**Scuola Internazionale Superiore di Studi Avanzati**
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# A multimodal investigation of matching mechanisms in automatic imitation

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# JURY

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# CONTENTS

# ABSTRACT

In recent years, research on imitation focused on investigating the underlying neural mechanisms; to this aim simple paradigms were developed to experimentally investigate the phenomenon. Following the natural tendency of humans to mimic gestures and postures of their conspecifics, paradigms of automatic imitation are nowadays widely used in the field. The main aim of my dissertation is to investigate how imitation occurs using an automatic imitation paradigm, in particular focusing on the matching processes that are required to map model and performer's actions.

The dissertation contains six chapters. In **chapter 1**, I will provide a brief background of the current theoretical accounts of imitation and of the concepts of automatic imitation and compatibility effects. I will particularly focus on the questions concerning automatic imitation that are still to be fully addressed, particularly those related to the distinction of imitative and spatial compatibility. I will also address the neuroimaging and neuropsychological literature on the neural correlates of imitation. In **chapter 2**, I will present a neuroimaging study I carried out to investigate the imitation components. Throughout all the studies of this thesis, we used a simple automatic imitation paradigm that is suitable to differentiate between the spatial compatibility and the imitative compatibility, due to the anatomical correspondence between model and performer. Results of the first study showed that the parietal opercula are active anytime the anatomical correspondence between model and performer is present. Hence, in **chapter 3** I will present a study in which double-pulse TMS was used to investigate the role of the parietal opercula in automatic imitation, and in particular in coding the imitative

compatibility. Results showed that when the activity in the parietal opercula is interfered by TMS, the imitative compatibility effect disappears.

In the second part of my thesis I have investigated the factors that can interact with and modulate imitative behaviors. **Chapter 4** contains an fMRI study in which the role of the model in imitation is investigated. Using a simplified version of the automatic imitation paradigm, I found that the fronto-parietal network, usually associated to imitation, is more active when participants perform actions that are compatible with those performed by a human model than by a non biological model. Moreover, in this study I have also investigated how different emotional contexts can influence the automatic tendency to imitate. The results showed that the activation of the fronto-parietal network is suppressed by emotional context, such as an angry face, that does not promote affiliative tendencies.

In **chapter 5** I will describe a neuropsychological study on brain damaged patients. Associations and dissociations between automatic imitation and action imitation were investigated, to analyze the differences between the two types of imitation. Moreover, the role of putative body representations in imitation and whether these body representations are needed for imitation has been investigated.

Lastly, in **chapter 6** I will wrap up the main results of my dissertation and I will argue that I was able to provide evidence that in automatic imitation an anatomical matching operates between the model and the performer, and that this is sustained by the parietal opercula. In addition I clarified the importance of the model, showing that the activity of fronto-parietal regions supporting imitative behaviors is modulated by model identity.

# Chapter 1

## INTRODUCTION

*1.1 What is imitation?*

Imitation is a complex behavior that can be used for different purposes, from development and learning to social communication. Although everybody intuitively knows what imitation is, there still is no total agreement among scholars on a definition of imitation. Even for the simplest imitative behavior to occur, a model to be imitated is required. Imitation can occur on purpose or automatically, without conscious awareness like, for instance, when we tend to take the same posture of the person near us. The correspondence between the model's and the performer's actions is another requirement for imitation to occur, with the output action that needs to be similar to the input action for imitation to be successful. Even though these seem straightforward issues, some of these mechanisms at the core of imitation and the neural underpinnings are still not well understood.

The *correspondence problem* is perhaps the most important of these open issues and deals with fundamental questions: How are the observed actions mapped onto the motor system of the observer? How does this matching process between model's and performer's movements occur? What are the cues used by the imitator to achieve the matching? And finally, where does this matching occur in the brain?

Whenever we move our body, we activate the body representations that constantly inform our brain, for example, about the location of our body parts in space.

The questions then are: Are the body representations necessary for imitation? Which information about our body is necessary in imitation and which is sufficient?

Moreover, as mentioned above, imitation always requires the presence of a model. But, which informational cues are extracted from the model in order to copy it is still debated. Can we imitate only a human model or can we speak about imitation even when we reproduce movements performed by abstract or robotic models? Is there something special about biological movement?

In the following paragraphs, I will review the state of the art of imitation research, with particular reference to the theoretical approaches for which strong experimental evidence is available. Overall these theoretical and empirical studies will constitute the starting point of my dissertation.

### *1.2 Automatic imitation and compatibility effects*

As imitation is a complex behavior, one of the main problems is to design paradigms suitable for investigating the phenomenon. The imitative behavior is better studied by segmenting the whole behavior into components that can be more easily manipulated. One problem in doing it, for instance when using techniques like functional magnetic resonance imaging (fMRI), transcranial magnetic stimulation (TMS), or electroencephalography (EEG), is that complex movements generate artifacts.

It is well known that the human being has a natural tendency to mimic gestures and postures of the interacting partner even without being aware of it, a phenomenon known as chameleon effect (Chartrand and Bargh, 1999). This modulation of the action by the observation of others' actions is called *automatic imitation* and paradigms on simple movements have been developed to experimentally generate this effect (e.g., Brass, Bekkering, Wohlschläger, Prinz, 2000; Stürmer Aschersleben, Prinz 2000; Brass, Bekkering, Prinz, 2001). An associated concept that needs to be explained to fully understand the automatic imitation phenomena is the *compatibility effect*, whereby when we simultaneously observe and perform an action, we are faster to execute our action when the observed action is the same rather than when it is different. The automatic imitation shares some common features with the more general framework of the

stimulus-response compatibility (SRC, Brebner, Shephard, Cairney, 1972), as well as some differences that I will discuss in the following paragraphs.

The first study showing how principles of SRC could be applied to imitation has been performed by Stürmer and colleagues (2000). They had participants see two types of gestures: a hand opening or closing. In each trial participants were required to perform one of the two gestures while observing the movement of the stimulus on the screen. The movement performed by the hand stimulus was irrelevant for the selection of the participants' action, as they were instructed to perform the two movements in response to two different colors that were superimposed on the hand stimulus. For example, if the hand color turned into red, participants had to open their hand while if it turned into blue, they had to close their hand. Results showed a compatibility effect between irrelevant observed movement and executed movement, with participants being slower when the two movements were different. The results were explained as being due mainly to the spatial correspondence between the trajectories of the two movements.

Subsequent studies found similar results, showing the presence of the compatibility effect in imitation with different finger actions (Brass, Bekkering, Wohlschläger, Prinz, 2000; Brass, Bekkering, Prinz, 2001). However, this automatic imitation seemed to be something more than pure SRC. In fact, the correspondence between observed and executed action cannot be attributed only to the overlapping of spatial features and, at least part of the compatibility effects observed should be attributed to the topographical or anatomical correspondence between model's and performer's actions. For this reason some scholars (Boyer, Longo, Bertenthal, 2012; Catmur & Heyes, 2011) have introduced the term of imitative compatibility to refer to the automatic imitation "cleaned" from spatial compatibility effects.

Many studies on automatic imitation tried to actively manipulate the spatial component in the attempt to isolate the imitative compatibility (Brass, Bekkering, Prinz, 2001 experiment 3; Heyes, Bird, Johnson, Haggard, 2005; Bertenthal, Longo, Kosobud, 2006; Press, Bird, Walsh, Heyes, 2008; Catmur & Heyes, 2011). Bertenthal and colleagues (2006) provided the first behavioral evidence in favor of the independency of imitative compatibility from spatial compatibility. They showed participants left and

right hands seen from a third-person perspective that could move by tapping either the index or the middle finger. In experiment 1, participants were instructed to respond with their right hand to the movement of the hand stimulus by moving the same finger that the hand was moving. In other words, if the presented hand was moving the index finger, the participant should move her index finger. The hand stimuli could be either a left or a right hand; thus in half of the trials, the hand stimulus (i.e., the left hand) and the hand used by the participant to respond (i.e., the right) were mirror-image of each other (i.e., specular), whereas in the other half of the trials, the hand stimulus (i.e., the right hand) and the one moved by the participant (i.e. the left hand) were different. In the former condition, with hand stimulus and participant's hand being the mirror image of each other, there exist spatial correspondence between the hand model and the participant's hand, whereas in the latter condition there was not spatial correspondence between the two. The anatomical correspondence between fingers moved by the hand stimuli and participants' was always kept constant, due to the instructions of the task. A spatial compatibility effect was observed by subtracting the reaction times (RTs) in the compatible condition from those in the incompatible condition. Experiment 2 was designed to test the complementary effect, that is the imitative compatibility. Using the same stimuli, participants were instructed to respond to the movements on the screen by moving the finger that was in the same spatial position with respect to the finger moved by the hand stimulus. In other words, if the hand was moving the finger more on the left side of the screen, participants should have moved their finger more on the left side of their hand. As in Experiment 1, when the hand stimulus was the mirror-image of the participants' hand there was the anatomical correspondence between moved fingers of the model and of the imitator, whereas when the hand was different the fingers moved by the model and the performer were also different. The analysis of the RTs revealed an imitative effect, in that when the anatomical identity of the fingers overlapped, participants were faster at executing the movement. Thus, these two experiments provided evidence for two independent compatibility effects, one due to the spatial correspondence between model's and performer's movement (i.e., the spatial compatibility) and the other due to the anatomical correspondence between the body

parts moved (i.e., imitative compatibility). However, despite this evidence has been replicated (Catmur & Heyes, 2011; Boyer, Longo, Bertenthal, 2012; Mengotti, Corradi-Dell'Acqua, Rumiati, 2012), it has not yet been established whether these two effects are sustained by independent mechanisms (Boyer, Longo, Bertenthal, 2012) or whether they are just two sides of a unique, possibly associative, mechanism (Catmur & Heyes, 2011). Whatever the explanation is, it is clear that gesture imitation can be accomplished throughout different parameters, based on spatial and/or anatomical correspondence with the model.

This happens also in real-life imitation when, for example in a gym lesson, we try to learn how to perform an exercise from an instructor who is in front of us. If the instructor moves her right arm, we can reproduce her movement by moving our right arm: in this case there will be an anatomical correspondence between the effector used by the instructor and the one used by the imitator; while the spatial position of our hand will be opposite to the one of the model: in this case we talk about anatomical imitation. However, if we perform the movement by using our left arm while she used the right arm, the two arms will be a mirror image of each other: in this case we talk about specular imitation. Studies on children showed that there is a certain degree of preference towards the specular imitation (Wapner & Cirillo, 1968; Schofield, 1976; Bekkering, Wohlschläger, Gattis, 2000; Gleissner, Melzoff, Bekkering, 2000), even though differences between specular and anatomical imitation have not been quantified in these studies. Moreover some results from these studies seem to suggest that the preference favors the dominant hand (Gleissener, Melzoff, Bekkering, 2000) rather than specular imitation, when the participant is asked to imitate the gesture freely choosing which hand to use, most of them will choose to imitate with their dominant hand, even if this means to imitate anatomically.

Intuitively, the specular imitation appears as more automatic and easier to perform because it implies the stimulus-response compatibility that facilitates the production of the action in the same direction of the model. However, other studies suggest that the activation of the motor system triggered by the observation of external action or by sensory stimuli follows an anatomical frame of reference rather than a

specular one (Belopolski, Olivers, Theeuwes, 2008; Thomas, Press, Haggard, 2006). Thomas and collaborators (2006), for instance, showed that participants were faster to respond to a tactile stimulation on their body when they observed a visual cue onto the same body location of a person in front of them rather than when the visual cue was presented onto a non-body control. Interestingly this facilitation was higher when the body parts involved of the model and the participant corresponded anatomically rather than in a specular way. The authors found that participants were faster to respond to a tactile cue onto their right arm when the visual cue appeared onto the model's right arm, even if this means that it was located in the opposite part of the body, as the model was facing the participant. Similar results were found in a study in which a Posner-like task was used (Belopolsky, Olivers, Theeuwes, 2008), with participants being faster to respond to a visual cue while observing the same movement performed by a model facing them and with a preference towards the anatomical correspondence of the two movements.

One can argue that the two types of imitation are selected depending to the requirement of the task, with a preference towards the specular imitation when the attention is focused on the goal of the action or the final position of the movement, and a reverse preference towards the anatomical imitation when attention is focused on the trajectory or other kinematics parameters. To date no studies have directly investigated this hypothesis.

*1.3 The different theories on imitation*

*1.3.1 The ideomotor approach*

The first formulation of the basic principle of the ideomotor framework originates at the end of the nineteen century, when the psychologist William James wrote that "Every representation of a movement awakens in some degree the actual movement which is its object" (James, 1890: vol. II, p. 526), thus suggesting a connection between representation and execution of motor acts (see also Greenwald, 1970). The more recent formulation of the ideomotor approach has been developed by Prinz and colleagues (Prinz, 1997; Hommel, Müsseler, Aschersleben, Prinz, 2001; Massen & Prinz, 2009).

The key concept of this approach is that motor and sensory representations are not entirely separate but share a *common coding*. The fact that perception and action planning have the same representations in common explains why observing the effect of an action facilitates its execution. This connection between perception and action allows a straightforward interpretation as to how imitation occurs. If the perceptual experience shares features with the processes controlling actions, then the former can induce and modulate the latter, with the strength of this modulation being dependent on the *similarity* between the observed and the to be performed action. Therefore, the correspondence problem that theories traditionally find hard to accommodate finds in this ideomotor theorization a solution.

      The ideomotor framework is based on rigorous experimental evidence demonstrating that the production of an action can be modulated by the observation of another action (i.e. similar or different) performed by an external agent. One of the first paradigms was developed by Brass and colleagues (Brass, Bekkering, Wohlschläger, Prinz, 2000; Brass, Bekkering, Prinz, 2001), thanks to which they showed how the observation of a different action interfered with the ongoing motor plan. In one of these studies (Brass, Bekkering, Wohlschläger, Prinz, 2000), participants were required to move one of two fingers in response to a spatial cue (i.e., a cross placed on the hand stimulus on the screen) while observing a moving hand as task-irrelevant cue. Results showed that when the movement performed by the hand stimulus was the same of the participants' RTs were smaller than in the opposite condition, when the two movements were different. Using a different version of the paradigm (Brass, Bekkering, Prinz, 2001), participants were pre-instructed to perform a simple finger movement while the same or a different movement was shown on the screen. Reaction times (RTs) were smaller when the observed movement was the same as the movement they were instructed to execute, that is a compatibility effect was observed. Subsequent studies manipulated this basic principle (Brass, Derrfuss, Matthes-von Cramon, von Cramon, 2003; Bertenthal, Longo, Kosobud, 2006; Longo, Kosobud A, Bertenthal, 2008; Longo & Bertenthal, 2009; Boyer, Longo, Bertenthal, 2012) and replicated the original observation that action is modulated by perception.

*1.3.2 The associative sequence learning model*

In alternative to the ideomotor theories, the Associative Sequence Learning (ASL) model, proposed by Heyes and Ray (2000) argues that perceiving an action at the same time as when we produce it develops associative links between sensory and motor processes, based on the classical concept of associative learning. Within this theoretical view, then, the correspondence problem of imitation is solved by assuming that the perception of an action influences the production of another (or the same) action insofar as the two actions have been performed together in the past (this is also known as *contiguity*). This is possible through the development with experience of vertical associations connecting the sensory representation of an action with the motor representation of the same action. Thus, imitation does not rely on cognitive mechanisms specific for imitation itself, but on more general associative processes.

This issue has been addressed experimentally in studies showing counter-imitation effects. In these studies incompatible sensorimotor training was used, thus the repeated association of an observed action with an opposite action will lead to associative links between the two actions. The incompatible training was able to abolish the compatibility effect, in that the participants did not showed the facilitation effect when the observed and the produced actions were the same (Heyes, Bird, Johnson, Haggard, 2005; Catmur, Walsh, Heyes, 2007; Cook, Press, Dickinson and Heyes, 2010). For example, after a period in which participants were trained to respond to an opening hand stimulus with the opposite movements, i.e., by closing of their hand, the compatibility effect that was normally observed when the two movements were the same was abolished (Heyes, Bird, Johnson, Haggard, 2005; Cook, Press, Dickinson & Heyes, 2010).

The neural mechanism underlying this account is the Hebbian principle whereby neurons that discharge in synchrony develop associations in the firing and tend to strengthen the synchronization of the firing itself. The mirror neurons system (Rizzolatti & Craighero, 2004) has been proposed to be the brain correlate of ASL: the repeated

experience of simultaneously observed and executed actions will develop neurons that fire both when the action is perceived and when the same action is performed.

### 1.3.3 The mirror neurons system

In the early '90s an Italian group of researchers first reported neurons in the inferior premotor cortex (area F5) of the macaque monkey brain that fired both when the monkey produced a specific upper limb action and when it observes the same action performed by the experimenter (di Pellegrino, Fadiga, Fogassi, Gallese, Rizzolatti, 1992; Gallese, Fadiga, Fogassi, Rizzolatti, 1996; for a review see Rizzolatti & Sinigaglia, 2010). This subset of neurons, that constituted about the 20% of the total amount of neurons recorded from the F5 region (Gallese, Fadiga, Fogassi, Rizzolatti, 1996), was later called "the mirror neurons". The mirror neurons showed some basic properties in their firing: they responded to goal-directed actions, in many cases they were specific of the type of action they responded to (i.e. a particular type of grasping) and usually they required an effector-object interaction. Mirror neurons did not show only to link the visual with motor modalities. Evidence of coupled response to auditory and motor stimuli was also reported (Kohler, Keysers, Umiltà, Fogassi, Gallese, Rizzolatti, 2002). Audiovisual mirror neurons were found in the F5 region of the macaque's brain that fired when the monkey produced an action but also when it heard the related sound (i.e., peanut breaking) (Kohler, Keysers, Umiltà, Fogassi, Gallese, Rizzolatti, 2002).

Further studies found neurons with the same mirror characteristics in other brain regions of the monkey such as the inferior parietal lobule (i.e. IPL, also known as PF region, Fogassi, Ferrari, Gesierich, Rozzi, Chersi, Rizzolatti, 2005), thus providing evidence of a distributed network of mirror neurons. Most of the registered neurons of the IPL (n = 165) showed firing selectivity in response to the observation of a particular type of action, i.e. for grasping to eat but not for grasping to place the food in a container and *vice versa*. About 25% of the neurons targeted showed mirror properties, that is they firing both when the action was observed and performed.

The superior temporal sulcus (STS) is the third region is held to be part of the mirror neurons system; in this region neurons have been found to respond selectively to

the observation of the biological actions (Perrett et al., 1989; Jellema, Baker, Oram, Perret, 2002 for a review) without having mirror motor properties. However, this region is considered to be a first stage of processing of biologically relevant movements that are then projected to the ventral premotor cortex, including F5. The visual analysis of the action is performed in the STS and then completed in the premotor cortex with information about the motor requirements. Connections between the IPL and F5 are also present to allow the correct execution of the action.

While the presence of mirror neurons in the monkey brain is widely accepted based on single cell recording, the evidence of similar neurons in humans is provided by neurophysiological and neuroimaging studies. In a TMS study, Fadiga and collaborators (1995) showed that when stimulating the primary motor cortex, the motor evoked potentials (MEPs) registered from the muscular activity of the hand and of the arm increased when the participants observed grasping movements performed by the experimenter. Surprisingly, the same increase was present also in the observation of intransitive meaningless gestures of the arm; this result is at variance with the monkey's MNS who remains silent when the monkey observes actions with no goals. Furthermore, the increase was registered in those muscles that were required to produce the movement participants observed. No increase in the MEPs amplitude was shown when participants observed only static objects without any human action directed towards them. This has been considered as the first evidence of a system matching actions observation and production. Subsequent studies replicated the original findings (Maeda, Kleiner-Fisman, Pascual-Leone, 2002) with very simple finger movements, suggesting that unlike monkey's MNS, the human mirror system codes for any type of movement, even these that are not goal directed.

In a similar vein, neuroimaging were performed to test if this supposed fronto-parietal mirror system activates both for observation and production of the same actions. Iacoboni and colleagues (1999) showed that two regions of the brain were active both in an observation condition of simple finger movements and in an observation-execution condition (i.e. imitation) of the same movement: the left inferior frontal gyrus (area 44) and the anterior part of the right superior parietal lobule. Similar results were found for

the right superior temporal sulcus in a follow-up study (Iacoboni et al. 2001). However, most recent fMRI studies provided contrasting evidences, in favor of the existence of a human mirror neurons system with the repetition suppression paradigm for the frontal regions (Kilner, Neal, Weiskopf, Friston, Frith, 2009) or against it with the multivariate pattern classification analysis in the parietal cortex (Dinstein, Gardner, Jazayeri, Heeger, 2008).

The main interpretation of the role of the mirror neurons systems is that it provides a direct mechanism for converting action understanding in production of behavior. In the monkey brain mirror neurons are showed to code for the goal of the action, activating only in response to actual or supposed transitive actions (Umiltà et al., 2001), hence supporting the idea that the function of these neurons is to promote action recognition or understanding. In the studies on humans however, the brain regions considered to have mirror properties activated in response to viewed and performed intransitive actions as well (Fadiga, Fogassi, Pavesi, Rizzolatti, 1995; Iacoboni et al., 1999, 2001; Maeda, Kleiner-Fisman, Pascual-Leone, 2002; Koski, Iacoboni, Dubeau, Woods, Mazziotta, 2003), accounting for a more complex mechanism tuned not only to recognize the action but to also reproduce and imitate it, maybe also to promote social interaction.

Recently, theories around the mirror neurons system have been pushed forward, suggesting a role of this system also in more complex cognitive functions, like empathy (Iacoboni, 2009), language understanding (Rizzolatti & Arbib, 1998), social cognition (Iacoboni & Mazziotta, 2007), or suggesting that the malfunctioning of this system can play a role in developmental diseases like autism (Dapretto et al., 2005).

