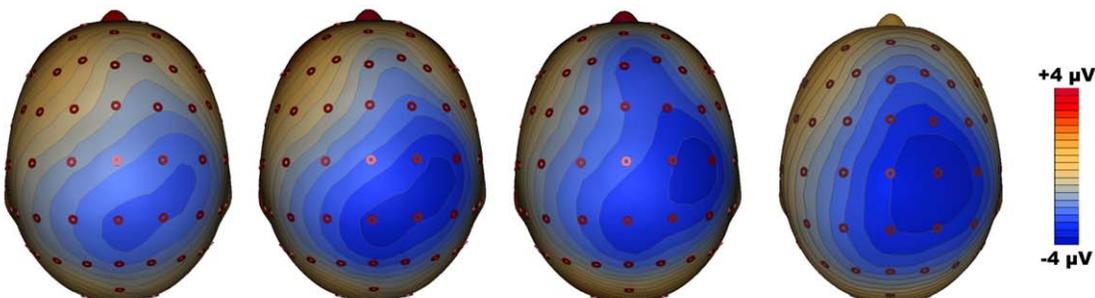
### Key-press



### Virtual Grasp



### Real Grasp

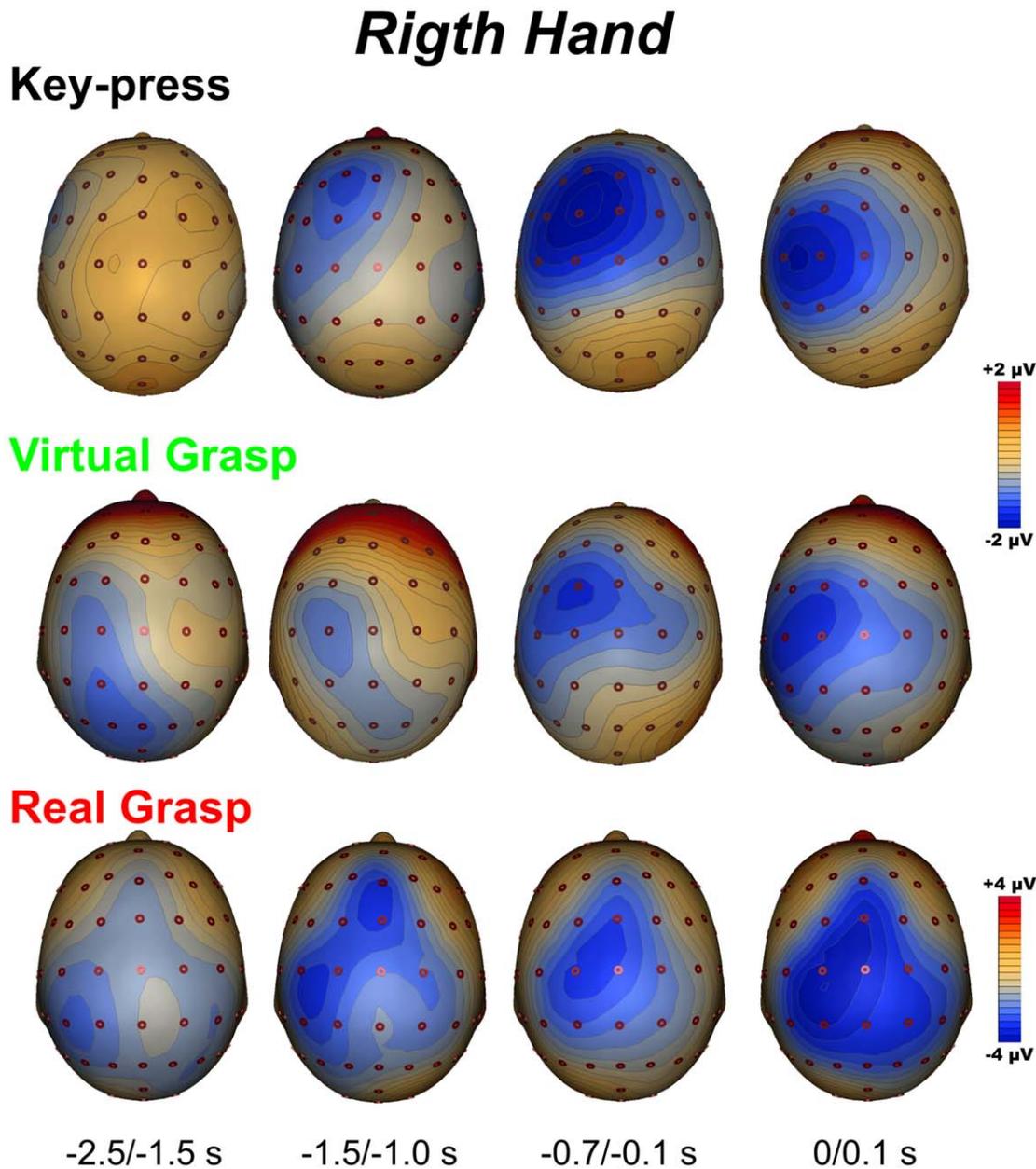


-2.5/-1.5 s      -1.5/-1.0 s      -0.7/-0.1 s      0/0.1 s

**Figure 3. Top view of topographic 3-D voltage maps for left movement in the *key-press*, *virtual* and *real grasp* conditions.** The four time windows shown correspond to the found MRCP components.  
doi:10.1371/journal.pone.0047783.g003

account for the anterior BP. The PMA/M1 source was fit into the interval between  $-0.7$  and  $0$  s to account for the NS' and MP. This sequence of intervals is the same of that used in several previous source localization studies of MRCPs (e.g. [6,23]). Figure 6B shows the time course of the aforementioned sources showing separately (with different colors) the source waveforms of the three conditions for each seeded area. For the *key-press* condition, the AIP source was not active before the movement. The SMA source started at approximately  $-1.5$  s before the movement, peaked at approximately  $-0.7$  s, and became inactive at approximately  $-0.2$  s. The PMA/M1 source started at  $-0.7$  s, first peaked at  $-0.2$  s (NS' peak) and then peaked concomitantly with the movement onset (MP). For the *virtual grasp* condition, the activity in the AIP source started at

approximately  $-2.8$  s, peaked at  $-0.8$  s and became inactive at  $-0.2$ . The SMA source started at approximately  $-1.9$  s, peaked at approximately  $-0.9$  s, and became inactive at the movement onset. The PMA/M1 source time course for the *virtual grasp* condition was very similar to the *key-press* condition, although the former condition produced larger peak amplitudes. For the *real grasp* condition, the activity in the AIP source started at approximately  $-3.0$  s, peaked at  $-0.9$  s and became inactive at  $-0.2$  s. The SMA source started at approximately  $-2.4$  s, peaked at approximately  $-1.0$  s, and became inactive at the movement onset. The PMA/M1 source time course was very similar to the two previous conditions but had larger peak amplitude.