However, strong criticisms have been raised against theories on mirror neurons. For example, empirical evidence on patients showed that the ability to recognize actions and objects dissociates from the ability to use those same objects or to produce the same actions, suggesting that the understanding of the actions is not necessary for the production of actions and that the two systems can be independently damaged (Negri, Rumiati, Zadini, Ukmar, Mahon, Caramazza, 2007; Tessari, Canessa, Ukmar, Rumiati, 2007; see also Mahon & Caramazza, 2005 for a review)

*1.4  Neural correlates of imitation*

*1.4.1 Neuroimaging evidences*

In many studies the neural underpinnings of action imitation were investigated and identified a putative fronto-parietal network associated with it (Iacoboni et al., 1999; Brass, Zysset, von Cramon, 2001; Koski et al., 2003; Chaminade, Meltzoff, Decety, 2005; Rumiati et al. 2005; Jackson, Meltzoff, Decety, 2006; Bien, Roebroeck, Goebel, Sack, 2009), with a certain degree of overlap with the regions associated with the processing of action observation (Iacoboni et al., 1999, Koski et al., 2003).

In a recent meta-analysis Caspers and collaborators (2010) analyzed data from a total 139 experiments on action observation and/or action imitation tasks to map the brain regions that are most commonly involved in the two functions. From the overlap of the activations reported in the 104 studies, the action observation network was found to extend bilaterally including fronto-parietal regions as the inferior frontal gyrus (BA 44/BA 45), the lateral dorsal premotor cortex (BA 6) and the supplementary motor area (SMA), the primary somatosensory cortex (SI, BA 1/2), the superior temporal sulcus (STS) and posterior middle temporal gyrus (pMTG), the inferior parietal lobule (IPL), the superior parietal lobule (SPL) and the intraparietal sulcus (IPS). Consistently, almost the same network resulted as being involved when only studies showing observation of hand actions were included. From the analysis of the activations of 35 studies, the imitation network was found to extend bilaterally throughout the inferior frontal gyrus (BA 44), the premotor cortex (BA 6) and supplementary motor area (SMA), the superior frontal gyrus, the primary somatosensory cortex (SI, BA 2), the inferior parietal lobule (IPL) and the visual area V5. In addition, the left posterior middle temporal gyrus (pMTG) was included in the network, as well as the right ventral part of the inferior parietal lobule including part of the secondary somatosensory cortex (SII, OP1), the fusiform face and body areas (FFA, FBA) and the more frontal part of the insula. These activations were consistent even when only studies of hand imitation were included.
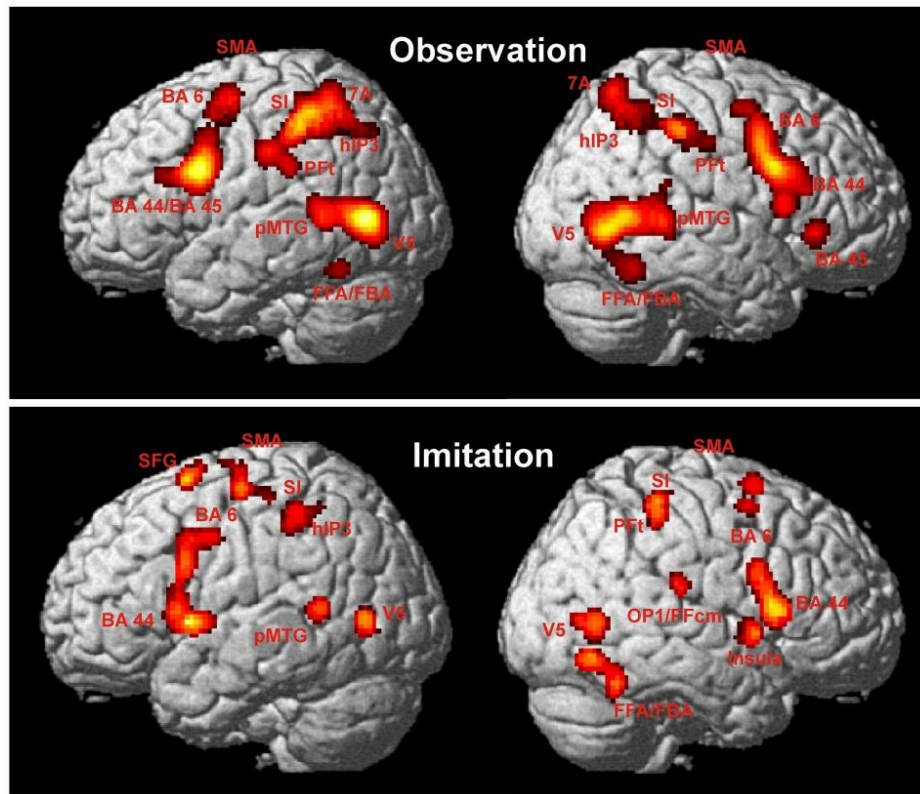
Figure 1.1 Regions significantly associated with the observation and imitation of actions, from the results of the meta-analysis performed by Caspers et al. 2010. Results are displayed on the left and right lateral surface view of the MNI single subject template.

Similar results were found in an fMRI study by Menz and colleagues (2009) in which they applied an independent component analysis (ICA) to an imitation task to analyze the brain networks associated with the different phases of the imitative behavior. They highlighted four different networks characterized by differential time windows. The first network included occipital regions and was associated to the perceptual processing of the observed action. The second network involved bilaterally the inferior frontal gyrus (BA 44/45), the primary sensory and motor areas (SI, M1), the supplementary motor area (SMA), the superior temporal gyrus, the superior parietal lobule, as well as the right precentral gyrus (BA 6). This network is supposed to code for the motor preparation and execution of the action. The third network is supposed to sustain processes of action planning and motor working memory and involves the cingulate gyrus, the superior temporal sulcus (STS) and the intraparietal sulcus (IPS)

bilaterally. Finally, the fourth network was specific to the conditions that involved objects interaction, thus activating the cingulate gyrus and the middle frontal gyrus, the dorsolateral prefrontal cortex and the superior parietal cortex bilaterally.

It is interesting to note how neuroimaging studies on imitation highlighted a bilateral network of regions underlined this process. At first glance, this pattern of results seems in contrast with neuropsychological evidence suggesting that a deficit in imitation of gestures is generally caused by left brain damage (see the next section for a discussion of the neuropsychological studies).

However, what the neuroimaging techniques cannot establish is whether the active regions are necessary for imitation to be accomplished. Moreover, what is still not well defined in the extant literature is the information about the role of the different regions of this widespread fronto-parietal network associated with imitation. For instance, the BA 44 (Broca's area) and the IPL/IPS, held to belong to the MNS, and are meant to be involved in matching the observed movement to the motor plans necessary to reproduce the movement, with the parietal regions coding for the kinesthetic aspects of the action and the frontal regions coding for the goal of the action itself (Iacoboni et al., 1999). The superior temporal sulcus and nearby temporal regions are supposed to code for the processing of body movements (Puce & Perret 2003, Iacoboni et al. 2001), whereas the dorsolateral prefrontal cortex (DLPFC, defined as middle frontal gyrus in some studies) has been found to play a role in inhibiting the imitative responses (Brass, Zysset, von Cramon, 2001; Bien, Roebroeck, Goebel, Sack, 2009).

*1.4.2 Neuropsychological evidences*

Ideomotor apraxia clinically refers to the patients' reduced ability to imitate gestures on purpose commonly caused by lesions of parietal and less frequently premotor regions of the left hemisphere (Liepmann, 1920; De Renzi, Motti, Nichelli, 1980; Papagno, Della Sala, Basso, 1993; Goldenberg, 1995; Haaland, Harrington, Knight, 2000; Tessari, Canessa, Ukmar, Rumiati, 2007; see also Leiguarda & Marsden, 2000 for a review). Thus, the study of neuropsychological patients with praxic deficits is fundamental in defining the cognitive processes and the neural correlates underlying imitation.

Papagno and collaborators (1993) showed that out of 10 apraxic non-aphasics patients with left brain damage the lesions were most commonly located in frontal and parietal regions. Seven patients had lesions restricted to subcortical structures and white matter, however the praxic deficit shown by these patients was less severe than the patients with lesions that involved also the cortex. Similarly, Goldenberg (1995) that in a group of 35 patients with left brain damage, frontal and parietal lesions were more frequent in those with apraxia than in those without praxic deficits. Among the patients with apraxia, two had lesions affecting only the subcortical structures and the white matter. Later Goldenberg and Karnath (2006) argue that the regions supporting the imitation of gestures are organized according to the body part involved in the action. They found that left brain damaged patients double dissociated in their ability to imitate hand and finger postures and that the anterior regions, such as the inferior frontal gyrus, were associated with the imitation of finger movements, and the parietal regions with the imitation of hand movements. More recently, Tessari and colleagues (2007) showed that out of eight left brain damaged patients with apraxia the regions that were more frequently lesioned were the temporo-parietal junction and the angular gyrus.

As mentioned earlier, neuroimaging studies differ from the neuropsychology studies on imitation in that the former documented bilateral representations and the latter reported apraxic patients with predominantly left brain damage. Patients with right brain damaged and signs of apraxia have also been reported (De Renzi, Motti, Nichelli, 1980; Tessari, Canessa, Ukmar, Rumiati, 2007) and, even if partly the errors can be attributed to the presence of neglect, there are nevertheless errors that cannot be attributed to the inattention of the left side of the space (Goldenberg, Münsinger, Karnath, 2009). However as the number of cases is very small, it is still difficult to understand the contribution of the right hemisphere in giving rise to ideomotor apraxia.

*1.5 Imitation and the other cognitive functions*
As imitation is a complex behavior it engages many different systems including perception, attention, emotion, language and most likely also body representations. In this interaction of imitation with other systems it is expected that it get influenced at

different levels. In the following sections I will review how imitation has been described to relate to these different systems. This review will constitute the starting point of my empirical work.

### 1.5.1 Imitation and the model

If we ask someone to define what imitation is, he/she will most probably answer that imitation is "to copy somebody's behavior". Thus, one necessary condition of imitation is the presence of the model. Part of the research on this topic has focused on the role of the model, trying to define what is special about the interaction between the imitator and a human model, compared with a robotic or non-biological model. Some studies suggest that humans are more inclined to imitate movements performed by a human model (see Gowen & Poliakoff, 2012 for a review). For example, Kilner and collaborators (Kilner, Paulignan, Blakemore, 2003; Kilner, Hamilton, Blakemore, 2007) found an interference on participants' movements of the arm when they observed incompatible movements performed by a human model. However, such interference did not occur when the model was non-biological. Furthermore, neuroimaging studies showed that when observing movements performed by a biological and a non-biological model, the fronto-parietal regions that are considered part of the mirror neurons systems are more active when observing the biological model (Perani et al. 2001; Tai, Scherfler, Brooks, Sawamoto, Castiello, 2004). What remains to be understood is if this preferential activation of fronto-parietal regions occurs also during imitation of a human model rather than a non-human one.

### 1.5.2 Imitation and emotions

Emotions are known to play a fundamental role in modulating behaviors (Pessoa, 2008 for a review) by eliciting affiliative tendencies or triggering avoidance from a situation or a particular individual. Facial expressions are known to be particularly effective in inducing emotional reactions as well as imitative behaviors (Carr, Iacoboni, Dubeau, Mazziotta, Lenzi, 2003). Some studies suggest that imitation can be modulated by emotional pictures presented immediately before the movement to be imitated (Grecucci,

Koch, Rumiati, 2011; Grecucci, Buiatti, Balaban, Budai, Rumiati, 2009). In these studies, participants were instructed to perform a simple finger movement meanwhile observing the same or an opposite movement performed by a model. When pictures with negative emotional content were presented before the movement the compatibility effect was enhanced, compared with conditions in which pictures with positive or neutral emotional content were used. To date, some imaging studies investigated the connections between emotion and imitation showing that fronto-parietal regions activated during imitation or simple observation of emotional faces (Carr, Iacoboni, Dubeau, Mazziotta, Lenzi, 2003), however, no neuroimaging study was performed to investigate the modulation of the emotions during imitation.

### 1.5.3 Imitation and the body representations

The body representations provide continuous information concerning the position of our body in space and the relative position of our body parts. Indeed, these cues are important to control and produce purposeful movements and are even more important when we have to compare the movement of another person with ours, like when we imitate. Previous studies suggested that, in addition to the motor and the somatosensory maps, the body information is represented in at least three more maps (Schwoebel & Coslett, 2005). According to the classification put forward by Sirigu and colleagues (Sirigu, Grafman, Bressler, Sunderland, 1991) and Buxbaum and Coslett (2001) and these maps are: The body schema that is an online sensorimotor representation of the location of the body parts in space, to guide and monitor movements; The body structural description that is a schematic topological map of the body that is used to define relationships between body parts; and the body image that refers to the semantic knowledge of the body, including names and definition of body parts and functions. Patients' studies (Schwoebel & Coslett, 2005) showed that these representations can be independently damaged and neuroimaging studies disentangled the different neural correlates of the body schema and the body structural description (Corradi-Dell'Acqua, Tomasino, Fink, 2009).

It is still under discussion which of these body representations is more important in order to imitate actions and how the different body representations interact with the motor system during imitation. For instance, Goldenberg (1995) asked patients with left brain damage to imitate actions and to reproduce such actions on a life-sized manikin and showed that patients with apraxia, thus not able to imitate gestures, were also impaired in reproducing the same gestures on the manikin. The author concluded that the underlying deficit resides "in the evocation and application of a general concept of the human body which applies regardless of whether one's own body is concerned or not", suggesting a disruption of the body structural description. However, this study was not suitable to properly disentangle the involvement of the different body representation because dedicated tasks tapping each of the representations were missing.

*1.6 Aims of the thesis*

The main aim of the thesis is to investigate the neural and cognitive mechanisms underlying imitation, using a paradigm of automatic imitation in neuroimaging and neuropsychological studies. In the first part I will investigate the neural correlates of the matching between the model and the performer, to define how this matching process occurs and what is the role of the different brain regions in supporting it. In the second part of the thesis I will focus on the factors that modulate the imitative response, like the emotional context and the identity of the model, and the connections of the neural network supporting imitation with the other cognitive systems of the brain, as the body representations.

# Chapter 2

## THE NEURAL CORRELATES OF IMITATION COMPONENTS: AN FMRI STUDY[1]

*2.1 Introduction*

As discussed in the previous chapter, in a typical automatic imitation paradigm (Brass, Bekkering, Wohlschläger, Prinz, 2000), participants are instructed to move one of two fingers in response to a spatial cue, while observing a task-irrelevant movement performed by a hand stimulus. When the seen movement performed by the hand stimulus and participant's movement were the same (i.e., compatible trials: both moving the index finger), reaction times (RT) were shorter than when they were different (i.e., incompatible trials: the hand stimulus moving the index finger and the participant moving the middle finger).

This automatic imitation effect can be interpreted in terms of a *common coding* between the observation of a movement and its execution (see Prinz, 1997). The key concept of common coding theories is that observing the effect of an action facilitates its execution because perception and action planning share the same representational domain.

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[1] The present study is published in NeuroImage [Mengotti P., Corradi-Dell'Acqua C., Rumiati R.I. (2012) Imitation components in the human brain: An fMRI study. NeuroImage 59(2): 1622-1630]

Brass et al. (2000) also added that the automatic imitation effects they observed with single finger movements are an instance of the stimulus-response compatibility (SRC), whereby a compatible mapping of stimulus and response leads to faster responses than an incompatible mapping (Brebner, Shephard, Cairney, 1972). The SRC and common coding accounts clearly have many common features, but differ for one fundamental aspect: whereas in SRC the compatibility is based on the spatial mapping of the stimulus and the effector (spatial compatibility, see Prinz, 1997), in the common coding the compatibility should, at least in principle, also involve an anatomical correspondence between observer's and model's motor commands (imitative compatibility).

Importantly, while in some studies (Brass, Bekkering, Wohlschläger, Prinz, 2000; Brass, Bekkering, Prinz, 2001 experiments 1 and 2), the hand displayed was the mirror-image of participants' hand (i.e., specular hand), thus making anatomically compatible finger movements also sharing the same spatial mapping, in others (experiment 3 of Brass, Bekkering, Prinz,, 2001; Bertenthal, Longo, Kosobud, 2006) the authors tried to disentangle, at the behavioral level, imitative compatibility, based on the identity between observer's and model's moved parts, from the spatial compatibility, based on the correspondence between the spatial location of the stimulus and of the effector. In the experiment 3, Brass and colleagues (2001) employed a modified version of their own task in which the observed hand was upside-down with respect to the participants' hand. This manipulation made movements that were anatomically compatible but spatially incompatible (i.e., a seen palm-up tapping hand and a response palm-down tapping hand with a different orientation but expressing the same movement), and vice versa (i.e., a seen palm-up tapping hand and a response lifting palm-down hand with the same orientation but expressing different movements). Brass and colleagues (2001) replicated the automatic imitation effect (Brass, Bekkering, Wohlschläger, Prinz, 2000; Brass, Bekkering, Prinz, 2001 experiments 1 and 2) even when participants were presented with upside-down hands, thus confirming that this effect was, at least partly, due to the anatomical compatibility between the observed and performed movement. However, the automatic imitation effect associated with upside-down hands stimuli was significantly

smaller than the effect associated with stimuli having the same orientation than the participants' responding hand. This result suggests that also the spatial compatibility between the stimulus and the responding hand played a role. In a similar vein, Bertenthal and collaborators (2006) asked participants to move either the finger anatomically compatible with the one moved by a model, independently of the spatial mapping (anatomical imitation), or the finger with the same spatial mapping, independently of the anatomical identity (spatial imitation). Stimuli were left and right moving hands, specular and non-specular to the hand of the participants. In either condition, participants were faster in the specular condition than in the non-specular condition: during anatomical imitation, participants were faster when their finger was also spatially compatible with the model's, thus highlighting the effect of the spatial compatibility, whereas during spatial imitation participants were faster when their finger was also anatomically compatible with the model's one, highlighting the effect of the imitative compatibility.

Neuroimaging studies (e.g., Iacoboni et al., 1999) showed that imitation of single movements recruited the left inferior frontal gyrus, the right anterior portion of the superior parietal cortex involving the intraparietal sulcus, and the right parietal operculum. These regions were active also during mere observation of the same movements, thus supporting the common coding hypothesis (Iacoboni et al., 1999). In addition, this brain network has been proposed to be the human homologous of the macaque mirror neurons system, engaged both when the monkey performs an action and when it observes an individual making a similar action (Rizzolatti & Sinigaglia, 2010).

However, as previous imaging studies did not manipulate both the spatial and anatomical mapping, it remains to be explored how these two components are implemented in the brain and, in particular, how they relate to inferior frontal, parietal and opercular structures whose activity in automatic imitation paradigms has been interpreted in terms of direct matching. In particular, Koski and colleagues (2003) asked participants to imitate, with their right hand, finger movements from displayed left (specular) and right (non-specular) hands. They found stronger activations of the inferior frontal and parietal activations when imitating specular, relative to non-specular hands,

thus describing regions sensitive to spatial compatibility effect. This study, however, was not designed to identify the brain regions coding for the imitative compatibility between observed and executed movement, as the anatomical correspondence between stimuli and responding hand was kept constant in both (specular vs. non specular) conditions.

We used fMRI and tested healthy volunteers using a paradigm derived from Bertenthal and collaborators (2006). Participants were presented with videos displaying moving hands which were either Specular or Non-Specular to their own responding hand (factor: STIMULI), and were engaged in both Anatomical and Spatial imitation tasks (factor: TASK). The crucial analysis is found in the TASK X STIMULI interaction, which reveals the putative neural signatures of imitative and spatial compatibilities emerging from the task-specific specularity effects. In particular, the neural structures specifically involved in the imitative compatibility are expected to be recruited not only during the Anatomical task (in which such compatibility is explicitly assessed) but also - following Bertenthal and colleagues (2006) - in the Spatial task and only for Specular (but not for Non-Specular) stimuli. On the other hand, neural structures specifically involved in spatial compatibility are expected to be recruited not only during the Spatial task (in which such compatibility is explicitly assessed) but also in the Anatomical task, specifically for Specular stimuli. Differently from previous neuroimaging research, our experimental paradigm can disentangle the anatomical components of imitation from the spatial effects (such as those associated with SRC) that are not specific to imitation, but that nevertheless might have played a crucial role in many studies in the field.

### 2.2 Materials and methods

### 2.2.1 Participants

Twenty-two healthy subjects (aged between 21 and 33 years, mean age 24.4+2.9, 12 females) were recruited. None of the participants had any history of neurological or psychiatric illness. They were all right-handed, as assessed with the Edinburgh Handedness Inventory (Oldfield, 1971; mean laterality quotient: 79). Written informed consent was obtained from all subjects. The study was approved by the Ethic Committee

of IRCCS E.MEDEA - Ass. La Nostra Famiglia and conducted in accordance with the Declaration of Helsinki.

### 2.2.2  Stimuli

On each trial, a short video (1 s) was presented to the participant, showing on a black background either a left (50% of the trials) or a right hand moving downwards either the index (50% of the trials) or the ring finger. Each video was preceded by the first frame of the video with the hand in the starting position and it was followed by the last frame of the video with the hand in the ending position of the movement. A black screen was shown in the intertrial intervals.

### 2.2.3  Experimental setup

In the scanner, participants laid supine with their head fixated by firm foam pads and their hands placed each on one button-box for manual responses. Stimuli were presented using Presentation 9.0 (Neurobehavioral Systems) and projected to a NordicNeuroLab VisualSystem goggles that subtended 30° x 23° (horizontal x vertical) of visual angle. For each experimental trial, the static picture of the first frame of the video was presented for 500 ms, followed by the 1000 ms video and the static picture of the last frame of the video for 300 ms. Each trial was followed by an inter-trial interval ranging from 3400 to 5800 ms with incremental steps of 600 ms in which the picture of the black background was displayed.

As videos displayed exclusively index and ring finger movements, participants were requested to tap exclusively their own index or ring fingers. In particular, in the Anatomical Imitation Task, subjects tapped with their left (50% of the trials) or right hand the finger that was anatomically compatible with the one moving on the screen: e.g., if the video displayed an index finger movement, than participants had to tap their own index finger, irrespective of whether the displayed and one's hand had the same/different handedness and, therefore, of whether the displayed and one's finger occupied the same/different position in space. In the Spatial Imitation Task, subjects were asked to tap with their left (50% of the trials) or right hand the finger that was

spatially compatible with the one moving on the screen: e.g., if the seen finger movement occurred closer to the right side of the screen (as in the case of a right hand moving its index finger), participants were asked to tap, between their index and ring finger, the one closest to the same side, irrespective of its anatomical identity. In either task, participants were told to focus their attention on the fingers being moved, irrespective of whether the hand seen was specular to their own moving hand.

Subjects were instructed to start the movement immediately as they became aware of which movement to perform. This results in an online imitation of the movement seen in the video.

When the displayed hand was the mirror-image of participants' moved hand (e.g., participants were requested to move their right hand whilst seeing a left-hand video), then Anatomical and Spatial tasks yielded to the same response. We labeled this condition as Specular. The condition in which Anatomical and Spatial tasks yielded to opposite responses was labeled Non-Specular. This yielded a 2 x 2 x 2 design with the factors TASK [Anatomical (AN) vs Spatial (SP)] and STIMULI [Specular (S) vs Non-Specular (NS)] and moved HAND [Right (R) vs. Left (L)] and eight conditions, corresponding to the following four conditions carried out responding either with their left (50% of the trials) or right hand: 1) AN_S, participants anatomically imitated a specular model; 2) AN_NS, participants anatomically imitated a non-specular model; 3) SP_S, participants spatially imitated a specular model; 4) SP_NS, participants spatially imitated a non-specular model (see Figure 1 for a schematic representation of the four conditions).

Trials were presented, during the whole experimental session, in four different blocks, the order of which was counterbalanced across subjects: two blocks were presented for each task, one to be performed with the left hand and the other with the right hand. Each block comprised 85 randomized trials, including 80 experimental trials [2 hand stimuli (left, right) x 2 finger movements displayed (index, ring) x 20 repetitions] and 5 "null events" in which the black background on the screen replaced the stimuli. Each block was introduced by instructions (8000 ms) informing the subjects about the hand to be used and task to perform. A total of 320 trials and 20 "null events"

were presented for each experimental session, with a total experimental duration of 38 minutes. Before the fMRI experiment, each subject performed a training session that included a shortened version of the four different blocks in each of which 16 randomized trials were delivered.
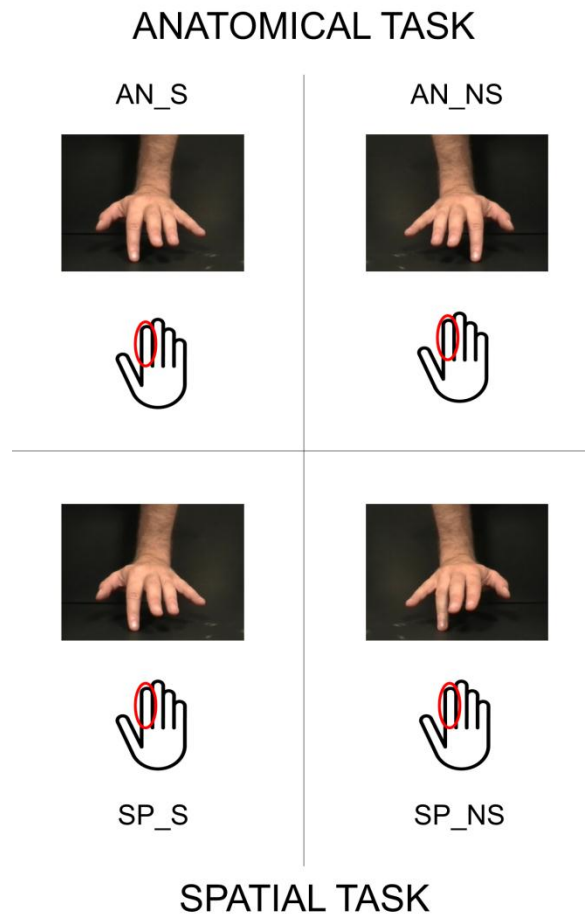


Figure 2.1 Experimental design and stimuli. For each of the four conditions a snapshot from the video-stimuli is displayed together with a schematic representation of participants' hand in which the appropriate finger movement is outlined.

### 2.2.4 fMRI data acquisition

A Philips Achieva 3-T scanner was used to acquire both T1-weighted anatomical images and gradient-echo planar T2*-weighted MRI images with blood oxygenation level

dependent (BOLD) contrast. Functional images were scanned using an echo-planar imaging (EPI) pulse sequence with a TR of 2500 ms, an echo time (TE) of 35 ms, a flip angle of 90°, a slice thickness of 3 mm, and no gap interval between the slices. Each volume comprised 30 axial slices with an in-plane resolution of 128×128 voxels and voxel size of 1.8x1.8x3 mm3, field of view (FOV) of 230 mm. For each subject, 910 volumes were acquired in a single experimental sessions. For the anatomical images the following parameters were used: TR = 8.2 ms, TE = 3.7 ms, number of slices = 190, slice thickness = 1 mm, no interslice gap, in-plane resolution of 1×1 mm2 and flip angle = 8°.

### 2.2.5 *fMRI data processing*

Statistical analysis was performed using the SPM8 software package (http://www.fil.ion.ucl.ac.uk/spm/) on MATLAB 7.8 (The Mathworks Inc., Natick, MA/USA). For each subject, the first six volumes were discarded. To correct for subject motion, the functional images were realigned to a first functional image (Ashburner & Friston, 2003), normalized to a template based on 152 brains from the Montreal Neurological Institute (MNI), and then spatially smoothed by convolution with an 6 mm full-width at half-maximum (FWHM) Gaussian kernel.

The data were analyzed using the general linear model framework (Kiebel & Holmes, 2003) implemented in SPM8. On the first level, for each individual subject, we fitted a linear regression model to the data, by modeling the event sequence of each of the experimental conditions of the 2 x 2 x 2 design and its first-order temporal derivative (null events were not explicitly modeled). Trials in which participants responded incorrectly were excluded from the analysis. We also included six differential realignment parameters assessed for each session as regressors of no interest. The first-level individual images describing the parameter estimates associated with each of the eight experimental conditions were then fed to a second-level flexible factorial design with a within-subjects factor with eight levels, using a random effects analysis (Penny & Holmes, 2003). Areas of activation were identified as significant if they passed a threshold of 65 consecutive voxels (corresponding to $p < 0.05$, family-wise corrected for multiple comparisons at the cluster-level, Friston, Jezzard, Turner, 1994) with an

underlying voxel-level height threshold of t = 3.15 (corresponding to p < 0.001, uncorrected).

Localization of activated regions with reference to cytoarchitectonic areas was analyzed based on probabilistic cytoarchitectonic maps derived from the analysis of cortical areas in a sample of 10 human post-mortem brains, which were subsequently normalized to the MNI reference space. The significant results of the random effects analysis were compared with the cytoarchitectonic maps using the SPM Anatomy toolbox (Eickhoff et al., 2005).

### 2.3 Results

#### 2.3.1 Behavioral results

A 2 x 2 x 2 repeated measures analysis of variance (ANOVA) was conducted on participant mean RT with TASK and STIMULI and HAND as variables. Error trials and trials in which RT was above two standard deviations from the mean RT for that condition were excluded from analysis. Excluded trials were about 1% of the overall trials. Statistical analyses were performed with SPSS 11.5 software. Mean RT and standard deviations for each condition are shown in Table 2.1.

There was a significant main effect of TASK ($F(1, 21) = 67.35$, $p < .0001$), indicating that participants responded faster during Spatial, rather than Anatomical imitation ($555 + 21$ ms vs $631 + 20$ ms, SEM). There was also a main effect of STIMULI ($F(1, 21) = 53.47$, $p < .0001$), responses were faster in the Specular ($578 + 20$ ms) than in the Non-Specular trials ($608 + 20$ ms) and a main effect of HAND ($F(1, 21) = 10.78$, $p < .005$), subjects being faster when using the dominant right hand ($585 + 19$ ms) than the left hand ($601 + 21$ ms). None of the two-way interactions were found to be significant, whereas the three-way interaction Task X Stimuli X Hand was significant ($F (1, 21) = 4.81$, $p < .05$): using the dominant right hand yielded to a smaller discrepancy between specular and non-specular stimuli (difference = 29 ms) than using the non-dominant left hand (39 ms). This, however, was the case only for the Anatomical task, but not for the Spatial task, in which the use of the dominant hand (compared with the use of the non-dominant hand, 21 ms) yielded to a larger specularity effect (30 ms).

We further analyzed our dataset with four paired-sample t-tests with a Bonferroni corrected threshold set at 0.0125. Significant differences were found between Specular and Non-Specular stimuli for each level of task. Significant differences were found for the Anatomical task was found between Specular and Non-Specular stimuli, for the right hand ($t(21) = -4.43$, $p < .001$) and the left hand ($t(21) = -4.35$, $p < .001$). Concerning the Spatial task, significant difference was found between Specular and Non-Specular stimuli, for the right hand ($t(21) = -3.75$, $p < .001$), whereas the effect for the left hand was slightly above the corrected significance threshold ($t(21) = -2.5$, $p = .02$). The analysis of accuracy showed a percentage of correct responses on average over all conditions of 99%, ANOVA on accuracy data revealed only a significant main effect of STIMULI ($F(1, 21) = 20.25$, $p < .0001$), with Non-Specular stimuli being more prone to errors with respect to the Specular ones (98.6% vs 99.6%).

Table 2.1 Behavioral data for each condition. Mean RTs (standard deviation) are shown in milliseconds.

| HAND | | Right hand | | Left hand | |
|---|---|---|---|---|---|
| TASK | | Anatomical | Spatial | Anatomical | Spatial |
| STIMULI | Specular | 605 (98) | 536 (88) | 623 (106) | 549 (95) |
| | Non-Specular | 634 (90) | 566 (96) | 662 (111) | 570 (104) |

*2.3.2  Functional imaging results*

Only clusters of activated voxels which survived a threshold of p <0.05, corrected for multiple comparisons (see Materials and methods Section), are reported on Table 2.2.

Table 2.2 Brain regions showing significant relative increases of BOLD response associated with each comparison of interest.

| | | MNI Coordinates | | | Cluster Size | T Scores |
|---|---|---|---|---|---|---|
| | Side | x | y | z | | |
| **Task main effect:** *Anatomical > Spatial* | | | | | | |
| | L | 48 | -74 | 6 | 12629*** | 7.01 |
| Occipital cortex, Superior/Inferior Parietal cortex, Precentral/Postcentral gyri, Inferior Frontal cortex | R | -20 | -60 | 44 | | 6.24 |
| Superior Temporal Gyrus | R | 54 | -32 | 6 | 144*** | 4.88 |
| | L | -28 | -2 | 54 | 245*** | 4.79 |
| Supplementary motor area | L/R | -4 | 6 | 46 | 132*** | 3.77 |
| | | 4 | 16 | 44 | | 3.63 |
| Insula/Inferior frontal gyrus | L | -32 | 22 | 16 | 103** | 4.70 |
| Middle frontal gyrus | L | -44 | 38 | 26 | 77* | 4.17 |
| Thalamus | R | 18 | -20 | 6 | 116** | 4.14 |
| **Stimuli main effect:** *Non-Specular > Specular* | | | | | | |
| Superior/Inferior Parietal cortex | R | 18 | -62 | 50 | 388*** | 4.75 |
| | R | 30 | 22 | 4 | 309*** | 4.45 |
| Anterior Insula | L | -28 | 32 | 4 | 81* | 3.80 |
| Precentral gyrus | L | -26 | -4 | 46 | 163*** | 4.43 |
| Supramarginal gyrus | R | 56 | -36 | 32 | 79* | 4.17 |

| Region | Side | x | y | z | Cluster | t |
|---|---|---|---|---|---|---|
| **Hand main effect: *Right > Left*** | | | | | | |
| Premotor cortex | L | -30 | -24 | 70 | 3309*** | 13.44 |
| Primary motor cortex | | -50 | -20 | 50 | | 7.68 |
| Supplementary motor area | L | -8 | -2 | 54 | 181*** | 4.58 |
| **Hand main effect: *Left > Right*** | | | | | | |
| Premotor cortex | R | 36 | -26 | 68 | 2928*** | 12.61 |
| Primary motor cortex | | 40 | -18 | 50 | | 8.82 |
| Parietal Operculum | R | 48 | -18 | 16 | 2155*** | 8.97 |
| Cerebellum | L | -6 | -54 | -8 | 98** | 6.03 |
| Supplementary motor area | R | 12 | -22 | 52 | 141** | 4.70 |
| **Task X Stimuli interaction: *(SP_S > SP_NS) > (AN_S > AN_NS)*** | | | | | | |
| Parietal operculum | R | 34 | -24 | 10 | 1018*** | 4.99 |
| | L | -50 | -12 | 24 | 734*** | 4.80 |
| Inferior frontal operculum | L | -38 | 20 | 34 | 221*** | 4.58 |
| Amygdala | L | -26 | 8 | -12 | 198*** | 4.55 |
| | R | 16 | -8 | -12 | 90* | 4.64 |
| Middle temporal gyrus | L | -46 | -26 | 0 | 87* | 4.42 |
| | | -50 | -56 | 18 | 70* | 4.02 |
| Putamen | R | 22 | 12 | 2 | 127*** | 4.36 |
| Postcentral gyrus | R | 24 | -38 | 54 | 110*** | 4.21 |
| Supplementary motor area | R | 8 | -16 | 56 | 108*** | 4.11 |
| Inferior frontal gyrus | L | -36 | 42 | 6 | 100** | 3.99 |
| Inferior parietal cortex | R | 58 | -54 | 14 | 92** | 3.82 |
| **Hand X Stimuli interaction: *(Specular Right & Non-Specular Left)*** | | | | | | |
| Lingual gyrus | R | 12 | -76 | 2 | 2350*** | 19.31 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Superior occipital gyrus | L | -18 | -98 | 14 | 744*** | 9.17 |
| Middle temporal gyrus | R | 50 | -68 | 8 | 91** | 4.25 |
| **Hand X Stimuli interaction:** *(Specular Left & Non-Specular Right)* | | | | | | |
| Superior occipital gyrus | R | 18 | -96 | 18 | 554*** | 11.53 |
| Lingual gyrus | L | -6 | -82 | 0 | 84* | 7.43 |
| Cuneus | L | -12 | -72 | 26 | 68* | 4.69 |
| **Conjunction analysis:** *Task X Stimuli ∩ (SP_S > SP_NS)* | | | | | | |
| Parietal operculum | L | -50 | -12 | 24 | 302*** | 4.80 |
| | R | 50 | -6 | 26 | 370*** | 4.76 |
| Superior temporal gyrus | R | 44 | -22 | 4 | 87* | 4.11 |
| **Conjunction analysis:** *Task X Stimuli ∩ (AN_NS > AN_S)* | | | | | | |
| Middle frontal gyrus | L | -38 | 24 | 36 | 145*** | 4.30 |
| Superior temporal gyrus | R | 50 | -32 | 10 | 131*** | 3.91 |

All clusters survived a threshold of $p < 0.05$ corrected for multiple comparisons at the cluster level for the whole brain. L, left hemisphere; R, right hemisphere.

*** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$.

*Main effect of TASK.* The contrast testing increased neural activity associated with the Anatomical, relative to the Spatial task [(AN_S+AN_NS)-(SP_S+SP_NS)], revealed an extensive network of bilateral areas including: occipital cortex, superior and inferior parietal cortex, precentral and postcentral gyri, supplementary motor area, together with right superior temporal gyrus, right thalamus, left insula, left inferior frontal gyrus and middle frontal gyrus (see Figure 2.2a). No suprathreshold activation was associated with the opposite contrast [(SP_S+SP_NS)-(AN_S+AN_NS)].

*Main effect of STIMULI.* Non-Specular, relative to Specular, stimuli [(AN_NS+SP_NS)-(AN_S+SP_S)] led to differential activation of the right parietal cortex extending in its superior and inferior part and involving the right supramarginal gyrus, bilateral insula

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and left precentral gyrus (see Figure 2.2b). No suprathreshold cluster was associated with Specular, relative to Non-Specular, stimuli [(AN_S+SP_S)-(AN_NS+SP_NS)].

*Main effect of HAND.* The main effect of Hand revealed the left primary motor, premotor and supplementary motor cortex involvement when participants moved the Right hand (relative to the Left hand), independently of the task employed. Similarly, right primary motor, premotor and supplementary motor cortex were associated with Left hand (as opposed to Right) hand movement.
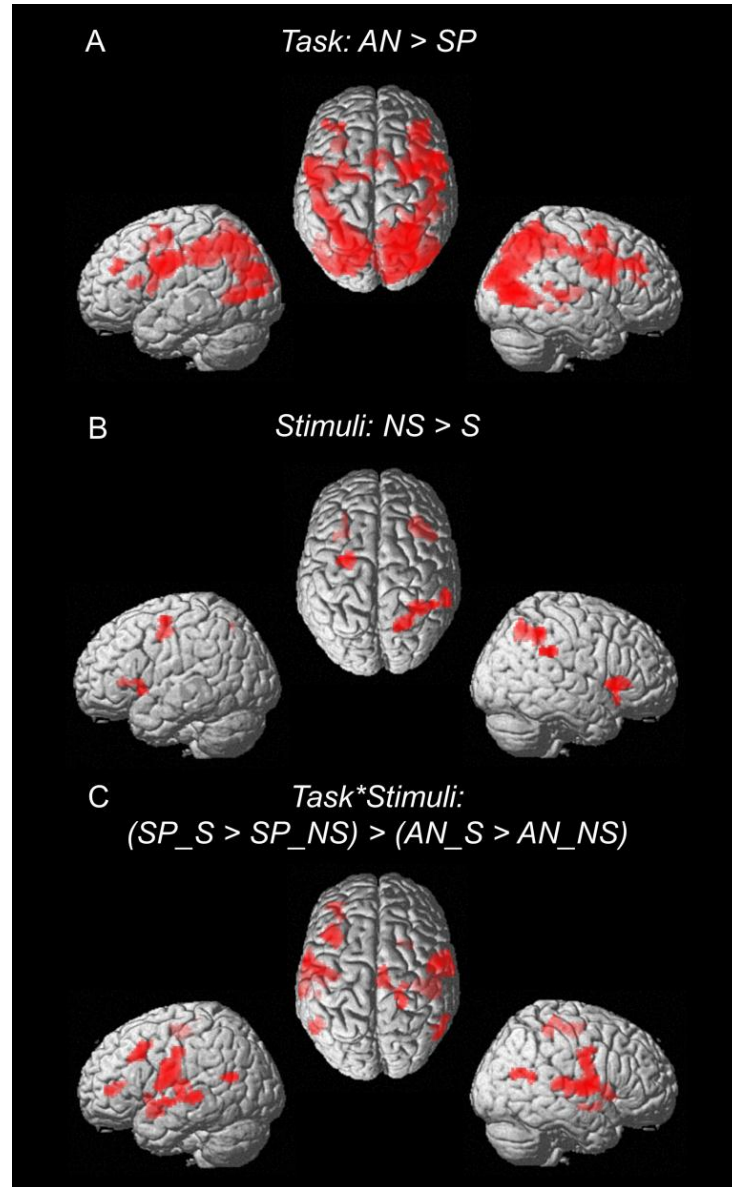
Figure 2.2 Neural activations. Suprathreshold activations are projected onto an MNI-normalized single-subject brain. (a) Regions associated with the Task main effect. (b) Regions associated with the Stimuli main effect. (c) Regions associated with the Task X Stimuli interaction.

*TASK X STIMULI Interaction*. We tested for the differential activity associated with the Specular (relative to Non-Specular) stimuli in Spatial (relative to Anatomical) imitation task [(SP_S-SP_NS)-(AN_S-AN_NS)]. We found a significant bilateral increase of activation of the parietal opercula, right inferior parietal cortex, postcentral gyrus, supplementary motor area and putamen, left inferior frontal operculum and inferior

frontal gyrus, left middle temporal gyrus and bilateral amygdala (see Figure 2c). The functional properties of these regions might reflect, as we predicted, an increase of neural activity when processing Specular, compared to Non-Specular, stimuli only during the Spatial imitation task (SP_S-SP_NS). Alternatively, these regions might exhibit increased neural activity when processing Non-Specular, relative to Specular, stimuli only during the Anatomical imitation task (AN_NS-AN_S). As only the activation of the former set of regions can be interpreted as due to anatomical compatibility of the moved and seen hand, we used the conjunction analysis to test which regions previously found associated with the interaction term were also associated with a specularity effect in the Spatial task  [(SP_S-SP_NS)-(AN_S-AN_NS)] ∩ (SP_S-SP_NS). This analysis implicated both the parietal opercula and right superior temporal gyrus. The Figure 3 displays the parameter estimates extracted from the clusters' local maxima, thus revealing how the opercula were most active during the anatomical imitation task (irrespective of the stimuli), and when specular stimuli were shown in the spatial imitation task.

Figure 2.3 Neural activations and parameter estimates extracted from the clusters' local maxima of the functional contrast testing the conjunction of the Task X Stimuli interaction and the simple effect (SP_S > SP_NS). Results are displayed onto a surface rendering and coronal (y= -6) section of an MNI-normalized single-subject brain. The surface rendering was obtained by removing the temporal lobes, thus allowing free vision of the surface of the parietal opercula.