**Figure 4. Topographic 3-D maps for right movement in the three conditions and in the four time windows.**  
doi:10.1371/journal.pone.0047783.g004

## Discussion

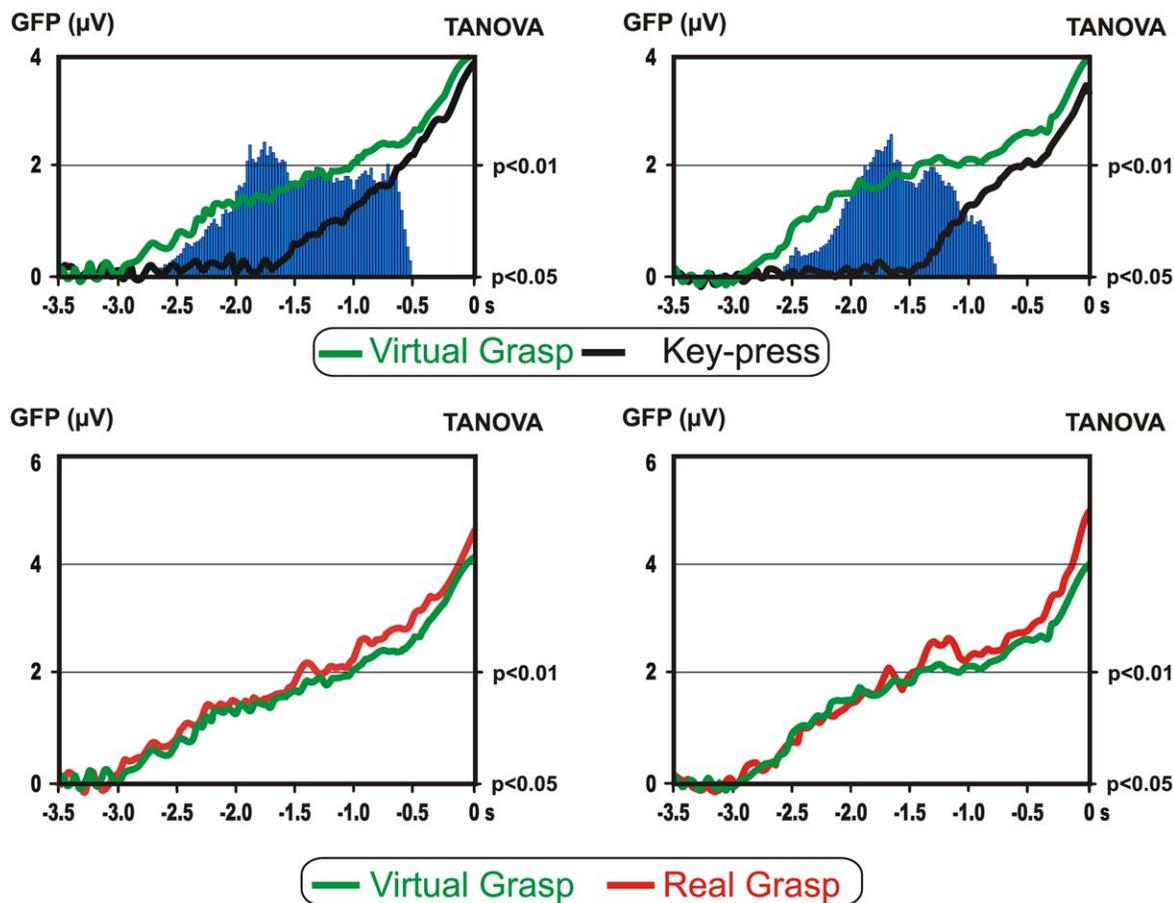
The present findings showed that motor preparation of a virtual grasp, mediated by pressing a key, was similar to that of a real grasp and was different from the preparation of a simple key-press. Although the movement in the two key-press tasks (*key-press* and *virtual grasp*) was the same, two major differences in their motor preparation were observed. The first difference concerns the BP onset latency: in the *key-press*, the BP onset was approximately 1.7 s before the movement, consistent with previous findings on simple movement preparation [24,25]; in contrast, for the *virtual grasp*, the BP onset was more than 1 s earlier and matched the onset recorded for the *real grasp* task. The second difference concerns the cortical areas involved in motor preparation. To prepare the *key-press*, the anterior motor and premotor areas contralateral to the

hand used accounted for all the recorded activity, as already observed in several previous studies (see 6 for review); in contrast, to prepare the *virtual grasp* task, the superior parietal areas also contributed at a very early stage, as in the case of the preparation for the *real grasp* task (called “posterior BP”; [4]). This latter result is a novel finding of the study. Thus, the present data suggest that the *virtual grasp* task and the *real grasp* task share the same preparatory cortical activities, in terms of both anatomy and timing.

Source analysis suggested that the posterior BP, for both *virtual* and *real grasp* tasks, was well accounted for by the source seeded in the anterior intra-parietal sulcus, corresponding to the typical anatomical position of the AIP area [20]. The AIP area is primarily involved in grasping action in which a transport phase of the hand prior to the grasp can be present or not [20,26,27]. This

## a) Left Hand

## b) Right Hand



**Figure 5. Global field power time course and TANOVA results (vertical bars) for *virtual grasp* vs. *key-press* conditions and for *virtual grasp* vs. *real grasp* conditions for a) left and b) right movement.** The differences (vertical bars) have been plotted only if significant for at least 150 ms.