We also investigated which regions exhibited a significant interaction term reflecting an increased BOLD signal during Anatomical imitation on Non-Specular stimuli [(SP_S-SP_NS)-(AN_S-AN_NS)] ∩ (AN_NS-AN_S): this analysis led to activation of right superior temporal and left middle frontal gyri. It should be mentioned that, a less

conservative threshold (e.g., 30 consecutive voxels) revealed as well the involvement of the right middle frontal gyrus (see Figure 4). We finally assessed for differential activity associated with the Specular (relative to Non-Specular) stimuli in Anatomical (relative to Spatial) imitation task [(AN_S-AN_NS)-(SP_S-SP_NS)]. We found no suprathreshold activation.
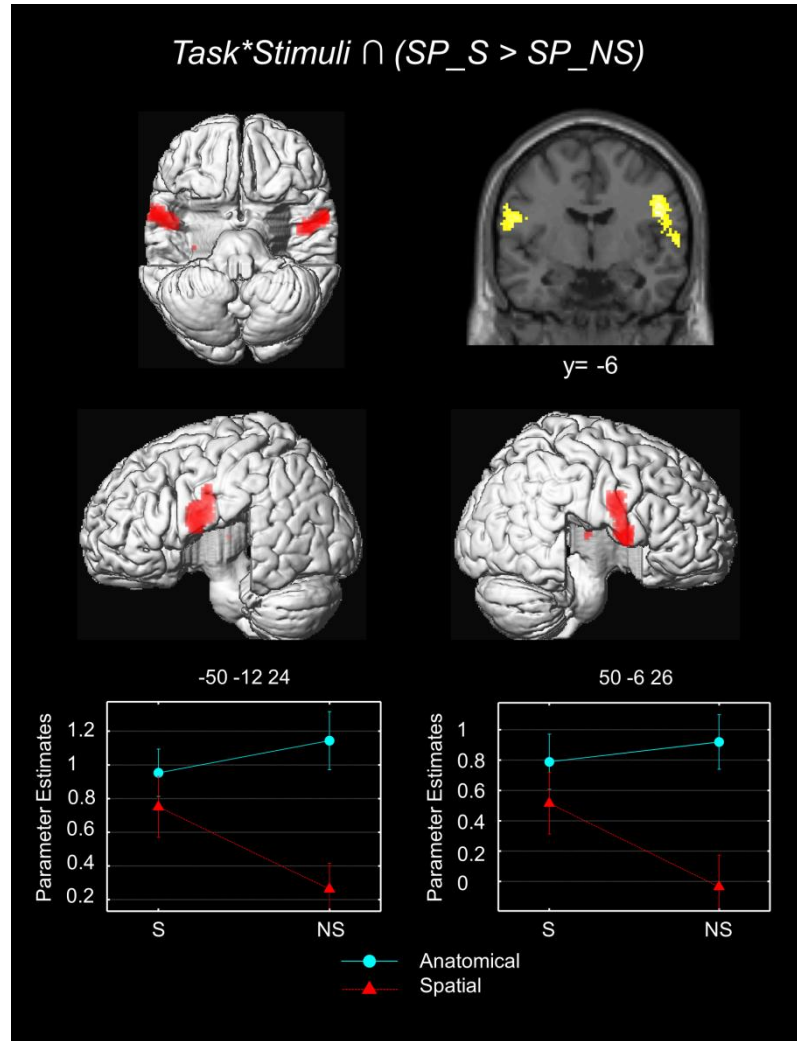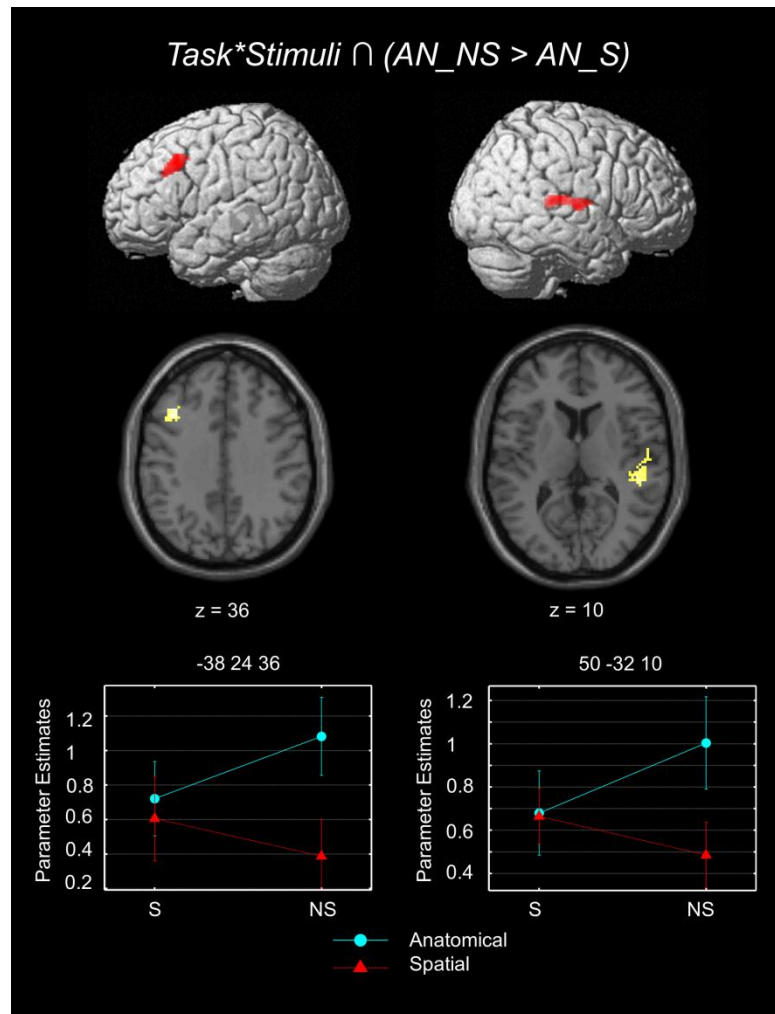


Figure 2.4 Neural activations and parameter estimates extracted from the clusters' local maxima of the functional contrast testing the conjunction of the Task X Stimuli interaction and the simple effect (AN_NS > AN_S). Results are displayed onto a surface rendering and axial (z = 36, z = 10) sections of an MNI-normalized single-subject brain.

*HAND X STIMULI Interaction*. The analysis of the interaction Hand X Stimuli showed an activation of the right lingual, right middle temporal and left superior occipital gyri when the stimuli were either Specular to a right moving hand, or Non-Specular to a left moving hand, that is when the stimuli depicted a left hand. Consistently, the left lingual gyrus, left cuneus and right superior occipital gyrus were associated to either stimuli Specular to a left moving hand, or Non-Specular to a right moving hand, i.e. a right hand stimuli. No suprathreshold activation was found for the Hand X Task interaction or in the three-way Hand X Task X Stimuli interaction.

### 2.4 Discussion

In the present study we used a paradigm that elicits automatic imitation to disentangle the neural correlates of the anatomical component of imitation from those associated with the spatial stimulus-response compatibility. Specifically, subjects were asked to move the finger that was either anatomically or spatially compatible with a visually-displayed finger movement. By asking participants to move a hand specular to the one displayed, we created a condition in which both tasks yielded to the same response, whereas by asking participants to move a hand non-specular to the one displayed we created a condition in which each task yielded to a different response.

Consistently with Bertenthal and colleagues (2006), we found that participants benefited from seeing Specular (relative to Non-Specular) hands: thus, in the Anatomical task, participants were faster when seeing a movement which was also spatially compatible, whereas in the Spatial task they were faster from seeing a movement which was also anatomically compatible.

The analysis of BOLD signal localized the imitative compatibility, based on the anatomical correspondence between model and performer, at the level of the parietal opercula bilaterally. These regions exhibited increased activation whenever the information about anatomical correspondence between seen and moved hand was accessed: during the Anatomical task in both Specular and Non-Specular conditions (where this information was explicitly accessed through task demands) and during the Spatial task, but only with the Specular stimuli (where implicit access to such

information was revealed by the behavioral data). Our results extend previous findings about the imitation of simple movements (Iacoboni et al., 1999; Brass, Zysset, von Cramon, 2001; Koski et al., 2003; Bien, Roebroeck, Goebel, Sack, 2009). More specifically, the activation of the parietal operculum has been reported in previous studies (Iacoboni et al., 1999; Koski et al., 2003), not only for finger movements, but also for imitation of limb movements (Chaminade, Meltzoff, Decety, 2005).

On the other hand, no region was significantly associated with the spatial compatibility effect.

Furthermore, we found that the right superior temporal sulcus, extending to temporo-parietal junction, and left middle frontal gyrus were recruited exclusively when participants engaged in the Anatomical task with Non-Specular stimuli. Finally, the Task main effect (Anatomical > Spatial) recruited an extensive bilateral fronto-parietal network, in line with behavioral data which describe the Anatomical task as the most time-consuming one, whereas the Stimuli main effect (Non-Specular > Specular) was associated with the activity of the right parietal cortex, bilateral insula and left precentral gyrus.

### 2.4.1 *When the anatomical information is relevant*

The anatomical component of imitation was associated with bilateral activation of the parietal opercula, involving cytoarchitectonical area OP 4 (Eickhoff, Schleicher, Zilles, Amunts, 2006; Eickhoff, Amunts, Mohlberg, Zilles, 2006) and extending to primary somatosensory and primary motor cortices (Brodmann areas, BA 3 and 4). The analysis of the beta values revealed that these regions were active in the SP_S condition as in the Anatomical task, whereas no modulation in the activation was found in SP_NS, that is the only condition in which the information about the anatomical identity between seen and moved fingers is neither task-relevant (as Anatomical task), nor affects participants' behavior (as in condition SP_S).

Electrophysiological research on the macaque brain (Burton, Fabri, Alloway, 1995; Krubitzer, Clarey, Tweedale, Elston, Calford, 1995) and neuroimaging imaging studies on humans (Disbrow, Roberts, Krubitzer, 2000; Eickhoff, Grefkes, Zilles, Fink,

2007), agree in describing the parietal operculum divided into distinct areas, among which the Secondary Somatosensory cortex and the Parietal Ventral Area (PV) processing tactile stimuli delivered to distinct body parts in a somatotopic fashion. In some recent studies, however, the parietal operculum has been implicated in processes which go beyond the mere sensitivity to tactile events, such as proprioceptive (Hari et al., 1998; Fitzgerald, Lane, Thakur, Hsiao, 2004; Hinkley, Krubitzer, Nagarajan, Disbrow, 2007) and motor coding (Iacoboni et al., 1999; Koski et al., 2003; Agnew & Wise, 2008; Bien, Roebroeck, Goebel, Sack, 2009), visual processing of sensorimotor activities in others (Avikainen, Forss, Hari, 2002; Keysers, Wicker, Gazzola, Anton, Fogassi, Gallese, 2004) or multisensory integration (Bremmer et al., 2001; Fitzgerald, Lane, Thakur, Hsiao, 2006a,b; Hinkley, Krubitzer, Nagarajan, Disbrow, 2007).

A close link between the activity of the parietal opecula and body perception and representation has also been suggested by imaging studies. For instance, Tsakiris and colleagues (2007) engaged participants in the rubber hand illusion, a paradigm in which participants feel one's hand being touched whilst seeing a replica of their hand being touched in a different spatial location. Although such experimental set-up usually gives participants the illusion of their hand being closer to the replica than it really is, the primary somatosensory cortex and the parietal operculum were most active in the cases in which participants are not affected by the incongruent visual input, and succeeded in keeping track of the real position of their hand. More recently, Corradi-Dell'Acqua and colleagues (2009) asked participants to perform a handedness task in which they assessed whether a visually-presented arm was right or left. Participants could accomplish the task by either comparing the arm to its position on a simultaneously-presented body shape (allocentric coding), or by ignoring the shape and comparing the arm to its homologous in their own body (intrinsic egocentric coding). The authors found the left parietal operculum active only during the egocentric coding, thus providing the evidence of opercular involvement in coding the representation of one's body even in absence of tactile stimulation (Corradi-Dell'Acqua, Tomasino, Fink, 2009).

Our data converge with, but also extend, findings from previous studies documenting the opercular's sensitivity in coding the relations between body parts.

Indeed, the majority of these studies focused on the integration of many sources of information arising from the same body (e.g, Bremmer et al., 2001; Fitzgerald, Lane, Thakur, Hsiao, 2006a,b; Hinkley Krubitzer, Nagarajan, Disbrow, 2007, Corradi-Dell'Acqua, Tomasino, Fink, 2009) rather than, as in the case of imitation, from homologous parts of distinct bodies. Chaminade and colleagues (2005) implicated the parietal operculum (together with parietal, prefrontal and insular structures) in imitation tasks and, in particular, in coding the body part that executes an action, and not the action itself. However, as for many studies testing imitation (see Introduction section), the design adopted by Chaminade and colleagues (2005) did not allow the authors to conclude whether their results reflected a real imitative compatibility between the seen and moved limb (which would be violated by responding with one's foot to a movement executed with a hand) or a spatial compatibility (which would be violated by responding to a hand a movement with a hand with the opposite spatial mapping). To the best of our knowledge, our study is the first to provide such control. Indeed, when accounting for spatial compatibility effects, it is only the parietal operculum who matches, for imitative purposes, the anatomical properties of one's body with the homologous properties of someone else's body.

Of crucial interest is also the subportion of the parietal operculum – i.e. cytoarchitectonic area OP 4 – which maximally exhibits our effect. Such region, presumably a human homologue of area PV in the macaque brain (Eickoff, Grefkes, Zilles, Fink, 2007), has been found associated with integrative sensory-motor processes in larger extent than other more somatosensory-oriented opercular subregions (Qi, Lyon, Kaas, 2002; Disbrow, Litinas, Recanzone, Padberg, Krubitzer, 2003; Kaas & Collins, 2003). Recently, a study of probabilistic tractography on diffusion tensor imaging data (Eickhoff et al., 2010) described OP 4 more strongly connected with the premotor and primary motor cortex than other opercular subportions (e.g., OP 1) which, instead, exhibited greater connectivity with anterior parietal cortex and thalamus. Our data, together with these tractography findings (Eickhoff et al., 2010), strongly suggest that OP 4 is a crucial interface point, in which the information about one's body orientation is compared with the orientation in space of the model's body.

Our study combines the neuroimaging findings obtained with paradigms investigating imitation (e.g., Iacoboni et al., 1999; Koski et al., 2003; Chaminade, Meltzoff, Decety, 2005) and spatial relation about body parts (e.g., Fitzgerald, Lane, Thakur, Hsiao, 2006a,b; Tsakiris, Hesse, Boy, Haggard, Fink, 2007; Corradi-Dell'Acqua, Tomasino, Fink, 2009) and better defines the role of the parietal operculum in the fronto-parietal imitation network. When spatial compatibility confounds are accounted for, the parietal operculum showed to be involved in coding the anatomical correspondence between parts of the model's body and similar parts in the body of the performer.

### 2.4.2 *When the spatial information is irrelevant*

The right inferior and superior parietal cortex, including the intraparietal sulcus, right supramarginal gyrus, bilateral anterior insula and left precentral gyrus were found to be active when participants processed Non-Specular (relative to Specular) stimuli, irrespective of the task performed. Furthermore, the middle frontal gyrus and the superior temporal sulcus extending to the temporo-parietal junction were found to be implicated in processing Non-Specular (relative to Specular) stimuli, but only when participants performed the Anatomical imitation task. Compared with Specular stimuli, non-Specular stimuli require additional control, as participants need to inhibit information which is task-irrelevant and might yield to an incorrect response. Such inhibition is not compulsory when Specular stimuli are shown, as the information, in principle task-irrelevant, might still lead to a correct response.

In agreement with our findings, many of these regions have been previously described to be active in SRC tasks, specifically in those conditions which (similarly to Non-Specular stimuli in our study) are associated with incompatible mapping between stimulus and response (e.g., Iacoboni, Woods, Mazziotta, 1996; Dassonville, Lewis, Zhu, Ugurbil, Kim, Ashe, 2001; Matsumoto, Misaki, Miyauchi, 2004; Schumacher, Cole, D'Esposito, 2007; Cieslik, Zilles, Kurth, Eickhoff, 2010). Similar activations were also associated with exertion of cognitive control, as documented by many studies showing their activity correlating with the performance of attention-demanding cognitive tasks

(Cabeza & Nyberg, 2000; Fox, Snyder, Vincent, Corbetta, Van Essen, Raichle, 2005). Furthermore, Corbetta and colleagues (2008) localized these regions as part of a network involved in the allocation of attentional resources, specifically in focusing the attention on the current goals, linking the stimulus to the correct response, coding the salience of task-relevant stimuli. Consistently, these regions have been previously isolated in the neuroimaging investigations in which Brass' paradigm has been employed (Bien, Roebroeck, Goebel, Sack, 2009; Brass, Derrfuss, von Cramon, 2005), specifically in those conditions in which the moved finger was incompatible with respect to the spatial cue.

Of crucial interest is the activation in the middle frontal gyrus and the superior temporal sulcus extending to the temporo-parietal junction, showing the highest activity in condition AN_NS, in which Non-Specular stimuli are displayed during the Anatomical imitation task. This is the only condition in which the anatomical compatibility between the observed and the seen hand is complete (participants imitate right hand movements with their own right hand and left hand movements with their own left hand) and the spatial mapping between participants' and the model's moved finger is detrimental to the task. Moreover this is the most difficult condition (see Table 1), although it should be reminded that the functional properties of the regions activated in this condition do not closely match the response time data (there is no difference in neural activity when comparing SP_NS and SP_S, see Figure 4), thus making the account of the temporal-frontal activity in our study as being due to task-difficulty unlikely.

One explanation of the functional role of the superior temporal sulcus and middle frontal gyrus suggests that these regions do not reflect the need to inhibit task-irrelevant features in general, but specifically information about the spatial mapping between stimulus and response.

In this perspective, our results are reminiscent of those in Bien's (2009) who found an involvement of the posterior portion of the superior temporal sulcus in the inhibition of the imitative response, even though, as only specular stimuli were used in their study, it is unclear whether the inhibited information pertained the spatial

component or anatomical component of such response. Our data are also in keeping with those of previous studies documenting portions of the superior temporal sulcus and temporo-parietal junction associated with the reorienting of the attention towards unattended spatial locations (Arrington, Carr, Mayer, Rao, 2000; Corbetta, Kincade, Ollinger, McAvoy, Shulman, 2000; Corbetta, Kincade, Shulman, 2002; Thiel, Zilles, Fink, 2004). Relevant to our issue are the findings reported in a recent study by Vossel and collaborators (2009) in which an association between the activation of the superior temporal sulcus specifically and the processing of spatial cues, but not of non-spatial cues, has been documented. The authors engaged participants in a Posner task in which both spatial and non-spatial (i.e. chromatic) irrelevant cues were presented: whereas regions such the intraparietal sulcus and the anterior insula were found active for any type of irrelevant information (both spatial and chromatic), the posterior portion of the superior temporal sulcus was specifically implicated in irrelevant spatial cues.

An alternative explanation of the functional role of the superior temporal sulcus and middle frontal gyrus deals with the role played by these regions in biological motion (Puce & Perrett, 2003; Thompson, Clarke, Stewart, Puce, 2005; Hein & Knight, 2008) and response selection (Cunnington, Windischberger, Robinson, Moser, 2006; Rowe & Passingham, 2001). Although all our experimental conditions require, at least in principle, the engagement of the neural structures involved in these processes, it is possible that a more sustained recruitment of these regions occurs when participants perform the Anatomical task. This is particularly true for AN_NS which requires also more processing of the displayed movement as biological than all other conditions.

Irrespective of the different interpretations of the neural underpinnings of condition AN_NS, our results unambiguously highlight the relevance of spatial compatibility effects in imitation, the absence of which yields not only to increases in execution time, but also to the additional recruitment of those neural structures involved in compensatory processes such as the inhibition of the spatial information or the enhanced coding of the seen displacement as a biological movement.

# Chapter 3

## THE IMITATIVE COMPATIBILITY IS CODED IN THE PARIETAL OPERCULA: EVIDENCE FROM DOUBLE-PULSE TMS[2]

### 3.1  Introduction

In recent years, at least 75 publications documented the phenomenon of automatic imitation (see Heyes, 2011, for a review). Two main theoretical backgrounds can be accounted for when investigating this phenomenon: the common coding and the Associative Sequence Learning (ASL).

According to common coding approach (Prinz, 1997; Hommel, Müsseler, Aschersleben, Prinz, 2001), within the more general ideomotor framework (Massen & Prinz, 2009), observing the effect of an action facilitates its execution because perception and action planning share the same representations. An alternative account is represented by the Associative Sequence Learning model proposed by Heyes and Ray (2000), that emphasizes the evolution of the connections between sensory and motor representations through associative learning. Both theoretical views consider automatic imitation as a phenomenon representative of more complex imitative behaviors and suitable to be implemented in simple experimental paradigms.

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[2] The present study has been accepted for publication in European Journal of Neuroscience [Mengotti P., Ticini L.F., Waszak F., Schütz-Bosbach S., Rumiati R.I. Imitating others' actions: transcranial magnetic stimulation of the parietal opercula reveals the processes underlying automatic imitation.]

In a series of behavioral studies, Brass, Bekkering, Wohlschläger and Prinz (2000) and Brass, Bekkering and Prinz (2001) provided evidence of a compatibility effect between executed and observed actions. In these studies, participants were faster when the executed movements, such as finger tapping or lifting, were triggered by a movement stimulus of the same type (e.g., tapping triggered by an observed tapping movement) than when they were triggered by the opposite type of movement (e.g., tapping triggered by an observed lifting movement). In some of these experiments, the observed and performed movements varied (i.e., tapping/lifting) while the finger moved was kept constant (index). In other experiments, observed and performed movements were kept constant (i.e., tapping/tapping or lifting/lifting), while the finger was varied (index or middle finger). In this latter case, the compatibility effect refers to the comparison between movements performed with the same (e.g., the model and the performer move the index finger, compatible condition) or with a different finger (e.g., the model moves the index finger and the performer moves instead the middle finger, incompatible condition). However, in all these experiments, the participants' responding hand was always specular to the left hand of the model (hence the right hand). As a consequence, also in the case of different finger movements compatible movements share the same spatial finger position, while incompatible movements have different spatial finger positions. Therefore, in most of these experiments, the compatibility effect could be attributed, at least in part, to a more general effect of spatial stimulus-response (S-R) compatibility.

As discussed in the previous chapters, some studies manipulated the spatial component to control for the general effect of the spatial S-R compatibility on the automatic imitation (Brass, Bekkering, Prinz, 2001, experiment 3; Heyes, Bird, Johnson, Haggard, 2005; Bertenthal, Longo & Kosobud, 2006; Press, Bird, Walsh, Heyes, 2008; Catmur & Heyes, 2011). Thus, we will refer to the effect of automatic imitation controlled for spatial compatibility as imitative compatibility (see also Catmur & Heyes, 2011; Boyer, Longo, Bertenthal, 2012).