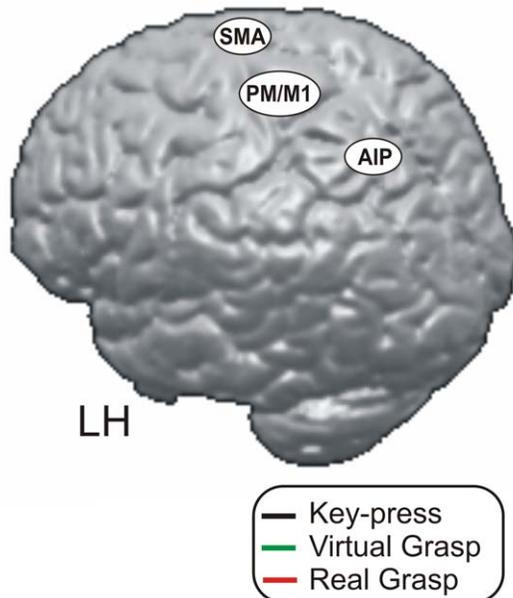
doi:10.1371/journal.pone.0047783.g005

area would encode the goal of grasping, rather than specify details such as the trajectory of hand movement [12,28,29,30]. Moreover, several fMRI studies investigating action execution and action observation have found a bilateral involvement of this area (as we found in the present study) in both modalities, reinforcing the concept that AIP function is not strictly related to the kinematics of the movement but to a broader representation of action [31]. This function might explain the very similar parietal activity recorded in the present study during preparation of the *virtual* and *real grasp* actions: the goal of the actions was indeed quite similar. Independent from the different kinematic complexities of the action performed in the two cases (which were very different), the anterior intraparietal area was the earliest activated region, and thus, it appears to be more related to the planning phase of motor preparation. According to the literature [5,32], the motor planning represents the phase related to the general idea of the action the individual is going to perform. In that phase, a general representation of the movement and its goal are created. During the subsequent phase (motor programming), the goal is transformed into a detailed kinematic program, and finally, the execution phase follows. The present findings are in line with the literature that shows a clear differentiation between the two sub-phases: when an

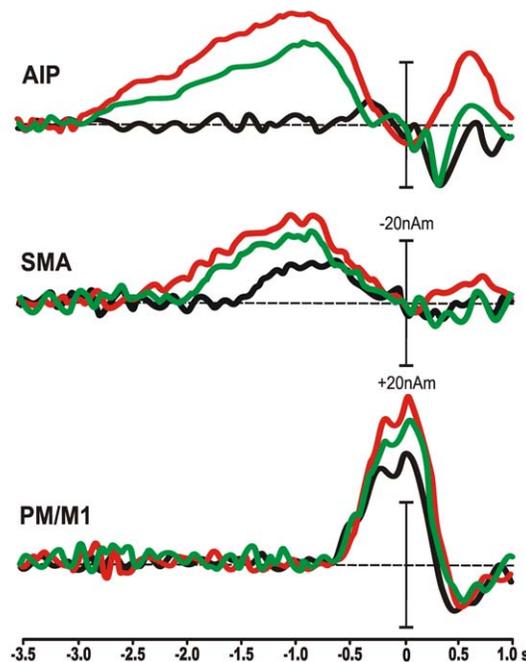
action involves an interaction with an object, the motor preparation includes a planning phase that takes place in the parietal areas, which are responsible for the tool affordance representation and the sensory-motor transformations required for executing movements directed at the external world. What is more appealing here is the finding that such parietal planning was also present in the *virtual grasp*, which just simulated the interaction with the object.

One could argue the possibility that the presence of the cup could have elicited an automatic response or an automatic motor behavior, as previous studies by Tucker and coll. [33] suggested. The lack of parietal activity in the preparation phase of the *key press* condition, however, does not support this hypothesis. Indeed, the cup was visible in the latter condition as well, conveying the same affordances as in the case of the *virtual grasp* task; however, in the *key-press* task, it represented only the cue to press the left or right key. The lack of consequence of the key-pressing confirmed the poorness of meaning of the *key-press* action: it was only the last step of the trial, and it did not produce any additional consequence; furthermore, the interaction with the object (the key) was minimal, reducing the task to finger flexion.

## a) Seeded Source Locations



## b) Source Time-Course



**Figure 6. Source model of the found MRCPs components.** a) Source locations seeded in the AIP, SMA, PMA/M1 and projected on a realistic model of the brain. b) Time course of each seeded cortical sources modeled separately for the three conditions and coded with different colors. doi:10.1371/journal.pone.0047783.g006

We proposed that the similar cortical preparation observed for *real grasp* and *virtual grasp* reflected the similarity of the goal/meaning of the action; however, the present finding is open to alternative interpretations. It is possible that this similarity reflects an anticipation of the visual consequences of the task; such anticipation might correspond to a mental representation or to an imagery process of the action subjects were going to perform or observe on the screen. Following this view, the present finding indicates that these representations would implicate all the motor preparation steps including the interaction with the object. While the imagery of an action may activate the same structures active in action execution [34], we would like to stress the novel aspect of the present finding represented by the fact that this activity starts well before the action initiation.

Future research should investigate the importance in the *virtual grasp* condition of the use of a video depicting a scene from an egocentric point of view. It would be interesting to understand whether the presentation of the hands from an allocentric point of view or the observation of another subject grasping, or making the cup move without interaction from the hands, produces comparable or different involvement of the parietal areas. Differences/similarities would allow us to evaluate whether the present results in the *virtual grasp* are due to a self-attribution of agency.

If our hypothesis that the parietal involvement during the preparation phase of *virtual grasp* represents the goal of the subject's action were supported by other studies, an interesting application of them would be in the Brain Computer Interface (BCI) field. BCI is a technique that uses electroencephalography to measure and detect the brain activity and turns it into the control commands of a computer device or artificial prostheses [35,36,37]. So far, BCIs have been used for neuro-rehabilitation of patients presenting severe motor and muscular disorders and who require basic

communication capabilities to interact with the outside world [38]. The primary purpose of BCI is to detect the user's intent [36]. If the action's goal plays an important role in motor preparation, it could be used to develop BCIs that are able to recognize this motor preparation pattern and anticipate the user's commands.

Finally, it is worth underlying that several differences between *real* and *virtual grasp* conditions were present for the anterior MRCPs components related to the last stage of preparation (NS') and the control of execution phase (MP), where the *real grasp* task produced the largest activity. The modulation of these components could be related to the amount of muscle districts (and their cortical representations) involved in the *real grasp* movement [8,39] and affecting the motor programming phase. Indeed, no differences were present between the two key-presses, confirming that both NS' and MP are mostly related to the kinematical and motor aspects of the action preparation. Moreover, Davare and coll. [40] showed, during grasping preparation, that activities in the ventral pre-motor cortex and the M1 were modulated by the interaction with the object to be grasped; hence, this can explain why the late components of the MRCPs, which are generated in those cortical areas, were found here enhanced in the *real grasp* condition, in which a real object interaction was actually performed.