Despite the fact that there is increasing evidence supporting the notion of an independency of imitative and spatial compatibility (Catmur & Heyes, 2011; Heyes,

2011; Boyer, Longo, Bertenthal, 2012), there are surprisingly few studies directly investigating the neurocognitive correlates of these components. Catmur, Walsh and Heyes (2009) used theta-burst TMS over the left inferior frontal gyrus and showed that the inactivation of this region disrupted the imitative compatibility effect.

In a recent fMRI study (see also Chapter 2 of this thesis), we found that, while the suppression of the tendency to imitate according to the spatial compatibility was associated with the activation of the left middle frontal gyrus and the right superior temporal sulcus, the parietal opercula bilaterally were activated in all conditions involving the anatomical matching between the model's and the performer's movements (Mengotti, Corradi-Dell'Acqua, Rumiati, 2012). This finding that the parietal opercula are activated in imitative tasks enriches our understanding of the functional role of this region, traditionally considered to be responsive to tactile stimuli (Burton, Fabri, Alloway, 1995; Krubitzer, Clarey, Tweedale, Elston, Calford, 1995; Eickhoff, Grefkes, Zilles, Fink, 2007).

The main aim of the present study was to clarify the role of the parietal opercula in processing the different components of imitation. Double-pulse transcranial magnetic stimulation allowed us to temporarily interfere with the activity of the parietal opercula while healthy participants performed finger tapping movements in response to observed tapping movements that were identical or different according to the spatial position or the anatomical identity of the finger. This paradigm is able to dissociate spatial and imitative compatibility effects (see also Mengotti, Corradi-Dell'Acqua, Rumiati, 2012). We predicted that the TMS would interfere with the activity of this region, thus selectively disrupting the imitative compatibility without affecting the spatial compatibility.

### 3.2 Materials and methods

#### 3.2.1 Participants

Twenty-three healthy individuals (aged between 19 and 35 years, mean age $26 \pm 4$ years, 9 females) participated in the study. All of them were native Italian speakers, they had

normal or corrected-to-normal visual acuity in both eyes, no neurological impairments and they were naïve to the purposes of the experiment. They were all right-handed, as assessed with the Edinburgh Handedness Inventory (Oldfield, 1971; mean laterality quotient 79+20) and gave written informed consent. The study was approved by the SISSA's Ethic Committee (Trieste, Italy) and conducted in accordance with the Declaration of Helsinki.

### 3.2.2 Task and procedure.

Participants were seated in front of a computer screen and their right hand was placed on a button-box for manual response. They observed five-frame video sequences presented on a black background, depicting a single tapping movement that could be performed either by a left (50% of the trials) or a right hand with the index (50% of the trials) or the ring finger (see Figure 3.1a-b). In each experimental trial, the first frame was presented for 500 ms, followed by three frames for 40 ms each depicting the intermediate positions of the finger and a final frame depicting the end position for 500 ms. Each trial was followed by an inter-trial interval of 5000 ms in which a black background was displayed. E-Prime 2 software (Psychology Software Tools, Pittsburgh, PA) was used for stimulus presentation and data collection. Reaction times (RTs) and accuracy data were collected, RTs being measured from the first 40 ms frame that followed the presentation of the first frame of 500 ms.

We asked participants to perform two tasks, in which they had to produce tapping movements similar to those performed by the hand stimulus. In the Anatomical Task, participants tapped with their right hand the finger that was anatomically compatible with the one moving on the screen: e.g., when the video displayed an index finger movement, participants had to tap their index finger, irrespective of whether the observed hand was a left or a right hand, thus whether the moved finger occupied the same or a different position in space relative to the observed moving finger. In the Spatial Task, participants had to tap with their right hand the finger that was spatially compatible with the one moving on the screen: e.g., when the observed finger movement occurred closer to the right side of the screen (as in case of a right hand tapping with its

index finger), participants had to tap using the finger closest to the same side, irrespective of its anatomical identity (i.e. the ring finger).

Participants were instructed to start the movement immediately as they became aware of which movement to perform. As participants' movement was not pre-instructed and totally dependent on the finger moved by the hand stimulus and the instructions of the task, no early start could occur.

When the observed hand was the mirror-image of the participants' hand, Anatomical and Spatial tasks triggered the same response. We labeled this condition as Specular. The condition in which Anatomical and Specular tasks triggered opposite responses was labeled Non-Specular.

The imitative compatibility is represented by the difference in RTs between Specular and Non-Specular conditions in the Spatial Task, whereas the spatial compatibility is represented by the difference in RTs between Specular and Non-Specular conditions in the Anatomical Task. This is of particular importance when considering that participants are always unaware of the effect of interest, which is exactly the opposite of the task they are performing (i.e. imitative compatibility embedded in the Spatial Task and vice versa).

The experimental design was 2 X 2 X 2 with TMS location [OP vs. Sham], Task [Anatomical vs. Spatial], and Stimuli [Specular vs. Non-Specular] as within subjects factors. The first two factors were blocked. The experiment consisted of six blocks, one for each Task in each anatomical location of TMS. The blocks were counterbalanced between subjects. There were 48 trials per block, for a total of 288 trials, with a pause every 12 trials. The experimental session lasted approximately 90 min.
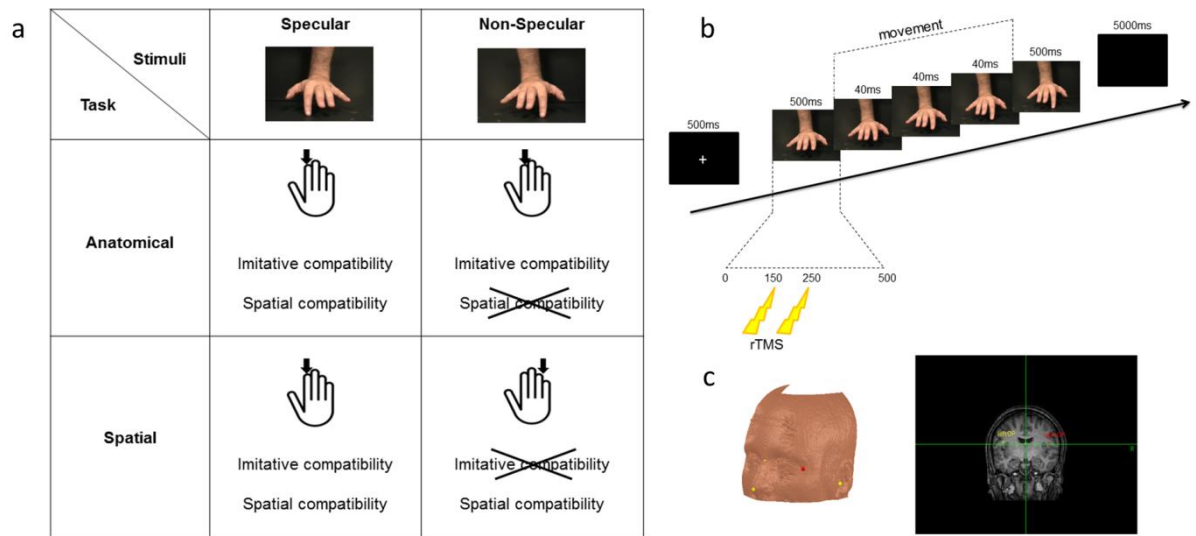
Figure 3.1 Experimental design and TMS protocol. **a.** Schematic representation of the four different conditions together with the appropriate finger movement. The presence or absence of the spatial and the imitative compatibility is shown for each condition. **b.** Timeline of the experiment. **c.** TMS neuronavigation. In the left part of the figure, anatomical landmarks are shown onto the skin reconstruction of one of the participants (yellow and red spots). In the right part of the figure, stimulated sites are shown onto a single participant's MRI scan.

### 3.2.3  TMS protocol

The sites of TMS interference for left and right OP were determined by using the Brainsight system (Rogue Research, Montreal, Canada). T1 structural MRI scans for each participant were used to define landmarks for coregisteration with the TMS coil and the actual position of the participant.  This procedure allowed to locate the target site of stimulation using MNI coordinates and the position of the TMS coil relative to the selected target site at millimeter precision level. The coil was mounted on an articulated arm while the participant's head and the TMS coil position was constantly tracked with an infra-red device (Polaris, Northern Digital, Ontario, Canada). MNI coordinates for the stimulation sites were x= -50 y= -12 z= 24 for the left OP and x= 50 y= -12 z= 24 for right OP, corresponding to cytoarchitectonical area OP4 (Eickhoff et al., 2010) and local maxima of a related fMRI study in which the same behavioral paradigm was used

(Mengotti, Corradi-Dell'Acqua, Rumiati, 2012). MNI coordinates were then converted into Talairach coordinates based on individual MRI scans. See Figure 3.1c.

Double-pulse TMS (Magstim Model 200 stimulators, Whitland, UK) was delivered with an interstimulus interval (ISI) of 100 ms by means of a 70 mm figure of eight stimulation coil. A stimulation paradigm with 100 ms ISI was chosen in order to elicit inhibitory effects on the activity of the target sites, based on previous findings (Chen, Wassermann, Caños, Hallett, 2007; Oshio, Tanaka, Sadato, Sokabe, Hanakawa, Honda, 2010). The first TMS pulse was delivered 150 ms after the onset of sample presentation. By stimulating 250 ms before the movement, we did not interfere with the production of the movement itself but with the coding of the anatomical information about body parts (see also Fiorio & Haggard, 2005, in which the same region was stimulated while participants performed a tactile task). Stimulation intensity was 120% of the resting motor threshold (rMT) for both pulses and ranged from 35% to 67% (mean 48+8%) of the maximum stimulator output. rMT was determined by delivering single TMS pulses at constant intensity on the optimal scalp position from which TMS-evoked twitch in the resting right hand was visually observed by one of the experimenters in at least 5 out of 10 trials. The optimal scalp position was detected by moving the coil positioned tangentially over the left motor cortex with the handle pointing backward and laterally 45° away from the midline.

During TMS stimulation, the coil was held tangential to the scalp, with the handle pointing backward. Participants were provided with earplugs to block the noise produced by the stimulating coil.

No discomfort or adverse effects during TMS were reported by participants. In the sham condition, the coil was held perpendicularly to the surface of the scalp over the vertex, in order to mimic the noise and the mechanical vibration of TMS but no magnetic stimulation actually reached the scalp.

*3.3 Results*

We first checked whether each participant showed a compatibility effect for the Spatial and the Anatomical Task in the sham condition. The compatibility effect is defined as the

difference in RTs between the Specular and the Non-Specular conditions. We excluded participants who showed a strong inversion of the compatibility effect for the Spatial or the Anatomical Task, using the analysis for outliers inbuilt in SPSS software. Outliers were defined as data points larger or smaller than 1.5 times the interquartile range (IQR) from the upper or lower limit of the IQR.

Following this criterion, three participants were outliers (one for the compatibility effect in the sham condition for the Anatomical Task, two participants for the Spatial Task) and therefore they were excluded from the further RTs and accuracies analysis. This exclusion procedure is essential for the aim of our study: indeed the presence of the imitative and the spatial compatibility effect in the Sham condition is necessary in order to test the modulation of the effect due to the disruption of the activity in the parietal opercula. The data during left and right OP TMS stimulation were collapsed for the first analysis in order to investigate the general contribution of this region in coding the two types of compatibility, in line with the previous fMRI data collected by our group using the same paradigm (Mengotti, Corradi-Dell'Acqua, Rumiati, 2012). However, to investigate more in depth putative differences in the role of the left and right OP, we reported an additional analysis in which data from left OP are directly compared with data coming from the right OP. Statistical analyses were performed with SPSS 11.5 software.

### 3.3.1 Accuracy rates

The analysis of accuracy showed an average percentage of correct responses over all conditions of 95%.

A 2x2x2 repeated measures ANOVA on correct responses revealed only a significant main effect of Stimuli ($F_{(1,22)} = 6.6$, $p < 0.05$, $\eta_p^2 = 0.232$), with responses to Non-Specular stimuli being more prone to errors than those to Specular stimuli (93% vs 96%).

Accuracy rates (in % of correct responses) are presented in Table 1 for each condition. Note that the only condition that seems to be different from the others is the

Non-Specular condition in the Spatial task. This suggests that the TMS interference over the OP diminishes the interference of the anatomical information when participants are asked to move their finger according to the spatial position of the hand stimulus' fingers, thus diminishing the effect of imitative compatibility and facilitating the performance on the Spatial task.

Table 3.1 Mean accuracy rates (in % of correct responses and SEM, standard error of the mean) for the spatial and the imitative compatibility in the two TMS locations are shown.

| | | Spatial compatibility | | Imitative compatibility | |
|---|---|---|---|---|---|
| **TASK** | | Anatomical | | Spatial | |
| **TMS LOCATION** | | OP | Sham | OP | Sham |
| **STIMULI** | Specular | 96 (1.3) | 96 (1.7) | 96 (1) | 95 (2) |
| | Non-Specular | 92 (2) | 93 (2) | 96 (1.1) | 93 (2) |

*3.3.2 Response times*

Mean RTs and standard errors of the mean (SEM) for each condition are reported in Table 3.2 and Figure 3.2.

RTs were significantly different between the Anatomical and Spatial Task, with the Anatomical Task having longer RTs than the Spatial Task (main effect of Task in a 2x2x2 ANOVA with all 23 participants, $F_{(1,22)} = 25.8$, $p < 0.001$, $\eta_p^2 = 0.54$), therefore the two tasks were considered separately in the following analysis.

Table 3.2 Mean RTs (SEM, standard error of the mean) in ms and compatibility effect size (in ms) for the spatial and the imitative compatibility effects in the two TMS locations are shown.

| | | Spatial compatibility | | Imitative compatibility | |
|---|---|---|---|---|---|
| **TASK** | | Anatomical | | Spatial | |
| **TMS LOCATION** | | OP | Sham | OP | Sham |
| **STIMULI** | Specular | 427.2 (43.6) | 410 (34.2) | 357.5 (31.2) | 356.3 (31.9) |
| | Non-Specular | 454.4 (40.2) | 450.5 (34.2) | 366.8 (30.5) | 376.8 (32.5) |
| | Compatibility effect | 27.2 | 40.5 | 9.4 | 20.4 |
| | Compatibility effect reduction | | 13.2 (32.7 %) | | 11.1 (54.2 %) |

Note: in brackets, the reduction of the compatibility effect in percentage due to the TMS is shown.

Figure 3.2 Mean RTs (in ms) as function of the TMS location (OP vs. Sham) and Stimuli for the spatial and imitative compatibility are shown. Note that for the Imitative compatibility the TMS over the OP reduced the compatibility effect relative to Sham, showing a significant TMS location X Stimuli interaction. Vertical bars represent the standard error of the mean (SEM).

### 3.3.2.1 Spatial compatibility

For the Anatomical Task, mean RTs of each condition for each participant were entered in a 2x2 repeated measures ANOVA with TMS location (OP vs. Sham) and Stimuli (Specular vs Non-Specular) as factors. There was a significant main effect of Stimuli ($F_{(1,21)} = 23.5$, $p < 0.001$, $\eta_p^2 = 0.529$) with responses being faster in Specular trials (418.6+38.6 ms, SEM) than in Non-Specular trials (452.4+36.8 ms). Neither the main effect of TMS location, nor the TMS location X Stimuli interaction was significant.

### 3.3.2.2 Imitative compatibility

As for the Spatial Task, mean RTs of each condition for each participant were entered in a 2x2 repeated measures ANOVA with TMS location (OP vs. Sham) and Stimuli (Specular vs. Non-Specular) as factors. There was a significant main effect of Stimuli ($F_{(1,20)} = 21.5$, $p < 0.001$, $\eta_p^2 = 0.518$) with responses being faster in Specular trials

(356.9+31.2 ms, SEM) than in Non-Specular trials (371.8+31.2 ms). No significant effect was found concerning the main effect of TMS location.

Interestingly a significant TMS location X Stimuli interaction was found ($F_{(1,20)}$ = 4.4, p <0.05, $\eta_p^2$ = 0.182), suggesting a selective modulation of the imitative compatibility by TMS on the OP region with respect to the Sham condition. Post hoc comparisons (Bonferroni's test, $\alpha$ <0.05) revealed that whereas a significant difference between Specular and Non-Specular stimuli was found in the Sham (p <0.0005), the same difference was not found when TMS was applied over the OP (p =0.12), suggesting that the imitative compatibility is removed when TMS is applied over the OP.

### 3.3.3 Reaction times on left and right OP

To further investigate the differential contribution of the left and right OP in coding the spatial and the imitative compatibility, we performed two 2x2 repeated measures ANOVAs on mean RTs associated with the left and right OP. As to the spatial compatibility, the 2x2 ANOVA with factors TMS location (L OP vs. R OP) and Stimuli (Specular vs. Non-Specular) showed only a main effect of Stimuli ($F_{(1,21)}$ = 22.2, p <0.001, $\eta_p^2$ = 0.513), with responses being faster in Specular trials (421.5+40.3 ms, SEM) than in Non-Specular trials (453.1+37.9 ms). Neither the main effect of TMS location nor the TMS location X Stimuli interaction was significant, suggesting that there was no difference between left and right OP. As to the imitative compatibility, the 2x2 ANOVA with factors TMS location (L OP vs. R OP) and Stimuli (Specular vs. Non-Specular) showed only a main effect of Stimuli ($F_{(1,20)}$ = 17.3, p <0.001, $\eta_p^2$ = 0.464), with responses being faster in Specular trials (357.1+31.2 ms, SEM) than in Non-Specular trials (369.8+30.6 ms). Neither the main effect of TMS location nor the TMS location X Stimuli interaction was significant, suggesting that, similarly to the spatial compatibility, left and right OP do not differ in coding the imitative compatibility.

In Figure 3.3 the mean RTs for each condition of the two tasks are shown: the pattern in the data is similar for left OP and right OP. Based on the available data no conclusions can be drawn concerning a differential contribution of the two parietal opercula in processing of the two types of compatibility.

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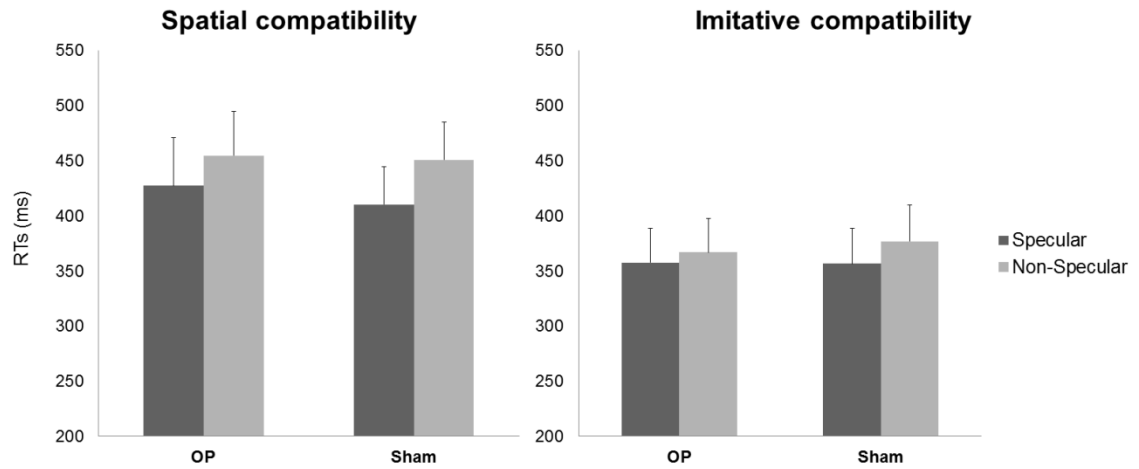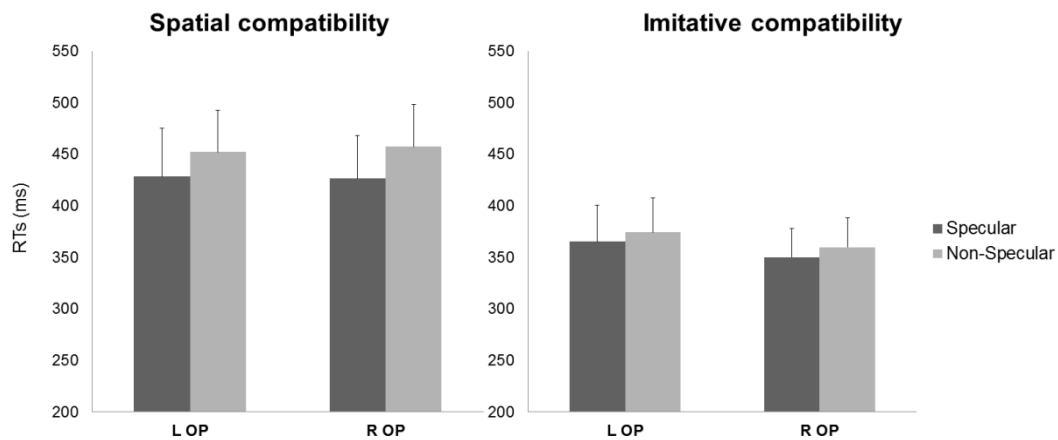
Figure 3.3 Mean RTs (in ms) as function of the TMS location (L OP vs. R OP) and Stimuli for the spatial and imitative compatibility are shown. Vertical bars represent the standard error of the mean (SEM).

## 3.4 Discussion

In the present study we used double-pulse TMS to temporarily interfere with the activity of the parietal opercula in order to investigate their role in the modulation of the imitative compatibility. When TMS was applied over the parietal opercula, we found a selective reduction of imitative but not of spatial compatibility.

The participant moved the finger that was either anatomically or spatially compatible with the observed finger movement, that could be either specular (i.e., a left hand stimulus, seen as in a mirror) or non-specular (i.e., right hand stimulus). In the Specular condition, the participant's finger was always anatomically and spatially compatible with the observed finger, independently of the task while in the Non-Specular condition, the participant's finger was compatible either anatomically or spatially with the observed finger, depending on the task. The imitative compatibility effect corresponds to the difference in RTs between the Specular and Non-Specular conditions in the Spatial Task, while the spatial compatibility effect corresponds to the difference in RTs between the Specular and Non-Specular conditions in the Anatomical Task. Imitative compatibility was modulated by TMS over the parietal opercula, as demonstrated by the significant interaction between TMS location and Stimuli (Specular

and Non-Specular): relative to the Sham condition, the imitative compatibility was reduced by about 54% when the activity in this region was temporarily disrupted. However, as for spatial compatibility, TMS location and Stimuli did not interact. These results suggest a selective influence of TMS on imitative compatibility.