Second, the effect of the "hand" factor deserves a comment. This effect was found for the BP amplitude of real grasp and for BP latency in the three tasks (however, less accentuate in the *key-press*). Compared to the right hand, the non-dominant left hand actions had both longer and larger amplitude, as shown in previous studies [4,23]. Such a difference suggests that for right-handers, left-hand actions require more demanding preparation (higher mental costs in action planning) than right-handed actions. This effect might be due to asymmetric motor representation in

the two hemispheres. Several studies have shown that the cortex M1 connectivity is asymmetric, being more extended in the left hemisphere, and that the movement of the right (dominant) hand only activates contralateral motor areas, whereas for the non-dominant hand, the activation is bilateral [41,42]. Thus, the programming of left-handed movement activates both left and right preparation areas, and the resulting activity would be more intense and widespread.

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In conclusion, the final effect of the action, not the kinematics of the movement, strongly influenced the early stages of the preparation phase.

## Author Contributions

Conceived and designed the experiments: CB MAG FDR DS. Performed the experiments: CB. Analyzed the data: CB FDR. Contributed reagents/materials/analysis tools: CB FDR. Wrote the paper: CD SP DS FDR.



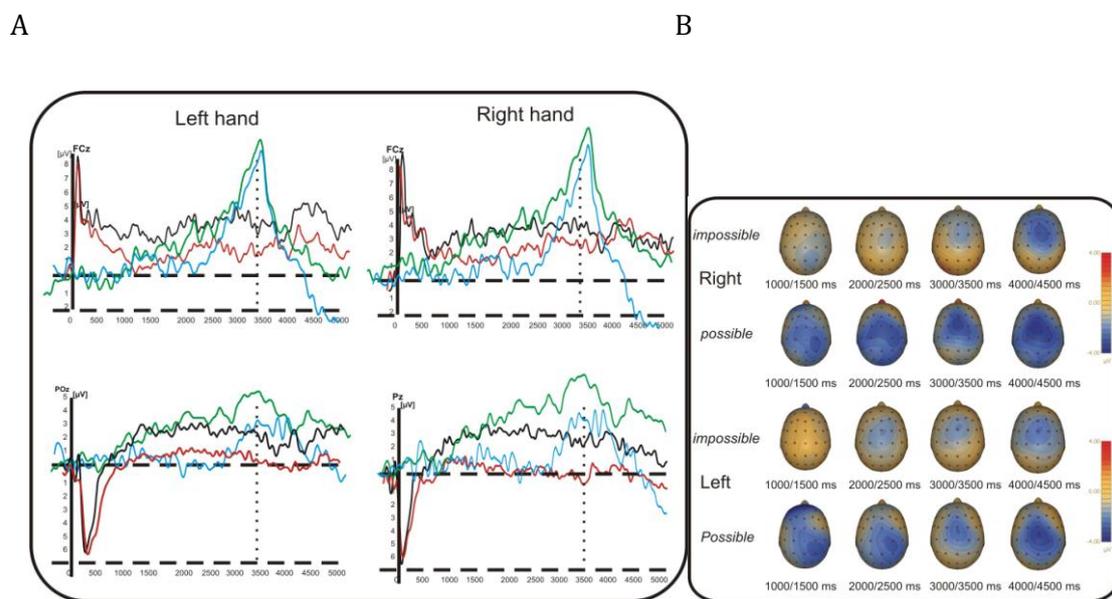
## Brief Communication

Recently, studies on motor preparation for object-oriented actions have highlighted the importance of the final goal of the movement for different cortical areas activation and the latency onset of the activity. In particular, it has been shown that it's not just the kinematical complexity of the movement that is coded but rather its meaning that modulates the pre-movement activity<sup>1-2-3</sup>. These studies have shown the complexity of the motor preparation activity that starts well before the initiation of the movement itself and the role of the parietal areas in encoding the aim and meaning of the action rather than the mechanical programming. Object-oriented actions have been subject to an intense scientific activity in the last decades thanks to the theories on the motor resonance and the mirror neuron system (MNS). Meaningful actions are able to activate in the spectator activity and networks very similar to those activated in the executor and such an ability has been thought to allow people to understand each other's intentions and give a sense to what the other is doing<sup>4-5-6</sup>. Some authors have even opened up to an interesting question about the possibility that this motor resonance would be involved well before the observation of the action execution, including the motor preparation process. They described an activity in the motor areas starting around 1.5s before the action onset, when subjects were just observing stable hands of which they could predict the starting moment. This interesting finding has suggested the possibility of a MNS involvement preceding the execution phase of the action, well accounting for its role in understanding and predicting other's intentions<sup>7</sup>. An appealing question still to be addressed to is in which degree the observation of a "motor preparation" actually reflects the

motor preparation activity for that kind of action. We already proved that during a real motor preparation of object-oriented actions the poorness of meaning and the impossibility of performing the action properly caused a lack of parietal activity and a constant pre-frontal positivity<sup>2</sup>. According to this, are the observation and the execution of different actions modulated in the same way? Here, we addressed to this new issue using the same actions we already tested in the execution experiment<sup>2</sup>, but this time asking subjects to passively observe them and we show that the observation of an upcoming action presents a motor preparation-like activity, but such an activity is modulated by the kind of action we are going to see. Moreover, this modulation reflects the one observed during the motor preparation for the execution of the same actions.

64-channels electroencephalogram (EEG) was recorded on 14 right handed subjects while they paid attention to videos showing two hands from an egocentric point of view performing object-oriented actions. Videos were divided in two separate blocks corresponding to two different conditions: a *real grasp* and an *impossible grasp* of a cup. Each block included 240 videos, 120 per hand, presented in 10 runs. In the *impossible grasp*, the actor's hands were tied up as fist in order to prevent the final grasp and the subject had the same handicap in order to enhance self-identification with videos (see **Supplementary Method**). Videos started with the image of the two hands laid on a table; after 3.5 sec one of the two hands moved toward the cup grasping (or trying to grasp) it. Subjects could predict which one of the hands was about to move based on the cup handle orientation. The video lasted 1.5 sec and the total trial duration was 5 sec.

Results showed different activities for the two conditions. Epochs considered for analysis lasted 3.5s corresponding to the motor preparation part until the onset of the hands movement. Differences were detected starting from 1s after the presentation of the image, where a stronger negativity was recorded for the *real grasp* condition and was particularly widespread all over the centroparietal electrodes with a bilateral distribution ( $F_{1,13}= 9.13, p= 0.009$ ). Starting from 2s after the image presentation the negativity moved more anteriorly, more intense for the *real grasp* rather than the *impossible grasp* ( $F_{1,13}= 6.14, p=0.02$ ) and more spread out for the right than for the left hand movement observation ( $F_{1,13}= 4.77, p= 0.04$ ). Finally, also for the observation of the *impossible grasp* movement, subjects presented a contralateral more positive pre-frontal activity, but significant only for the right hand movement ( $F_{1,13}= 9.38, p= 0.009$ ).



**Figure1:** A. Waveforms for the observation of the real (black line) and impossible (red line) grasping conditions. The dot line represents the movement onset. the activity is compared with the one previously observed for the execution of the real (green line) and impossible (blue line) grasping movements (Bozzacchi et al., 2012). B. Topographic representation of the cortical activity for observation of real and impossible grasping at significant time intervals.

We confirmed that the observation of an upcoming action presents a motor preparation-like activity, but such an activity is modulated by the kind of action we are going to see. Moreover, this modulation reflects the one observed during the motor preparation for the execution of the same actions. Compared to the execution paradigm, the observation showed a centroparietal negativity, corresponding to the posterior BP component, but bilaterally distributed as shown for the execution. Such an anterior switch might be due to the two different tasks and, therefore, aims: elaboration of the final goal to act or to predict a movement. We also recorded an anterior positivity corresponding to the prefrontal positivity for the execution paradigm, but only for the right hand movement. This activity was considered as related to the awareness of not being able to accomplish the action, thus, like an inhibition of the action to perform. The same activity here reflects how subjects were really understanding the actions observed; being all of them right-handed, it's possible that such an identification was stronger for observation of movements performed with the right rather than the left hand. These findings confirm the pre-movement activity as neural correlate of motor prediction but showing for the first time how this activity is able to differentiate between actions creating a real correspondence between what we see and what we do.

## Supplementary Method

### Partecipants

Data were recorded from 14 subjects, all volunteers and university students (mean age 24.7 years; SD 6.2; 8 females). None presented neurological or psychiatric disease. All subjects were right-handed, and we evaluated their manual preference by of the Edinburgh Handedness Inventory (Oldfield, 1971) ( $LI > 60$ ; mean score 85). After a full explanation of the procedures, all subjects provided written informed consent. The study was approved by the local ethical committee.

### Stimuli

Video clips were filmed by the experimenters. They represented grasping actions in two conditions: a *real grasp* and an *impossible grasp*. In order to better match the stimuli for left and right hand movements, video clips were also flipped left to right and right to left using a video editing software (Ulead VideoStudio 9.0), and their presentation was counterbalanced so that 50% of the videos of one hand's movement were mirrored movements of the other hand. Video clips showed the movement from an egocentric point of view and only the two hands and the tea cup were visible on the screen. The model's limbs wore yellow rubber gloves and a white coat and in the *impossible grasp* condition the hands were tied as fist by a band. We selected the first frame of the video clip to create a static image of the two hands laid on the table in a resting position with the tea cup located in the middle. Each condition had its own static image that lasted 3400 ms and was followed by the video presenting one of the two hands moving towards the cup, grasping it and lifting it up (in the *real grasping* condition), or just reaching the cup (in the *impossible grasping* condition). All video lasted 1500 ms. The total duration of each trial was 5000 ms and the interval between trials was 1s. Stimuli timing and presentation were controlled by the Presentation software (Neurobehavioral System, Davis, CA). The size of the hands and the cup in the static images and the video were create in order to simulate the real size of the object when presented at a distance of 35 cm from the subject.

## Procedure

Subjects were comfortably seated on a chair in front of a table with a monitor on top and were not required to perform any tasks except for observing the videos presented. The monitor was located ca 35 cm in front of them. They underwent a passive observation task in which they had to pay attention to videos showing action performed in two different conditions: a *real* and an *impossible grasp* of a tea-cup. The tea cup was located in the middle. Participants were instructed to fix their eyes on the centre of the tea cup. Since the model's hands in the videos wore yellow gloves and a white coat, even subjects were requested to wear the same gloves and coat in order to enhance an identification process. For the same reason, when subjects were presented with the *impossible grasp* videos, they also wore the band over the gloves that blocked their hands as fist, in order to facilitate the identification in that condition either. Subjects didn't see their own hands that were laid on their legs under the table. Actions in the video were performed with both left and right hand and subjects could predict the following movement based on the cup handle orientation. The two conditions were performed in separate blocks because subjects had to wear the band during the *impossible grasp* and it would had been impossible to set up them trial by trial. The orientation of the cup was instead presented in a randomized order: cup handle was rightward or leftward oriented and according to it the corresponding hand moved. Each block included 10 runs and each run was composed by 24 trials (12 per hand). Every 5 runs the condition was switched. Half of the sample started the experiment with the *real grasp* condition and the others with the *impossible grasp* condition.

## Electrophysiological Recording and Data Analysis

Electrical brain activity was recorded during the experiment using a BrainVision™ 64-active channel system (Brain Products GmbH, Munich, Germany) connected to an active sensor system (ActiCap™ by Brain Products GmbH, Munich, Germany), adopting the standard 10-10 International system montage. Eye movements were recorded. Left mastoid (M1) was used as initial reference electrode for all scalp channels. Finally two EOG channels located on the outer canthy were used for blinks and eye movement detection. Signal was