*3.4.1 Are imitative and spatial compatibility based on independent mechanisms?*
It has been widely debated whether automatic imitation is independent from spatial compatibility. Automatic imitation can be considered as a special instance of stimulus-response compatibility (Brass, Bekkering, Wohlschläger, Prinz, 2000) in which the performance of the participant is modulated by the anatomical or topographical correspondence between his movement and the task-irrelevant action of the model (Heyes, 2011). However, some behavioral studies dissociated automatic imitation (Brass, Bekkering, Prinz, 2001; Bertenthal, Longo, Kosobud, 2006; Press, Bird, Walsh, Heyes, 2008; Catmur & Heyes, 2011) from spatial compatibility.

The question is whether the two effects reflect a unique or two different cognitive processes. Along the lines of the ASL theory, Catmur and Heyes (2011) argued in favor of a unique process based on associative learning. On this account, the empirical dissociation between imitative and spatial compatibility and the differences in the time course of the two effects that they have also found, is due to differences in processing the stimuli, faster and easier for the side of space in the spatial compatibility and a slower and more complex for body parts moving in space in the imitative compatibility.

However, Boyer and colleagues (2012) tested two different connectionist models (Sauser & Billard, 2006) against each other, one based on a single mechanism underlying imitative and spatial compatibility and the other based on two different mechanisms. The latter model predicts that if participants are asked to respond to the opposite of the stimulus cue, a reverse compatibility effect for the spatial compatibility should appear, as previously reported for the Simon effect (Simon, 1969; Simon, Sly, Vilapakkam, 1981). However, if the imitative compatibility is based on a different mechanism, the inversion should not appear. Boyer and colleagues (2012) observed the inversion of the effect for the spatial compatibility, but not for the imitative compatibility. The results, thus,

provide evidence not only for a dissociation of the behavioral effects but also for the independence of the cognitive processes associated with them. The current study corroborates this independent-processes account.

### 3.4.2 *Neural substrates of imitative compatibility*

While to date there is ample behavioral evidence of imitative compatibility, to the best of our knowledge, there are only a few studies that directly investigated its neural correlates. Using fMRI, frontal and parietal regions have been found active when participants observed a finger movement and when they performed the same action (Iacoboni et al., 1999; Koski et al., 2003). These activations have been interpreted in terms of a human mirror neurons system, analogous to that found in the macaque monkey's brain, with premotor and parietal neurons firing when the animal observes an action as well as when it performs it (see Rizzolatti, Sinigaglia, 2010, for a review). Thus, it has been proposed that this human mirror neuron system could represent the neural substrate of imitation (Heyes, 2011; Iacoboni et al., 1999; Koski et al., 2003). However, in the above mentioned imaging studies, imitative compatibility was not disentangled from spatial compatibility.

In a recent fMRI study performed by some of us (Mengotti, Corradi-Dell'Acqua, Rumiati, 2012), a paradigm suitable to disentangle imitative from spatial compatibility led to bilateral activation of the parietal opercula in all conditions in which an anatomical matching between model and performer was present. This finding is fully corroborated by the present study, in that it shows that the imitative compatibility effect is attenuated when interfering by means of TMS with the activity of this region.

Similar behavioral results have been reported before by Catmur, Walsh and Heyes (2009) but in association with a different anatomical region. The authors showed how inactivating by theta-burst TMS the left inferior frontal gyrus, but not the posterior parietal cortex (or in the sham condition), disrupted the imitative compatibility effect. These two regions - the inferior frontal gyrus and the parietal opercula - are likely to be part of the same network that supports imitation particularly when the anatomical matching is required.

Furthermore, Alaerts, Swinnen and Wenderoth (2009) showed that the stimulation by means of single-pulse TMS over the primary motor cortex enhanced MEPs in the muscle that was involved in the action observed by the participant, even if the direction of the movement was different, suggesting a preference of the motor system for the anatomical rather than the spatial matching. Our results suggest that this type of anatomical matching should occur in a previous stage of processing in the region of the parietal opercula, which are in strict connection with parietal and premotor and motor areas (Eickhoff et al., 2010).

### 3.4.3 *The parietal operculum and connections with body representations*

The region of the parietal operculum has been extensively described by Eickhoff and colleagues (Eickhoff, Grefkes, Zilles, Fink, 2007; Eickhoff et al., 2010) in terms of cytoarchitecture and connectivity. This region is considered to be analogous to two different areas of the macaque monkey's brain, the Secondary Somatosensory cortex and the Parietal Ventral Area, processing tactile stimuli with a somatotopic code (Burton, Fabri, Alloway, 1995; Krubitzer, Clarey, Tweedale, Elston, Calford, 1995; Eickhoff, Grefkes, Zilles, Fink, 2007). However, the involvement of the parietal operculum is not limited to tactile events, but it has also been associated with motor coding and imitation (Iacoboni et al., 1999; Koski et al., 2003; Chaminade, Meltzoff, Decety, 2005; Agnew & Wise, 2008; Bien, Roebroeck, Goebel, Sack, 2009) and with the processing of body representations, in particular the body schema (Corradi-Dell'Acqua, Tomasino, Fink, 2009).

In a study of probabilistic tractography on diffusion tensor imaging data, Eickhoff and colleagues (2010) showed that a subportion of the parietal operculum, named OP 4, is strongly connected with premotor and primary motor cortex, suggesting an interaction with the motor system. We argue that the parietal operculum can be considered as a crucial interface point, in which during imitation the information about the body part in space of the model is compared with the orientation in space of the body of the performer. It is worth noticing that this region has also been associated with the

processing of the body schema, thus suggesting a connection of the imitation network with the body representations (Corradi-Dell'Acqua, Tomasino, Fink, 2009).

Similarly, Forss and colleagues (2012) showed that the activation of the parietal operculum correlated with hand motor recovery in stroke patients. These data support the notion of a continuous interaction of this region with sensory and motor systems, and thus suggests that the parietal operculum is important in mediating modulatory afferent input to motor cortex.

# Chapter 4

## THE ROLE OF THE MODEL AND THE EMOTIONAL CONTEXT IN AUTOMATIC IMITATION: AN FMRI STUDY[3]

*4.1 Introduction*

As extensively described in Chapter 1, according to the common coding theory (Prinz, 1997) the observation of an action facilitates the production of the same action. On this account, imitation is achieved by activation of motor representations through action observation; the ease with which a stimulus is transformed into an action would depend on the similarity between the observed and the executed action (see Brass, Bekkering, Wohlschläger, Prinz, 2000).

There is now increasing evidence that, in humans, action observation and imitation share a broad network of brain regions, including the inferior frontal gyrus, the ventral and dorsal premotor cortex, and the superior and inferior parietal lobes (see Brass & Heyes, 2005, for a review).

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[3] The present study is published in Brain Research [Crescentini C., Mengotti P., Grecucci A., Rumiati R.I. (2011) The effect of observed biological and non biological movements on action imitation: An fMRI study. *Brain Research*, 1420: 80-92.]

Consistent with the view that imitation relies on shared representations for perceived and executed actions, it has been shown that the mere observation of biological actions (e.g., realistic actions performed by a human agent) is especially effective in activating the fronto-parietal network abovementioned, possibly because this type of actions is already present in the imitator's motor repertoire (e.g., Stevens, Fonlupt, Shiffrar, Decety, 2000; Perani et al., 2001; Tai, Scherfler, Brooks, Sawamoto, Castiello, 2004). Likewise, several behavioral studies have reported larger visuomotor priming effects (i.e., the generation of motor activation by visual stimuli) for biological stimuli (such as moving hands or limbs) compared with non biological stimuli (such as moving objects or robotic limbs), hence suggesting that human perception–action coupling may be tuned to biological actions (e.g., Brass, Bekkering, Prinz, 2001; Castiello, Lusher, Mari, Edwards, Humphreys, 2002; Press, Bird, Flach, Heyes, 2005; Press, Gillmeister, Heyes, 2006, 2007; Bird, Leighton, Press, Heyes, 2007; Jonas et al., 2007; Liepelt & Brass, 2010; but see Gazzola, Rizzolatti, Wicker, Keysers, 2007; Newman-Norlund, Ondobaka, van Schie, van Elswijk, Bekkering, 2010, for a different account). Furthermore, behavioral studies have reported specific interference effects of observed movements on action execution (Kilner, Paulignan, Blakemore, 2003; Kilner, Hamilton, Blakemore, 2007). In particular, in Kilner and colleagues (2003), the interference was only found when observed movements were incompatible with the executed movements and the former were performed by a biological model, compared with a non biological model. The interference was held to be mediated by an activation of the parietal and premotor cortices, namely of a common neural network that would encode both observed and executed movements and respond preferentially to biological actions.

The preference in imitation for the biological model follows directly the evidences on imitative compatibility (Brass, Bekkering, Prinz, 2001, experiment 3; Heyes, Bird, Johnson, Haggard, 2005; Bertenthal, Longo, Kosobud 2006; Press, Bird, Walsh, Heyes, 2008; Catmur & Heyes, 2011), that, unlike the pure stimulus-response compatibility, is supposed to emerge when the anatomical correspondence between model and performer is present.

To the best of our knowledge, no past fMRI study has been designed to investigate the neural correlates of the interference effect of observed biological and non biological movements on automatic imitation. In the present fMRI study we used a paradigm similar to that employed by Brass and colleagues (2001, experiment 2). We compared patterns of activation observed when participants executed finger movements (e.g., tapping) after having observed either a hand or a moving dot (biological/non biological movement) performing compatible (i.e., tapping or downward movements for biological and non biological movements, respectively) or incompatible movements (lifting or upward movements, respectively). Our main prediction concerned the interaction term testing for areas more active when participants saw biological model compared with non biological model and performed compatible movements vs. incompatible movements. Activation in the parietal and motor/premotor regions would suggest that observed biological movements affect action production, by facilitating the execution of compatible movements and/or interfering with the execution of incompatible movements.

We also aimed at examining whether the type of emotional facial expression presented before the observed movement influences imitative responses. In a previous study (Grecucci, Buiatti, Balaban, Budai, Rumiati, 2009; Grecucci, Koch, Rumiati, 2011), some of us examined how emotional pictures, presented as primes, affect imitative tendencies using a Brass' (2001) modified automatic imitation paradigm. The key result was that when seen index finger movements (tapping or lifting) and pre-instructed finger movements (tapping or lifting) were the same (tapping–tapping or lifting–lifting, compatible trials), subjects were faster than when they were different (lifting–tapping or tapping–lifting, incompatible trials). This compatibility effect was enhanced when the seen finger movement was preceded by negative primes compared with positive or neutral primes; we proposed that this could be due to negative stimuli being particularly effective in rapidly preparing the organismfor actions in potential flight-or-fight situations (Grecucci, Koch, Rumiati, 2011).

In the present study, we used instead facial expressions (neutral, sad and angry) because of their known role in inducing empathic and imitative reactions (e.g., Carr,

Iacoboni, Dubeau, Mazziotta, Lenzi, 2003), and predicted that participants would show a stronger imitative tendency following sad but also neutral facial expressions than angry facial expressions. This is because while we are inclined to empathize with a person expressing sadness (Blair, Morris, Frith, Perrett, Dolan, 1999; Blair, 2003), we are not likely to do so with a person expressing anger: the former case elicits prosocial behavior and may involve mirroring the expression (Chakrabarti, Bullmore, Baron-Cohen, 2006), while the latter can be perceived as a threat and thus trigger avoidance behavior in the observer (e.g., Pichon, de Gelder, Grèzes, 2008, 2009; see also social response reversal, Blair, Morris, Frith, Perrett, Dolan, 1999; Blair, 2003).

Premotor and motor areas were found to be robustly activated when participants observed emotional facial expressions, in particular in the imitative condition (Carr Iacoboni, Dubeau, Mazziotta, Lenzi, 2003); however, based on their study, it is not possible to establish the contribution of the different expressions presented or their effects on imitative responses as they were not measured. Nevertheless, it was later showed that empathy may rely on a perception–action mechanism that shares with hand imitation a common neural network involving motor/premotor brain regions (Leslie, Johnson-Frey, Grafton, 2004).

As far as the brain activations are concerned, we expected the activity of parietal and motor/premotor regions during imitation of biological vs. non biological movements to be particularly influenced by an emotional context promoting empathy (i.e. with sad and neutral facial expressions).

*4.2 Materials and methods*

*4.2.1 Participants*

Nineteen healthy volunteers (10 females, 24.6 ± 3.7 years) participated in the study. All participants had no existing neurological or psychiatric illness. All but one were right-handed, as assessed with the Edinburgh Handedness Inventory (Oldfield, 1971; mean laterality quotient: 71.5, range: -67/100). All participants gave written informed consent, and the study was approved by the Ethics Committee of the "E. Medea" Institute.

*4.2.2 Stimuli and design*

In the present experiment, we modified the overall paradigm of Brass and colleagues (2001) in three ways. First, similarly to their experiment 2, participants were pre-instructed to either lift or tap the index finger when they saw tapping and lifting finger movements on the screen (biological model) or a white dot moving upward (mimicking a lifting movement) or downward (mimicking a tapping movement) on the screen (non biological model). The white dot stimuli were obtained by superimposing a small white circle (1 cm of radius) on the index fingertip of the animated hand frames; after this was done, the hand itself was removed. The final stimuli consisted of a sequence of five frames containing each a white dot and presented as in the case of the moving hand: in the first frame the dot was at the center of the screen while the following four frames successively displaced the dot moving either upward (lifting-like movement) or downward (tapping-like movement) on the screen (see also below). Thus, the trajectory and the velocity of the two movements (biological and non biological) were exactly the same.

Second, prior to the stimulus movement we presented facial expressions that varied for emotional valence (angry, sad, and neutral). Third, unlike Brass and colleagues, who had participants respond to the onset of the presented finger movement, in our study participants responded at movement offset. It has become a standard procedure in imitation studies to ask participants to not respond until the stimulus movement has reached completion (e.g., Rumiati & Tessari, 2007).

Each experimental trial consisted of the following succession of events (Figure 4.1): an attention cue (fixation cross) presented for 500 ms in the middle of the screen, a facial expression presented for 1000 ms, a digitized video-sequence of 1120 ms consisting of five frames showing either an animated hand or a moving dot performing a lifting or a tapping movement (or a downward and an upward movement), and an interstimulus interval of variable duration consisting of a blank screen (jitter of 3000-6000 ms). Pictures of facial expressions with Neutral (N = 20), Sad (N = 20) and Angry (N = 20) emotional valence were selected from the NimSet collection of facial expressions (http://www.macbrain.org/resources.htm; see also Tottenham et al., 2009)

and were presented prior to the stimulus movement. Each facial expression was presented twice in the experiment in two different fMRI-runs. As mentioned above, each video depicting a moving hand or a moving dot consisted of five different frames. The first frame lasted for 500 ms and was identical for the tapping and lifting finger movements, as well as for the upward and downward dot movements, and it depicted either a still hand or a still dot in the middle of the screen. The following three frames lasted for about 40 ms each and displaced the finger or the dot either upward (lifting movement) or downward (tapping movement) in the screen. The last frame showed the final position of the finger or of the dot and lasted for 500 ms. The animated hand mirrored the orientation of the subject's right hand. See Figure 4.1A.

Participants were asked to perform a pre-instructed movement for an entire block of trials, independently of whether the observed movement was tapping or lifting (or downward and upward). There were blocks of trials in which participants performed finger-tapping and others in which they were required to execute finger-lifting (see the experimental procedure for more details). In some blocks, the observed movement was executed by a biological model (i.e. hand) while in other blocks it was performed by a non biological model (i.e. dot). Thus, in each block there were compatible trials, occurring when seen and performed movements were the same (e.g., tapping-tapping or downward-tapping), and incompatible trials when seen and performed movements were different (e.g., lifting-tapping or upward-tapping). Although we collected participants' responses for both lifting and tapping movements, the data reported here only relate to tapping movements. Importantly, subjects were required to perform one single movement for every trial (either tap or lift) and to begin moving only when the observed hand or dot movement reached completion. This was specifically done to better assess the neurocognitive mechanisms associated to each single response as well as to reduce the influence of habituation effects potentially arising from repeated tapping-lifting movements (Grecucci, Buiatti, Balaban, Budai, Rumiati, 2009; Grecucci, Koch, Rumiati, 2011).

*4.2.3 Experimental procedure*

The experimental procedure involved 240 trials in total which were organized into 2 fMRI runs of 120 trials each. Each fMRI run was divided into four blocks of 30 trials each depending on the pre-instructed movement the participants were required to execute (lifting blocks or tapping blocks), and on whether the observed movement was executed by a biological model or a non biological model (biological blocks and non biological blocks). Presentation order of the blocks was fixed and, for 10 participants, it was: biological-tapping; non biological-lifting; biological-lifting; non-biological-tapping for the first fMRI run and: non biological-lifting; biological-tapping; non-biological-tapping; biological-lifting for the second fMRI run. The order of the two fMRI runs was reversed for the remaining 9 participants. Each block of 30 trials contained an equal number (N = 10) of neutral, sad, and angry facial expressions, as well as an equal number (N =15) of compatible and incompatible trials. The latter were equally distributed across the three different types of facial expression. As already mentioned, each facial expression was repeated twice in the experiment, once in each run. Moreover, each of them was used in two totally different types of block (e.g., a given neutral expression was used in a biological-tapping block in the first run and in a non-biological- lifting block in the second run). The order of trials was randomized within each block. Fixation blocks of 15 sec each were added at the beginning, at the end, and between blocks of each run. The fixation cross appeared in the middle of the screen during these blocks and subjects were required to keep fixating for the entire duration of the block. Before each block of trials, an instruction appeared on the screen warning the participants about the upcoming block of trials. Each instruction disappeared from the screen and the relative block of trials started only when participants pressed the button associated with the specific block of trials. Two buttons of a response-pad were used in the experiment. One button was associated with lifting movements and another was associated with tapping movements. RT and accuracy of both tapping and lifting movements were recorded (only the data referred to tapping movements are reported here). In particular, participants' responses were recorded from the onset of the last frame of the video-sequence until they pressed (tapping) or released (lifting) the appropriate button on the response-pad or until 3.5 sec

with no response had passed. Participants had to press (tapping) or release (lifting) each button with the index finger of their right hand.

Before the fMRI scanning, participants practiced the tasks for approximately 5 min outside the scanner room. Participants were first explained the test and then presented with four mini-blocks of six trials each. The order of the blocks was: biological-tapping; non biological-lifting; biological-lifting; and non biological tapping. The same procedure used in the practice phase was also employed in the fMRI phase except that the facial expressions used during practice were different from those used during fMRI. In particular they were classified as having a "calm" expression in the NimSet battery. The fMRI session lasted approximately 32 min (two fMRI runs of 16 min each).

### 4.2.4 fMRI methods: acquisition and processing

Images were acquired using a 3-T MRI scanner (Achieva 3.0T Philips Medical Systems, Netherlands) equipped with a standard quadrature head coil and for echo-planar imaging (EPI). Head movement was minimized by mild restraint and cushioning. Thirty-four slices of functional MR images were acquired using blood oxygenation level-dependent (3.59 x 3.59 mm, 4 mm thick, repetition time = 2 s, time echo = 35 ms; flip angle: 90; field of view, FOV: 23 cm x 23 cm, acquisition matrix: 64x64; SENSE factors: 2 in anterior-posterior direction), covering the entire cortex. At the beginning of the scanning session, anatomical scans were also acquired for each participant (TR/TE: 8.2/3.7, 190 transverse axial slices; flip angle: 8; 1 mm$^3$ voxel size; FOV=24 cm x 24 cm; acquisition matrix: 240×240; no SENSE factors).

The experimental task was presented using the Presentation software (Neurobehavioral Systems, Inc.), and delivered within the scanner by means of MR-compatible goggles mounted on the coil. SPM8 (http://www.fil.ion.ucl.ac.uk/spm/software/spm8/) was used for data preprocessing and statistical analyses. For all participants we acquired on average 966 volumes (483 volumes on average for each fMRI-run); the first five volumes were discarded for each run to allow the magnetization reach steady state. Slice-acquisition delays were corrected

using the middle slice as reference. All images were corrected for head movements. All images were then normalized to the standard SPM8 EPI template and spatially smoothed using an 8 mm FWHM Gaussian filter. The high-pass filter was set to the cut-off value of 128 s.

All subsequent analyses of the functional images were performed using the general linear model implemented in SPM8. First, for each subject, the data were fitted at every voxel using a combination of effects of interest. For each trial of the biological-tapping and non biological-tapping blocks we modelled the onset of each digitized video-sequence separately for the emotional valence of the facial expression (neutral, sad, and angry) and for the compatibility (compatible and incompatible) and observed movement (biological and non biological) status of the trial and convolved with the hemodynamic response function (HRF). Each of the 12 trial types was modelled as a separate event (duration = 0). In addition, the model comprised the onset of each instruction period (block-duration dependent on participants' response; average duration = 7.1 s), and, as a separate regressor, the onset of the trials associated with an incorrect response (in the biological-tapping and non biological-tapping blocks) (duration = 0) and the onset of each trial in the biological-lifting and non biological-lifting blocks (duration = 0), convolved with the HRF. The latter two regressors were excluded from subsequent group-level analyses. Finally, the first-level analyses also included the parameters of the realignment (motion correction) as covariates of no interest.

Next, we obtained 12 contrast images per participant, corresponding to the 12 conditions of interest (given by crossing the following factors: facial expression, compatibility, and observed movement) and pooling across the two fMRI-runs. These 12 contrasts were then submitted to a full factorial ANOVA for group-level random effects statistical inference. In this ANOVA we tested for i) the main effects related to the three factors, ii) the interaction between the two factors compatibility and observed movement.

Correction for non-sphericity (Friston et al., 2002) was used in the ANOVA to account for possible differences in error variance across conditions and any non-independent error terms for the repeated measures. Statistical threshold was set to p-corr.