digitized at 250 Hz, with an amplifier band-pass from 0.001 to 60 Hz with 50 Hz notch filter. Data were analyzed off-line using BrainVision™ Analyzer 1.5 software (Brain Products GmbH, Munich, Germany). To further reduce high frequency noise, the time-averaged MRCPs were subsequently low-pass filtered at 8 Hz. Trials presented artifacts were discarded from subsequent analysis and eye movement artifacts were reduced using a specific algorithm. The trigger used for the analysis was the onset of the static image and data were segmented into non overlapping epochs of 5000 ms duration with 100 ms baseline. 3500 ms after the onset of the image, the video started lasting 1500 ms. The first 3000 ms were considered as time related to motor preparation and the following part of the video as the execution part. Semi-automatic computerized artefacts rejection was performed prior to signal averaging in order to discard epochs with ocular or muscular contraction artefacts from further analysis. No more than 20% of the trials were rejected. Blinks were found to be the most frequent cause for rejection. Baseline was calculated for the 100 ms before the stimulus onset. The period used for statistical analysis started 500 ms after the presentation of the stimulus in order to avoid all activity related to the visual response to the stimuli. Significant differences in the activity amplitudes between *real grasp* and *impossible grasp* were assessed sample by sample using a running paired t-test with the alpha level set at  $p < 0.05$ . Bonferroni correction was employed. To visualize the voltage topography of the MRCPs components, spline-interpolated 3D maps were constructed using the Brain Electrical Source Analysis system (BESA 2000 version 5.18, MEGIS Software GmbH, Gräfelfing, Germany). To visualize the scalp topography, spline interpolated 3-D maps were generated using BESA 2000 software (MEGIS Software GmbH, Gräfelfing, Germany).

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## General discussion and conclusions

The main results obtained in these studies can be summarized as follows:

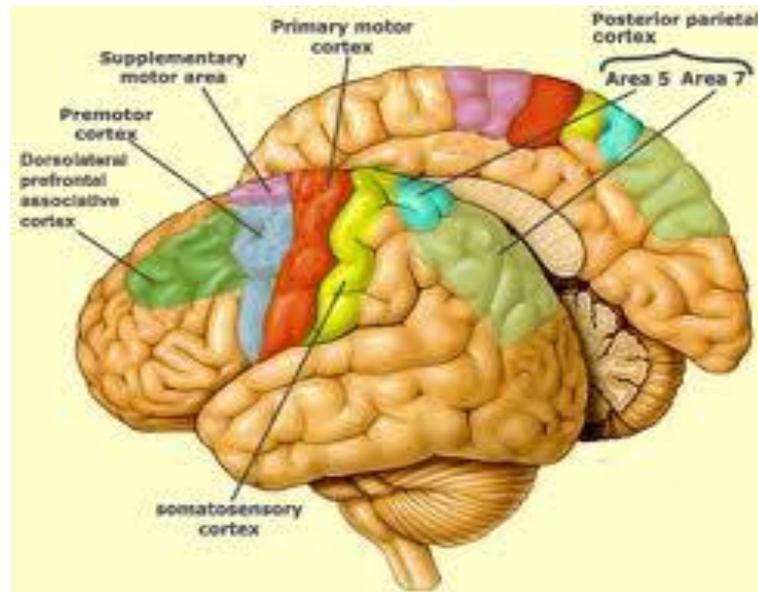
1. It has been confirmed that motor preparation for praxic actions is a well more complex process compared to simple or sequential movements, involving parietal areas and starting even 3 s before action execution.
2. The complexity of this activity is not just due to the amount of muscular districts involved but even to more cognitive aspects related to the possibility of being able to perform the action and, therefore, to the meaning of that action.
3. In particular, the posterior BP component seems to be the one more affected by the final goal of the action regardless of its complexity, whereas the more anterior activities (BP, NS', MP), seem to be more affected by the mechanical complexity of the action and the amount of muscular districts involved.
4. Even the observation of object-oriented actions shows an activity very similar to that one observed during the motor preparation phase for the execution of the same actions; more important, this pre-movement-like activity in the observation task seems to be modulated in the same way as the real execution of those actions.

All these statements well generalize results produced by all the experiments, although several more specific comments rise up from singular data. Even though all connected to each other, according to the results found I want to comment the studies gathering them separately and considering the first two studies first and subsequently the third one. Because of the paradigm that didn't involve a motor part, indeed, this study cannot be directly matched with the other two, but only with the first one in terms of kind of actions used. Therefore, I will consider it in a second moment.

The first experiment allowed the description, for the first time, of a motor preparation activity for object-oriented actions actually performed in a more ecological setting. In this study, indeed, subjects were really interacting (not miming) with the object, performing a meaningful action. Data showed that motor preparation activity described for grasping and reaching conditions was quite different, although literature has largely reported similar cortical

responses for the two movements, in particular in terms of parietal structures. Our data have presented, indeed, a complex activity starting very early before movement onset in parietal areas (Superior Parietal lobe SPL), but only in association with grasping action. We called this activity *posterior BP* in order to distinguish it from the anterior BP component originating in the supplementary motor area (SMA). Although a similar activity was already reported by Wheaton and colleagues in 2005, unlike their results here we described a broader activity, not lateralized on the left hemisphere as Wheaton showed, but bilateral and more dorsal. Such a difference can be due actually to the different paradigms used between our two studies. The left hemisphere has been described as associated to praxic movements, but particularly pantomime of gestures, as studies on patients with left hemisphere lesions and studies on mirror neuron system have reported (De Renzi and Lucchelli, 1988; Gallese et al., 1994; Rizzolatti and Craighero, 2004). On the contrary, the activity described in our study was more bilateral and also more anterior, probably ascribed to the SPL and the anterior part of the intraparietal sulcus (aIPS), a structure already shown as responsible for grasping actions (Sakata et al., 1995; 1997; Binkofsky et al., 1998). Such a difference in distribution might be related to all information and sensory transformations needed for actually accomplish a grasping action. Literature has indeed shown the role of SPL and aIPS in providing frontal areas with grasp related information in order to prepare and guide hand shaping and visually guided transformations (see Figure 5) (Rizzolatti and Matelli, 2003; Culham et al., 2003; Davare et al., 2010).