= 0.05 corrected for multiple comparisons at the cluster level using FWE (cluster size estimated at p-unc. = 0.001), considering the whole brain as the volume of interest.
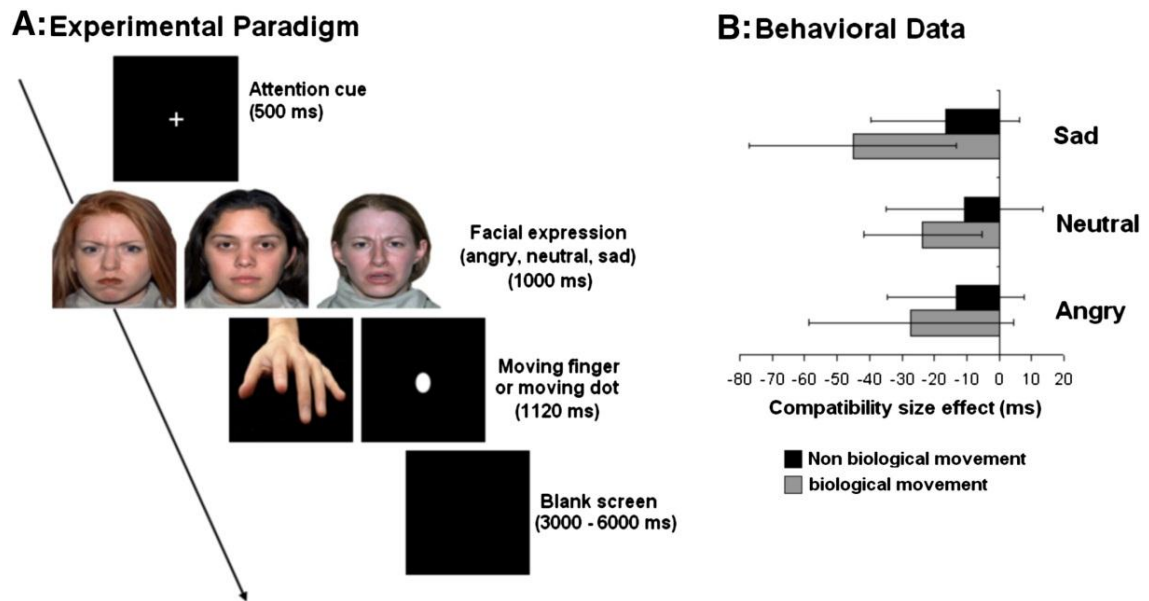


Figure 4.1 A) Experimental paradigm. After an attention cue, the emotional facial expression was presented for 1000 ms. This was given by an angry, a neutral or a sad expression. At the end of the finger movement (biological movement blocks) or the dot movement (non biological movement blocks), participants performed the pre-instructed movement (tapping or lifting). A blank screen of variable duration was presented before the next trial. B) Behavioral results during fMRI. A compatibility size effect (RT compatible movements minus RT incompatible movements) is reported in millisecond for each type of facial expression (angry, neutral, and sad) and for both observed movements (biological, non biological).

## 4.3 Results

### 4.3.1 Behavioral results

The behavioural and imaging data refer to tapping movements only. Participants' accuracy was very high (98.5%). The RT results are plotted in Figure 4.1B: a compatibility size effect (RT compatible movements minus RT incompatible

movements) is plotted in millisecond for each type of facial expression (angry, neutral, and sad) and for both types of observed movements (biological, non biological). A 3 (Facial expression) x 2 (Observed movement) x 2 (Compatibility) repeated measures ANOVA on RT of correct responses returned a main effect of Compatibility (compatible movements faster than incompatible movements; 309 ms vs. 332 ms respectively) [$F_{(1, 18)} = 12.37$, $p < 0.01$] but not the main effects of Facial expression [$F_{(2, 18)} = 0.42$, $p = 0.66$] and Observed movement [$F_{(1, 18)} = 0.38$, $p = 0.54$]. Moreover, there was a trend for a Compatibility x Observed movement interaction [$F_{(1, 18)} = 3.47$, $p = 0.07$]. The interaction was due to marginally larger compatibility effects for observed biological (-32 ms; [$F_{(1, 18)} = 10.86$, $p < 0.01$]) than non biological movements (-13 ms; [$F_{(1, 18)} = 4.66$, $p < 0.05$]). Moreover, observed biological and non biological movements differed more on incompatible (341 vs. 322 ms, respectively) than compatible trials (309 ms for both biological and non biological movements). The remaining two or three-factor interactions were not significant (all $p > 0.3$). Finally, the main effect of compatibility was analysed separately for the three facial expressions, even though the corresponding two-factor interaction was not significant. As expected, a main effect of Compatibility was fully significant for both the sad and the neutral facial expressions ([$F_{(1, 18)} = 16.29$, $p < 0.01$] and [$F_{(1, 18)} = 5.18$, $p < 0.05$], respectively), but was only a trend for the angry expressions ([$F_{(1, 18)} = 4.17$, $p = 0.06$]). Overall these results are consistent with those of past behavioural experiments showing larger compatibility effects after observation of biological than non biological movements (e.g., Brass, Bekkering, Wohlschläger, Prinz, 2000; Kilner, Paulignan, Blakemore, 2003; see Introduction).

### 4.3.2 Functional imaging results

The main aim of the functional imaging analyses was to investigate whether executing actions previously observed in a biological model and in a non biological model relied on similar brain regions. A related and more specific goal was to examine to what extent such activations are modulated by whether the actions to be executed are compatible (i.e., tapping-tapping, respectively for observed and executed movements) or

incompatible (i.e., lifting-tapping). We therefore first investigated whether there were regions that were globally more active when participants responded to movements carried out by a biological compared with a non biological model or were globally more active when compatible actions had to be carried out (relative to incompatible actions). More importantly, we then tested for the interaction between compatibility and observed movement. In the main analyses, we first averaged activations across the three types of facial expression and then we examined whether the emotional valence of the expressions differentially affected the brain activations observed in the main analyses.

*4.3.2.1 Main effects of observed movement, compatibility and facial expression*

Table 4.1 Brain regions showing significant relative increases of BOLD response for the main effects of Observed movement and Compatibility

| | | MNI coordinates | | | | Z | Voxels |
|---|---|---|---|---|---|---|---|
| **Anatomical localization** | **~BA** | **x y z** | | | **P corr.** | **Value** | **per cluster** |
| *1) Regions more active during biological movement than non biological movement* | | | | | | | |
| R Inferior Temporal Gyrus | 37 | 52 | -72 | -4 | < 0.001 | > 8 | 29512 |
| L Middle Occipital Gyrus | 19 | -50 | -82 | 4 | | > 8 | |
| R Cerebellum | // | 38 | -42 | -30 | | 7.09 | |
| L Cuneus | 17 | -14 | -94 | 2 | | 6.85 | |
| L Cerebellum | // | -42 | -42 | -28 | | 6.35 | |
| L Cuneus | 18 | -14 | -106 | 6 | | 5.82 | |
| R Inferior Parietal lobe | 40/3 | 40 | -32 | 46 | | 5.75 | |
| R Postcentral Gyrus | 2 | 46 | -26 | 38 | | 5.58 | |
| L Middle Temporal Gyrus | 21 | -62 | -50 | 8 | | 5.38 | |
| R Precentral Gyrus | 4 | 58 | -22 | 36 | | 5.34 | |
| R Middle Frontal Gyrus | 6 | 36 | -6 | 64 | | 5.30 | |
| L Middle Frontal Gyrus | 6 | -38 | 8 | 32 | | 5.12 | |
| L Postcentral Gyrus | 2 | -48 | -30 | 34 | < 0.001 | 6.28 | 4020 |
| L Inferior Parietal lobe | 40 | -58 | -26 | 32 | | 5.49 | |

| Region | BA | x | y | z | P | z | voxels |
|---|---|---|---|---|---|---|---|
| L Precentral Gyrus | 6 | -32 | -16 | 66 | | 4.99 | |
| L Postcentral Gyrus | 3/4 | -30 | -28 | 68 | | 4.50 | |
| L Postcentral Gyrus | 5 | -22 | -44 | 72 | | 3.86 | |
| L Transv. Temporal Gyrus | 42 | -58 | -18 | 16 | | 3.80 | |
| L Precuneus | 7 | -30 | -48 | 50 | | 3.34 | |
| R Inferior Frontal Gyrus | 45 | 54 | 36 | 10 | =0.27 = 0.029 FWE | 4.76 | 118 |
| R Precuneus | 7 | 26 | -78 | 38 | < 0.008 | 4.64 | 382 |

*2) Regions more active during non biological movement than biological movement*

| Region | BA | x | y | z | P | z | voxels |
|---|---|---|---|---|---|---|---|
| R Cuneus | 19 | 2 | -90 | 30 | < 0.05 | 4.77 | 242 |
| L Middle Temporal Gyrus | 19 | -32 | -60 | 12 | = 0.29 = 0.065 FWE | 4.57 | 114 |

*3) Regions more active during compatible movements than incompatible movements*

| Region | BA | x | y | z | P | z | voxels |
|---|---|---|---|---|---|---|---|
| L Cuneus | 18 | -18 | -106 | 2 | < 0.03 | 5.56 | 284 |
| R Cuneus | 18 | 18 | -106 | 8 | < 0.005 | 5.55 | 435 |
| R Cuneus | 19 | 14 | -100 | 22 | | 4.37 | |

*4) Regions more active during incompatible movements than compatible movements*

| Region | BA | x | y | z | P | z | voxels |
|---|---|---|---|---|---|---|---|
| R Insula | 13 | 42 | 18 | 6 | = 0.42 = 0.06 uncorr | 3.82 | 90 |

Stereotactic MNI coordinates for significant clusters (random effects, cluster-level P < 0.05 corrected, estimated at p < 0.001 uncorrected) given in millimeter with effect sizes (z scores) and cluster extent. In the Voxels per cluster column, cluster extent is reported in correspondence of the main peak. Subpeaks were selected dividing each cluster into Brodmann areas (BA) and then selecting peaks within each area.

First, we compared activation during the execution of tapping movements following a biological minus non biological model. This contrast revealed activation in three clusters (Table 4.1, contrast 1, and top part of Figure 4.2). The largest cluster was a swathe of cortex that involved the posterior/inferior and middle temporal gyri bilaterally, extending to the cerebellum bilaterally, right inferior parietal lobe, right postcentral and

precentral gyri and to the left ventral premotor cortex. A second cluster was centred in the left hemisphere and activated the postcentral and precentral gyri, the inferior parietal lobe, and extended to the precuneus. The right precuneus was also activated as a separate cluster. Finally, the right inferior frontal gyrus was also more active when the model was biological than non biological. Activation in this region did not survive our specific cluster-level correction criterion, but the peak voxel was significant for voxel-level correction.
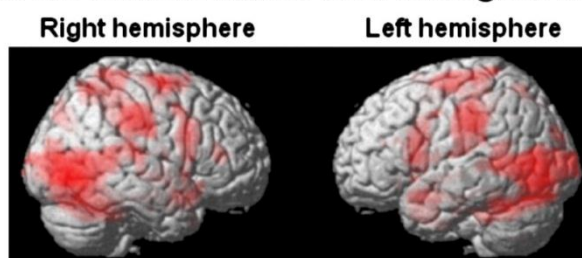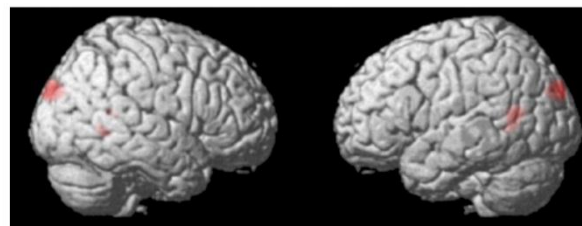


Figure 4.2 Neural activations. Suprathreshold activations are projected onto an MNI-normalized single-subject brain. Main effects of Biological movement minus Non biological movement (top part of the figure) and Non biological movement minus Biological movement (bottom part of the figure). Brain activation in both hemispheres is reported.

The opposite contrast tested for areas more active with the non biological model than the biological model. We found that the superior part of the right cuneus and marginally the medial/posterior part of the left middle temporal gyrus were more active when participants carried out tapping movements after having observed a non biological vs. a biological model doing compatible and incompatible movements (Table 4.1, contrast 2, and bottom part of Figure 4.2).

When we compared patterns of activation associated with the execution of compatible movements (tapping-tapping) and those associated with the execution of incompatible movements (lifting-tapping), we found that the cuneus was bilaterally more active during the execution of compatible than incompatible movements (Table 4.1, contrast 3). Activation in the right hemisphere extended dorsally to a region reasonably close to that showing an effect of observed movement (non biological minus biological) in the previous analysis. Nevertheless, the contrast testing for the areas more active during the execution of incompatible movements than compatible movements, only led to the activation, marginally significant when uncorrected for multiple comparisons, of the right insula (Table 4.1, contrast 4). Moreover, the contrasts testing for the effects of compatibility separately for observed biological movements and non biological movements did not show any activation. Finally, also the contrasts aimed to test for any potential overall differences between the three facial expressions did not lead to any significant activation.

We carried an additional analysis in which, for each trial, we modelled the onset of each facial expression (rather than the onset of each digitized-video as in the main analysis), separately for its emotional valence (angry, neutral, and sad) and for the compatibility (compatible and incompatible) and observed movement (biological and non biological) status of the trial. This analysis may be more appropriate for detecting possible differences between the three types of facial expression. We found that the right insula, the left cerebellum, and the posterior cingulate gyrus were more active when an angry facial expression was presented relative to a sad facial expression (Right insula: MNI: 40 8 -16, $z = 4.22$, p corr = 0.08, cluster extent: 184 voxels; left cerebellum: MNI: -28 -52 -46, $z = 3.57$, p corr = 0.02, cluster extent: 261 voxels; posterior cingulate gyrus: MNI: 4 -26 24, $z = 3.90$, p corr = 0.05, cluster extent: 212 voxels ). No other region was significantly modulated by the emotional valence of the facial expression presented before the observed movement.

### 4.3.2.2 Interaction between compatibility and observed movement and conjunction analyses

Table 4.2 Brain regions showing significant relative increases of BOLD response for Interactions and Conjunctions analyses

| Anatomical localization | ~BA | MNI coordinates x y z | | | P corr. | Z Value | Voxels per cluster |
|---|---|---|---|---|---|---|---|
| *1) Regions showing a Compatibility (compatible/incompatible) by Observed movement (biological/non biological) interaction for neutral and sad facial expressions* | | | | | | | |
| R Caudate | // | 16 | 16 | 2 | < 0.02 | 4.66 | 302 |
| R Putamen | // | 20 | 20 | -2 | | 4.62 | |
| R Postcentral Gyrus | 3/4 | 38 | -34 | 64 | < 0.001 | 4.52 | 1636 |
| R Postcentral Gyrus | 3 | 48 | -28 | 60 | | 4.29 | |
| R Precentral Gyrus | 6 | 38 | -12 | 64 | | 4.13 | |
| R Inferior Parietal Lobe | 40 | 42 | -34 | 48 | | 4.13 | |
| R Postcentral Gyrus | 1 | 54 | -20 | 56 | | 4.11 | |
| R Precentral Gyrus | 6 | 32 | -2 | 36 | | 3.69 | |
| R Postcentral Gyrus | 2 | 32 | -30 | 40 | | 3.62 | |
| R Middle Frontal Gyrus | 9 | 40 | 8 | 34 | | 3.39 | |
| L Caudate | // | -12 | 10 | 4 | < 0.003 | 4.41 | 482 |
| L Thalamus | // | -10 | -2 | 6 | | 3.91 | |
| L Putamen | // | -20 | 22 | -2 | | 3.83 | |
| L Inferior Frontal Gyrus | 47 | -22 | 26 | -2 | | 3.81 | |
| R Superior Parietal Lobe | 7 | 18 | -52 | 66 | < 0.002 | 4.38 | 521 |
| R Precuneus | 7 | 22 | -62 | 48 | | 3.32 | |
| L Precentral Gyrus | 4 | -30 | -20 | 40 | = 0.078 | 4.16 | 201 |
| L Middle Frontal Gyrus | 6 | -32 | -10 | 42 | | 3.64 | |
| L Cingulate Gyrus | 24 | -18 | -8 | 42 | | 3.49 | |
| L Postcentral Gyrus | 2/3 | -30 | -26 | 38 | | 3.34 | |
| R Thalamus | // | 12 | -8 | 8 | = 0.088 | 3.71 | 193 |
| L Lingual Gyrus | 18 | -6 | -78 | -10 | < 0.005 | 3.67 | 422 |

| *2) Conjunction of biological/compatible minus non biological/compatible simple main effects for neutral and sad facial expressions* | | | | | | | |
|---|---|---|---|---|---|---|---|
| R Inferior Temporal Gyrus | 37 | 52 | -72 | -4 | < 0.001 | > 8 | 10060 |
| L Middle Occipital Gyrus | 19 | -50 | -82 | 4 | | 7.81 | |
| L Cuneus | 17 | -14 | -94 | 0 | | 5.51 | |
| R Cerebellum | // | 38 | -40 | -28 | | 5.15 | |
| L Cerebellum | // | -40 | -40 | -28 | | 4.69 | |
| L Middle Temporal Gyrus | 21/22 | -62 | -50 | 8 | | 4.51 | |
| L Inferior Temporal Gyrus | 37 | -48 | -44 | -26 | | 4.50 | |
| L Lingual Gyrus | 18 | -20 | -76 | -10 | | 4.10 | |
| R Superior Temporal Gyrus | 22 | 56 | -40 | 12 | | 4.01 | |
| R Inferior Parietal Lobe | 40 | 40 | -38 | 46 | < 0.001 | 5.05 | 2740 |
| R Postcentral gyrus | 3 | 36 | -38 | 50 | | 4.96 | |
| R Postcentral gyrus | 2 | 44 | -24 | 34 | | 4.86 | |
| R Precuneus | 7 | 24 | -80 | 38 | | 4.40 | |
| R Postcentral gyrus | 5 | 24 | -50 | 68 | | 4.19 | |
| R Superior Parietal Lobe | 7 | 32 | -58 | 56 | | 4.02 | |
| R Precentral Gyrus | 6 | 62 | -20 | 44 | | 3.84 | |
| R Precentral Gyrus | 4 | 28 | -26 | 50 | | 3.76 | |
| R Cingulate Gyrus | 24 | 26 | -22 | 46 | | 3.37 | |
| L Postcentral Gyrus | 2 | -48 | -28 | 36 | < 0.001 | 5.04 | 914 |
| L Precentral Gyrus | 4 | -56 | -22 | 36 | | 4.88 | |
| R Middle Frontal Gyrus | 6 | 36 | -6 | 60 | < 0.001 | 4.85 | 613 |
| R Medial Frontal Gyrus | 6 | 4 | -14 | 64 | < 0.02 | 4.53 | 343 |
| R Superior Frontal Gyrus | 6 | 10 | 12 | 64 | | 3.56 | |
| L Middle Frontal Gyrus | 6 | -30 | -14 | 64 | < 0.004 | 4.50 | 463 |
| L Precentral Gyrus | 4 | -28 | -26 | 64 | | 3.17 | |
| L Middle Frontal Gyrus | 9/44 | -52 | 8 | 26 | < 0.04 | 4.38 | 265 |
| L Superior Temporal Gyrus | 38 | -36 | 10 | -30 | < 0.05 | 4.21 | 234 |
| R Middle Frontal Gyrus | 46 | 46 | 16 | 28 | = 0.05 | 3.90 | 229 |
| R Middle Frontal Gyrus | 44 | 56 | 8 | 24 | | 3.68 | |

| *3) Conjunction of biological/incompatible minus non biological/incompatible simple main effects for neutral and sad facial expressions* | | | | | | | |
|---|---|---|---|---|---|---|---|
| R Inferior Temporal Gyrus | 37 | 52 | -74 | -4 | < 0.001 | 7.58 | 2061 |
| R Cerebellum | // | 40 | -44 | -28 | | 4.99 | |
| L Middle Occipital Gyrus | 19 | -50 | -82 | 4 | < 0.001 | 5.83 | 1035 |
| L Middle Temporal Gyrus | 21/22 | -62 | -46 | 2 | | 3.74 | |
| L Cerebellum | // | -44 | -70 | -22 | | 3.24 | |
| L Inferior Occipital Gyrus | 18 | -42 | -86 | -14 | | 3.22 | |
| L Cuneus | 18 | -14 | -102 | 2 | < 0.04 | 4.31 | 249 |

Stereotactic MNI coordinates for significant clusters (random effects, cluster-level $P < 0.05$ corrected, estimated at $p < 0.001$ uncorrected) given in millimeter with effect sizes (z scores) and cluster extent. In the Voxels per cluster column, cluster extent is reported in correspondence of the main peak. Subpeaks were selected dividing each cluster into Brodmann areas (BA) and then selecting peaks within each area.