The result that sounded more controversial, though, was the one related to the reaching condition. Although in the literature there are plenty of results in both humans and monkeys about a parietal activity for reaching actions, we didn't detect any significant parietal contribution in both *reaching* and *impossible grasping* conditions



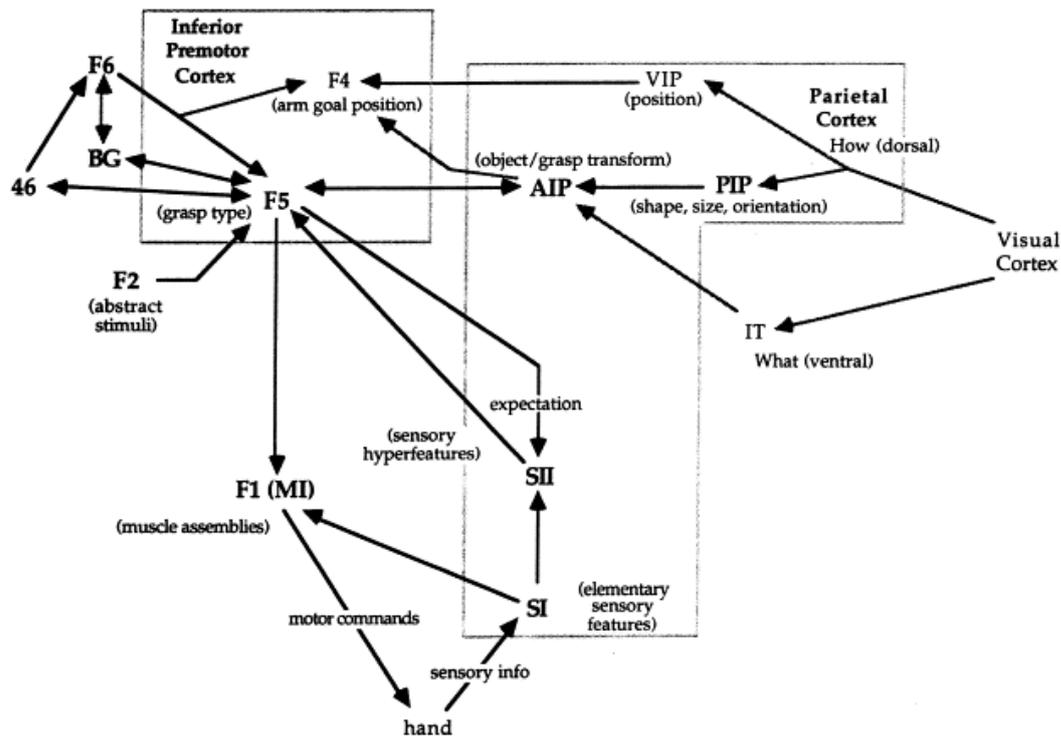
**Figure 5:** The picture shows all the areas involved in object-oriented action planning (reaching and grasping). Our results show the main contribution of the SPL (area 5 in PPC) in forwarding information to the more anterior motor areas, particularly the premotor cortex and SMA responsible for the earlier MRCP component BP and 'NS and finally MP. Area 5 is particularly suitable for accomplishing the sensori motor transformations needed for planning the action thanks to its proximity to the primary sensorimotor area.

We counted several reasons for that but, even according to the subsequent results found in the second experiment, we can now try to put an hypothesis forward: it is possible that the way the brain prepares to move is triggered and modulated by the type of interaction we are going to have with that specific object, which is supposed to be approached in a specific way according to its features and affordances. This hypothesis actually combines the sensorimotor transformation studies with studies on movement intentions, the high level cognitive plans for movement (Hemilton and Grafton, 2008; Andersen and Buneo, 2002; Buneo and Andersen, 2006; Beurze et al., 2007) and affordances (Fagg and Arbib, 1998).

To date, two principal models have been suggested for explaining dynamics and elaboration of object-oriented actions highlighting the role played by the posterior parietal cortex (PPC) and motor areas. The first model lays on the "affordances theory". Affordances represent those parameters for motor interaction signaled by sensory cues without invocation of high-level object recognition processes (Gibson, 1966). That means that objects have some

particular features that trigger our response and the way to interact with them (Tucker and Ellis, 1998). Fagg and Arbib have developed a model for grasping actions that accounts for the affordances perception and representation in movement programming and execution. According to this model, called FARS, the AIP has the main role in extracting affordances from the visual stream, whereas area F5 is responsible for selecting one of the corresponding grasping and manage the execution (Fagg and Arbib, 1998). Specifically, AIP is supposed to be the first stage in the grasping programming phase as responsible for integrating object-related information coming from the dorsal and ventral streams, related to decoding the “where” and “what” information about the object, and relevant for grasping it properly. F5, then, applies constraint, as visual information, task information etc., to select a grasp and informs AIP of the status of execution. F5 is responsible for the high level execution and monitoring of the planned action. This model well account for the different affordances an object can have and, thus, the different grasping we can apply on it in terms of grip aperture, arm extension and strength to put it on (see Figure 6) (Fagg and Arbib, 1998).

This hypothesis seems to be only partly true in our studies: in all conditions indeed, we always kept the same setting, that is, the same object was always shown producing the same features and input (the cup in the real action execution of the first experiment and in the key-press conditions of the second experiment). Despite that, we didn't record the same activity in these conditions, but differences related to the kind of interaction subjects had to have with that object. If actually the object features had elicited a particular response related to them, we would have expected to find similar activity in all our conditions.



**Figure 6:** Graphic representation of the FARS model: visual information about object properties goes from visual cortex to areas in PPC to end up eventually to frontal areas, particularly F5, responsible for selecting the correct action and monitor its execution.

On the other hand, the second model suggested by Buneo and Andersen along with other researchers (Beurze et al., 2007), claims the importance of the PPC in movement planning as related to its role in sensorimotor transformation and formation of intentions (Andersen and Buneo, 2002; Buneo and Andersen, 2006). PPC doesn't seem to be just a motor or a sensory area, but a fundamental bridge between the two functions. It has the task of extracting the coordinates related to the object and those related to our body in different frames of references (eye or hand-centered) in order to create a map and representation of the environment around us and of the best way for interacting with it. Because of that, PPC seems to be involved in motor preparation since its very early stage of movement planning. Unlike what suggested by the FARS model, according to these authors PPC has the monitoring control over the action before and during its execution (Wolpert et al., 1998; Buneo and Andersen, 2006). Although this model well account for what we found in the key press experiment, on the other hand, also this model is not able to explain extensively our findings. The main role of PPC as an area related to specify the goal and intention of the action, can

explain results found in the “virtual grasp” condition of the second experiment: as we also suggested indeed, the parietal activity here found has a principal cognitive function of representing the final goal of the action, no matter the action actually to perform. Nevertheless, if it also specifies the type of movement, without necessarily containing information about muscle activations and other motor details, why in the impossible grasping condition, as well as in reaching condition, the activity in PPC is missing, although the intention was the same as for grasping for the former movement, and it was different but totally satisfied in the latter one (subject had the task to reach the cup). Finally, if all the types of real interaction with the object elicited a parietal activity because of the coordinates transformation and sensorimotor integration processes in this area, we would have found it even for reaching and impossible grasping movements but not for the key press one.

What our data may suggest, therefore, is that objects actually provide us some information related to their features that we use to interact with them, but those information generate a particular response involving specific areas of the posterior parietal cortex (PPC) only when our gesture is coherent with that object, according to the experience we have of it, its affordances and still our final intentions and goal. Hence, the reason why in both *reaching* and *impossible grasping* we didn't detect any parietal activity could be related to the fact that a cup represents a powerful stimulus we everyday interact with, having very clear features. The role of PPC, thanks to its connection with visual areas, seems to be the role of integrating these features with the correct movement and our final goal to create a coherent action making all these aspects well matched to each other. The *reaching* and *impossible grasping*, although kinematically object-oriented movements, created a mismatch between object features and the kind of interaction we are supposed to have with it: indeed, it doesn't really happen to us to approach a cup just touching it. In the *impossible grasping* condition such a mismatch was even more marked: the incongruence between features and actual movement was strengthened by the impossibility of achieving the real goal subjects had to pursue. Such awareness was probably responsible of the frontal positivity related to the will of grasping the cup but the physical constraint.

Also the second experiment well accounts for this hypothesis: again in this study, indeed, the object and its features were the same in both conditions, but only in that one in which the “interaction” was actually coherent with these object features, a parietal activity was detected. Even more appealing in this second study was the fact that our act on the object doesn't necessary need to be real, thus taking the motor component away from the parietal areas. This data, indeed, enforces the idea that parietal contribution to motor preparation is more related to match the right goal and movement to the environmental situation, in order to produce the correct and appropriate outcome. It doesn't matter whether the interaction is going to be real or virtual: our brain seems to see beyond the kinematical aspects considering the action as a whole.

Thus, the new model we suggest agrees with the previous about the importance of PPC, and in particular IPS, in planning the correct action to be executed. Thanks to the connections with striate cortices which forward information about what and where objects are around us (Mishkin and Ungerleider, 1982), the PPC extracts affordances information that uses for planning the action, but in order to do that, it matches these information with the goal of the action, that is already known. If goal and affordances well match, PPC and IPS are active and start planning the movement forwarding to motor areas information (in terms of coordinates, frames of reference and intention to move, as suggested by the sensorimotor model) about how to do it mechanically. This is demonstrated by the fact that the anterior areas (pre motor cortex, SMA and M1) start their response after the parietal one and are those areas whose activity is more modulated by action complexity in terms of joints, muscles and strength involved. Therefore, we can conclude that PPC, especially aIPS, doesn't have any motor component, since not affected by the kinematical parameters of movement, but its role is strictly related to the final goal of actions; in particular, it is related to the evaluation and matching of goal and object parameters, thus showing 'object-goal' properties. After having carried out this evaluation, it forwards the coordinates information about the object and us, in order to produce the best interaction and it does it during the second part of the motor preparation, that is, the motor programming, during which this area keep maintaining its activity. We agree, indeed, with Andersen and Buneo about the

monitoring role PPC has during both preparation and execution processes, showed by the fact that in our data parietal activity was always present, even in concomitance with activity in motor areas.

Data collected in the last experiment can enforce this theory about the non-motor role played by the PPC. In this study, indeed, no motor component were involved but subjects were just requested to observe videos presenting some grasping actions. We collected data from the same sample we previously tested with the execution task in the first experiment and we did so because we wanted subjects being familiar with the actions and, moreover, to better compare the two results. Although different in terms of task, indeed, the actions were the same and even in the observation experiment subjects were dressed up like the actor in the videos in order to better facilitate a self-identification process.

The performance of object-oriented action or other meaningful actions produces in the person that observes them an activity very similar to the one recorded in the person performing the action. The reason beyond this study was to investigate whether the motor resonance was actually present even before the observation of the execution of an action, as already extensively shown in the literature. That is: is there an activity similar to the motor preparation one even when we observe someone about to move and of whom we can predict the movement? A similar issue was already addressed by Kilner and colleagues in 2004 and it gave us a baseline to work on. Knowing that such an activity is actually present, that we don't only simulate the execution of an action we see but also its motor preparation, and because of the finding that motor preparations for object-oriented actions are pretty different to each other because of all the reasons explained so far, we put together all these information to see how much reliable this motor resonance is. According to the results in the execution experiment, showing different motor preparations for different actions, we expected to find similar differences also during the observation of the two hands before their movement. And it is exactly what we found. We recorded a strong negative activity elicited by the presentation of the fixed image of the two hands, but with some differences in the two conditions. First of all, the



activity related to the real grasp condition was stronger and earlier, but also it was more spread on the posterior parietal areas rather than on the anterior electrodes as recorded for the impossible grasp condition. Although some substantial differences between the execution and the observation results, particularly related to the distribution of this parietal activity, more anterior for the observation task, we can highlight the overall similarity between a real grasp really performed and one just observed. But more important, the similarity is between and impossible grasp actually performed and one observed. This data straightened the theory about the mental simulation and representation of what we see performed by other people, as suggested by the mirror neuron system theory and the motor resonance theory. But what they do more is to demonstrate that such a correspondence between what we see and do starts already before the action starts and it's not just a general activation related to an arousal effect of something we know it's going to happen, but is strictly related to what we are going to see. Again, the parietal areas seem to be fundamental in this discriminative task, although no movement component were present in this task.

The parietal areas, thus, seem to account for several aspects related to movement execution or action computation: some of its structures are related with grasping and reaching actions involving a transport phase of the limb (Culham et al., 2003), others with grip adjustment (Davare et al., 2010) and others with the action meaning (Rizzolatti et al., 1988). It seems that during motor preparation, at least in the very early period (the planning one), what counts more in the parietal areas is the selection of the correct action, but not only in terms of the task requested, but rather in terms of the appropriate output for that particular environmental condition.

Altogether these data put forward that the hypothesis suggesting that the PPC would be involved in sensory motor transformation, can actually present some limits, as well as the FARS model considering the PPC as the area delegated to catch affordances from the environment to send to motor areas. Such a finding opens up to the possibility of being applied to other fields, in particular those related to BCI and rehabilitation field. If control experiments will confirm these results, indeed, it would be possible to extend them for making subjects interact

with the environment, creating devices having ecological features and meanings and making patients interacting with them in the correct way to achieving their final goal that could be to communicate, move, or other fundamental functions.

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