We then assessed whether any of the activations found in the regions showing a main effect of observed movement (Table 4.1, contrasts 1 and 2) or in any other region, varied as a function of the type of movement performed: compatible or incompatible. The compatibility by observed movement interaction [compatible movements: biological minus non biological] minus [incompatible movements: biological minus non biological] did not lead to any significant activation when all types of emotional facial expression were considered together, but produced significant activations in several clusters when only neutral and sad expressions were considered (Table 4.2, contrast 1). In particular, the largest cluster was found in the right hemisphere including the somatosensory and motor cortices in the postcentral gyrus, the rostral part of the inferior parietal lobe, and both the dorsal and ventral parts of the premotor cortex. As part of another cluster, the intraparietal sulcus in the right superior parietal lobe and the right preceneus were also activated. The left somatosensory, motor and premotor cortices also showed a marginally significant compatibility by observed movement interaction. All these areas were similar to those showing a main effect of biological minus non biological movement. Moreover, basal ganglia structures such as the head of the caudate and the putamen and the thalamus, were also activated bilaterally in the interaction. The opposite interaction

([compatible movements: non biological minus biological] minus [incompatible movements: non biological minus biological]) did not lead to any significant activation, either when all facial expressions were considered together or when only the neutral and sad ones were considered. Moreover, it is important to note that none of the two interactions led to significant activations when only the angry facial expressions were considered, thus suggesting that incompatible and compatible movements were similar whether the model was biological or non biological when an angry emotional context was "primed". The interactions were not significant also when the angry expressions were considered together with the sad or the neutral expressions.
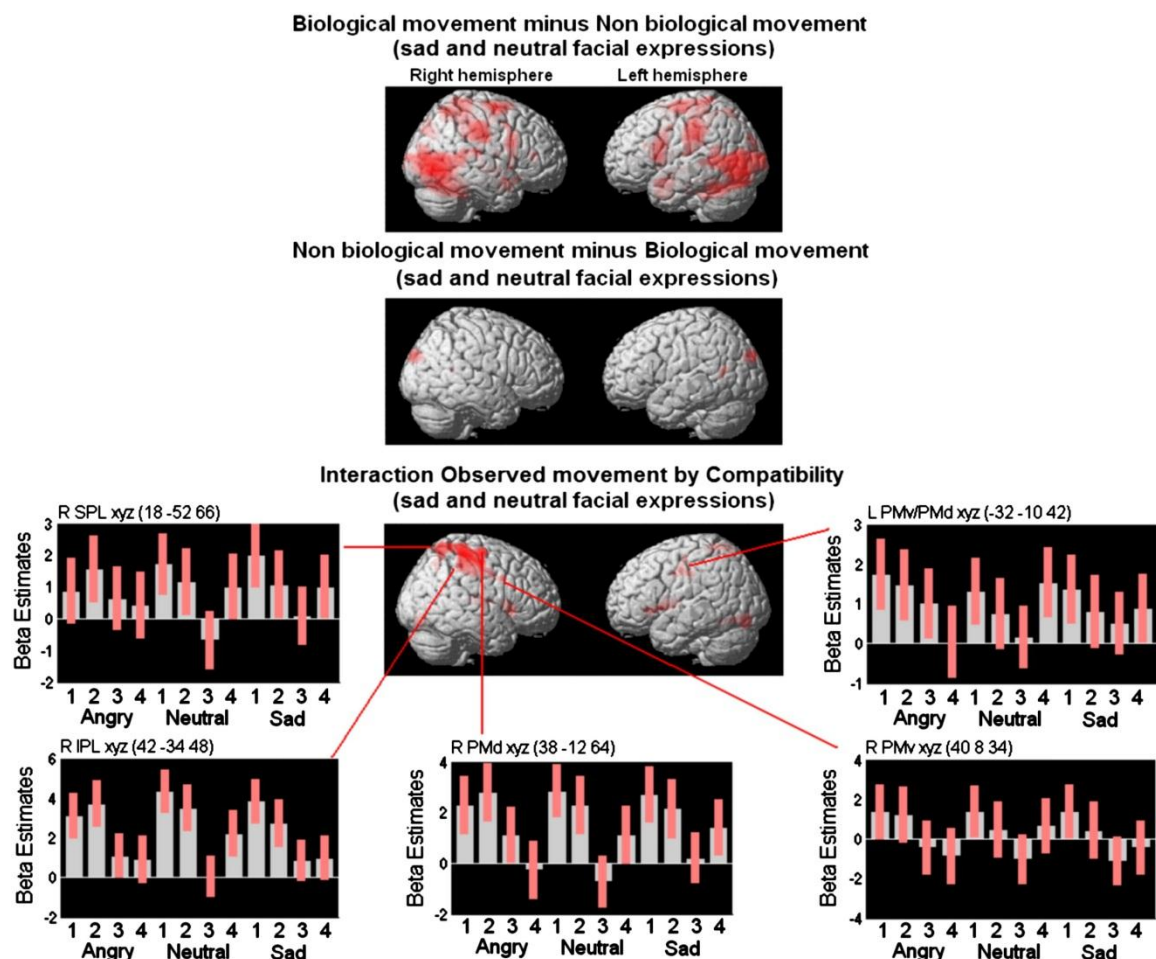


Figure 4.3 The effect of Biological movement minus Non biological movement, measured for the neutral and sad facial expressions, is shown in the top part of the figure. The effect of Non biological movement minus Biological movement, measured for the neutral and sad facial expressions, is shown in the middle

part of the figure. The effect of the interaction between Compatibility and Observed movement (i.e. [compatible: (biological minus non biological)] minus [incompatible: (biological minus non biological)] is shown in the bottom part of the figure. For the interaction, the signal plots for each of the 12 event types are reported for the right superior parietal lobe (SPL), right inferior parietal lobe (IPL), right dorsal premotor cortex (PMd), right ventral premotor cortex (PMv), and for the left premotor cortex (PMv/PMd). All signal plots depict activity in experimental conditions relative to baseline (in arbitrary units [a.u.], ± 90% confidence interval); plots report the pattern of activity at activation's peaks (i.e. single voxels) selected from the whole-brain contrast SPM maps. The 12 event types are obtained by crossing the following factors: facial expression (angry, neutral, and sad), observed movement (biological, non biological), and compatibility (compatible, incompatible). In the plots, 1-2-3-4 respectively refer to biological/compatible, biological/incompatible, non biological/compatible, and non biological/incompatible.

The top and middle parts of Figure 4.3 respectively illustrate the areas that showed an effect of biological minus non biological movement and non biological minus biological movement for the neutral and sad facial expressions. These patterns of activation were very similar to those reported in Figure 4.2, obtained when all three types of facial expression were considered. The bottom part of Figure 4.3 shows the areas that showed a significant compatibility by observed movement interaction for the neutral and sad facial expressions plus the signal plots for the right superior and inferior parietal lobe, right ventral and dorsal premotor cortex and left premotor cortex, including all the 12 event types obtained by crossing the factors of Facial expression, Compatibility, and Observed movement. For each region, the plots show that, especially for the neutral and sad facial expressions, biological movement and non biological movement differ particularly on compatible trials (1 minus 3 in the plots). The difference appears less evident for the incompatible movements (2 minus 4 in the plots). By contrast, in the case of angry expressions, the same five regions seem to be uniformly more active with biological movement than non biological movement (1&2 minus 3&4 in the plots). Moreover, concerning the neutral and sad facial expressions, each of the above five regions tended to be globally more active for compatible than incompatible movements in the trials in which the model was biological (1 minus 2 in the plots; the difference not

being statistically significant); this difference took the opposite direction in the trials in which the model was non biological (4 minus 3 in the plots).

As mentioned above, in the case of neutral and sad facial expressions, whether the model is or not biological seems to affect the execution of compatible movements more than the incompatible ones. We formally assessed these findings by performing two conjunction analyses. In the first analysis, we tested for the conjunction of the significant simple main effect of biological/compatible minus non biological/compatible for the neutral and sad facial expressions. In the second analysis, we investigated the areas that conjointly showed an effect of biological/incompatible minus non biological/incompatible in the neutral and sad facial expressions. The first conjunction revealed an activation in an extensive bilateral network of brain regions including the somatosensory, motor, and premotor cortices and the inferior/posterior part of the temporal gyrus (Table 4.2, contrast 2, and top part of Figure 4.4). Some of these regions were very similar to those, already discussed, that showed compatibility by observed movement interaction. By contrast, the execution of incompatible movements was less affected by whether the previously observed movement was performed by a biological model or not. An effect of biological movement greater than non biological movement for the incompatible trials was only found in the inferior and middle/posterior parts of the temporal cortex, in the cerebellum bilaterally and in the left cuneus (Table 4.2, contrast 3, and middle part of Figure 4.4). Of importance, the latter pattern of results was very similar to the one found when the effect of biological/compatible minus non biological/compatible was tested using the angry facial expressions only (bottom part of Figure 4.4). Finally, for the neutral and sad expressions, the conjunctions opposite to the two described above (e.g., non biological/compatible minus biological/compatible) did not lead to any significant activation.

**Conjunction of biological/compatible minus non biological/compatible effects for neutral and sad facial expressions**

Right hemisphere | Left hemisphere
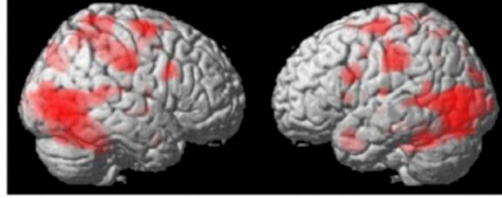
**Conjunction of biological/incompatible minus non biological/incompatible effects for neutral and sad facial expressions**
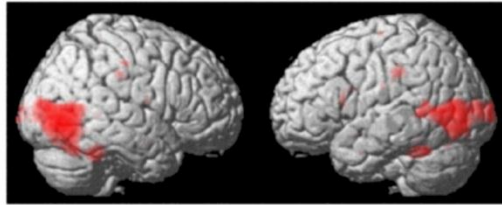
**Biological/compatible minus non biological/compatible for angry facial expressions**
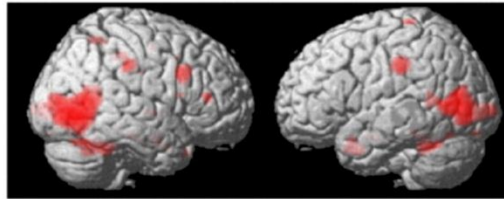
Figure 4.4 Top part: Conjunction analysis of biological/compatible minus non biological/compatible for the neutral and sad facial expressions. Middle part: Conjunction analysis of biological/incompatible minus non biological/incompatible for the neutral and sad facial expressions. The first conjunction was given by: Neutral expressions: biological/compatible minus non biological/compatible ∩ Sad expressions: biological/compatible minus non biological/compatible. The second conjunction was given by: Neutral expressions: biological/incompatible minus non biological/incompatible ∩ Sad expressions: biological/incompatible minus non biological/incompatible. In the bottom part of the figure, the effect of biological/compatible minus non biological/compatible is shown for the angry facial expressions.

## *4.4 Discussion*

In the present fMRI study we investigated whether the observation of movements performed by a biological or a non biological model affects the successive execution of compatible and incompatible actions. To this end we scanned participants while they

were performing a finger imitation task. Moreover, we also investigated whether imitative responses were influenced by the type of emotional facial expression presented before the observed movement. Behaviorally, participants showed a marginally larger compatibility effect when the model was biological compared with when it was non biological; furthermore, a statistically reliable compatibility effect was present for both the sad and the neutral facial expressions but not for the angry expressions.

The brain imaging data showed bilateral activation in parietal, posterior/temporal, motor and premotor regions when participants responded to movements carried out by a biological model vs. a non biological model (main effect of biological minus non biological movement). The opposite contrast revealed activation of the right cuneus. Despite the large behavioral effects, Compatibility did not have a major impact on the brain activations.

However, the interaction testing for areas more active in biological compared with non biological movement and performed by compatible vs. incompatible actions, activated parietal, motor, premotor and basal ganglia regions. Importantly, we observed the significant interaction only for the neutral and sad facial expressions. In particular, the conjunction analyses carried out for the neutral and sad expressions showed that, except for the basal ganglia, all other regions were more active for biological than non biological movement during compatible trials but not during incompatibles ones. The Compatibility by Observed movement interaction was not significant whether the angry facial expressions were considered alone or together with the other expressions; this result indicated that incompatible and compatible movements were similar when an angry emotional context was elicited independently of the type of model (biological or non biological).

The activation of a network involving parietal, motor and premotor regions in the biological movement condition (compared with the non biological movement condition) is consistent with previous fMRI studies in which similar activations were reported when participants observed movements executed by a biological as opposed to a non biological agent (Stevens, Fonlupt, Shiffrar, Decety, 2000; Perani et al., 2001; Tai, Scherfler, Brooks, Sawamoto, Castiello, 2004), but also with behavioral studies showing stronger

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automatic imitation effects for biological than non biological movements (e.g., Castiello et al., 2002; Press, Bird, Flach, Heyes, 2005). For instance, Tai and colleagues (2004) found that the premotor cortex was particularly active when participants observed manual grasping actions performed by a human rather than a non human model. Together with these findings, our results further support the proposal that biological and non biological movements are processed differently by the brain (e.g., Kilner, Paulignan, Blakemore, 2003). Nevertheless, our results extend those of previous studies by showing that activation in these regions was critically modulated by whether the movements to be executed were compatible or incompatible.

According to the ideomotor theory (see also the Introduction), imitation occurs as motor representations are activated through action observation, with the similarity between the observed and the executed action affecting the ease with which a stimulus is directly transformed into an action (e.g., Brass, Bekkering, Wohlschläger, Prinz, 2000; Brass & Heyes, 2005). On this view, this similarity is higher, and the motor system is better tuned to execute observed movements, in the compatible trials in which the model is biological compared with the compatible trials in which the model is non biological. While the spatial components of the observed movements are the same in the biological and non biological model (e.g., upward and downward movements of the dot and lifting and tapping movements of the finger), the movement displayed by the biological model is more similar to the executed movement than the observed non biological movement.

By contrast, the biological and non biological models differ less in terms of ideomotor compatibility on the incompatible trials where the observed movement is different from the executed movement. On these trials, the observation of a finger-lifting movement or an upward dot movement interferes with the performance of the required tapping movement (Figure 4.1B; see also Brass, Bekkering, Prinz, 2001). In line with past studies (Kilner, Paulignan, Blakemore, 2003; Press, Bird, Flach, Heyes, 2005; Kilner, Hamilton, Blakemore, 2007), our behavioral findings show that this interference is larger when the model is biological than when it is non biological. In our study, as the Observed movement by Compatibility interaction was only marginally significant, it needs to be interpreted with caution. However it is interesting to note that, specifically in

the trials in which the model is biological, the parietal and premotor regions tended to be less active on the incompatible than compatible trials (cf. signal plots of Figure 4.3). This may suggest a relative inhibition of these regions in conditions in which imitative compatibility is present (with the biological model) but imitative responses are not adaptive.

The present account of the Compatibility by Observed movement interaction suggests that activations in regions of a putative human MNS following imitative compatibility may facilitate performance on compatible trials or interfere with the execution of incompatible movements. Based on the present findings, it is difficult to establish which of the two factors contributed most to the large compatibility effect observed when the model was biological. Nevertheless, in line with a possible general facilitation effect of compatible movements, we found that occipital regions projecting to somatosensory and motor-related areas, such as the cuneus, were more active on compatible than incompatible trials, showing also a main effect of biological movement minus non biological movement. These findings suggest that imitative tendencies elicited by the observation of compatible actions, may depend, at least in part, on the visual properties of the stimuli and that human stimuli may be particularly effective in triggering such tendencies (Press, Gillmeister, Heyes, 2006). Admittedly, this hypothesis still awaits confirmation by future studies, in which biological and non biological models will be made perceptually more similar.

A secondary aim of our study was to investigate the relation between emotional context and action imitation. On the hypothesis that facial expressions of emotion have a communicatory function (Blair, 2007) and enhance imitative behavior (Chartrard & Bargh, 1999), we presented participants with angry, neutral and sad facial expressions before that the hand or the dot movement was displayed, with the intent to differentially affect participants' imitative behaviour. Differently from sad and neutral facial expressions, when an angry expression was shown, the parietal and premotor regions were not preferentially more active for biological than non biological movements in the

compatible trials relative to the incompatible trials (cf. signal plots of Figure 4.3; see also bottom part of Figure 4.4).

The difference in activation for the angry facial expressions compared with the sad and neutral facial expressions may reflect the extent to which we tend to empathize with others. Thus, angry expressions signal a potential attack and are likely to be perceived as a threat and thus trigger avoidance behavior in the observer (e.g., Pichon, de Gelder, Grèzes, 2008, 2009; see also social response reversal, Blair, Morris, Frith, Perrett, Dolan, 1999; Blair, 2003). By contrast, individuals showing sad expressions elicit prosocial behavior (Blair, 2003) and empathizing with them involves mirroring their expressions (Chakrabarti, Bullmore, Baron-Cohen, 2006). Thus, it is possible that empathizing with the sad individuals but also the neutral individuals presented before the observed movement has contributed to increase the compatibility effects in the trials in which the model was biological and performed the same movements.

In line with this possibility, it has been suggested that empathy, likewise the hand imitation, depends on a perception-action mechanism whereby the same premotor areas involved in the generation of one's own emotional facial expression may be also active during the recognition of that emotion in others. Thus, according to Preston and de Waal (2002), a motor resonance system plays a critical role in a perception-action model (PAM) of empathy. Consistent with this view, it has recently been found that a motor resonance system for emotional facial expressions may exist, and that this system shares with biological hand imitation a common neural circuit involving the premotor cortex, particularly in the right hemisphere, a region which thus seems to be crucially linked to emphatic processes (Leslie, Johnson-Frey, Grafton, 2004).

In conclusion, the present study showed that observed biological movement affects action imitation. Motor-related regions were more active when participants responded to movements carried out by a biological model than a non biological model. Critically, this was especially the case when participants performed imitative rather than non imitative actions. Moreover, we provided evidence that an emotional context promoting empathy plays a major role in distinguishing a biological model from a non biological model in imitative trials.

# Chapter 5

## AUTOMATIC IMITATION, ACTION IMITATION AND BODY REPRESENTATIONS IN PATIENTS WITH LEFT AND RIGHT BRAIN DAMAGE

*5.1 Introduction*

In the previous chapters, I have extensively discussed the phenomenon of automatic imitation. The ideomotor theory and the associative sequence learning theory, both predicting an effect of the action observation on the production of the same actions, inspired automatic imitation paradigms in the experimental practice. The underlying assumption is that automatic imitation can be used as an effective model of imitation, and that the basic mechanisms involved in the former are shared by more complex imitative behaviors.

The results of neuroimaging and neuropsychological studies on imitation present some variability, particularly with respect to the lateralization of the function. Neuropsychological studies showed that apraxia is more commonly caused by lesions to the left hemisphere (Liepmann, 1920; De Renzi, Motti, Nichelli, 1980; Papagno, Della Sala, Basso, 1993; Goldenberg 1995; Haaland, Harrington, Knight, 2000; Tessari, Canessa, Ukmar, Rumiati, 2007), some evidence of defective imitation were also found following right hemisphere damage, even if most, but not all, of the errors were due to the presence of the unilateral neglect (Goldenberg, Münsinger, Karnath, 2009). On the

contrary, neuroimaging evidences are considered, bilateral activations are associated with imitation, both when automatic imitation paradigms are used (Iacoboni et al. 1999; Brass, Zysset, von Cramon, 2001; Koski et al. 2003; Bien, Roebroeck, Goebel, Sack, 2009; Mengotti, Corradi-Dell'Acqua, Rumiati, 2012) and when action imitation tasks are performed (Rumiati et al. 2005; Menz, McNamara, Klemen, Binkofski, 2009).

To date no study directly compared automatic imitation and action imitation tasks, hence one of the aims of the present study was to test whether the former can be used as a simplified model of imitation or whether some differences can be detected. We tested left and right brain damaged patients to highlight the differential contribution of the two hemispheres to the different components of imitation. To this aim, patients were administered with an automatic imitation task that is suitable to disentangle between anatomical and specular types of imitation. Action imitation as well was administered according to anatomical and specular perspective, to compare with automatic imitation. Even though some studies on children suggested a preference towards specular compared with anatomical imitation (Wapner & Cirillo, 1968; Schofield, 1976; Bekkering, Wohlschläger, Gattis, 2000; Gleissner, Melzoff, Bekkering, 2000), a systematic investigation of the phenomenon has not yet been carried out.

A second aim of the study was to test the role of the body representations in imitation. As discussed in chapter 1, three body representations have been hypothesized in addition to the primary somatosensory and motor maps (Schwoebel & Coslett, 2005): the body schema, the body structural description and the body image. It is still an open debate which of the body representations may underlie imitation (see Rumiati, Carmo, Corradi-Dell'Acqua, 2009, for a review). Only few studies investigated this issue, obtaining inconclusive results. While Goldenberg (1995) argued that deficits in imitation can rise from a disruption of a general knowledge of the human body, a concept near to the body structural description, Buxbaum, Giovannetti and Libon (2000) and Schwoebel, Buxbaum and Coslett (2004) suggested a general involvement of the body schema in imitation tasks.

We used a body part rotation task recently developed (Corradi-Dell'Acqua, Tomasino, Fink, 2009) that takes advantage of two different rotation perspectives,

relaying on egocentric and allocentric coordinates, and that have been argued to tap the body schema and the body structural description representations respectively.


## 5.2 Materials and methods

### 5.2.1 Participants

A total of 15 consecutive patients (mean age $65 \pm 11$ years; education $8.5 \pm 4$; 7 females) entered in the study, seven of them suffered from a focal unilateral brain lesion to the left hemisphere (LBD) and eight of them had a focal unilateral brain lesion to the right hemisphere (RBD). Patients were recruited from the rehabilitation ward of the Ospedali Riuniti in Trieste. They were all right-handed and without previous neurological history. All patients were tested within 4 months from the recovery and no significant difference is found for LBD and RBD in the mean time between the occurrence of the lesion and the neuropsychological evaluation ($t_{(6)} = 0.7$, $p = 0.53$).

Fifteen healthy individuals were recruited as controls, matched for age and education (mean age $67 \pm 9$ years; education $11 \pm 2.5$; 8 females). They were all right-handed and with no neurological history. They were screened with the Mini Mental State Examination (Folstein, Folstein, McHugh, 1975) to ensure that they were not suffering from any form of cognitive decline (mean score: 29, range 27-30). All participants accepted to participate in the study by signing an informative consent. The study was approved by the local Ethics Committee.


### 5.2.2 Neuropsychological assessment

All 15 patients underwent a neuropsychological assessment evaluating language, visuo-perceptual and visuo-spatial abilities, attention, executive functions, praxis and memory. The results of the neuropsychological evaluation for LBD patients are shown in Table 5.1 and those of the RBD patients are shown in Table 5.2. Five out of seven LBD patients were aphasics and six out of eight RBD patients showed unilateral neglect. Overall the group of the RBD patients seems to be more impaired at the neuropsychological assessment with respect to the LBD patients. For the neuropsychological tests in common to both groups (AAT and BIT tests were excluded),

we calculated for each patient a percentage score by comparing the total number of tests performed and the number of tests in which the performance was pathological. Overall RBD patients' performance was pathological on the 37% of the tests, whereas LBD patients' performance was pathological on the 26% of the tests.

Table 5.1 Demographic data and results of the neuropsychological evaluation for LBD patients.

| Case | Sex | Age | Education (years) | Testing Post Onset (months) | Handedness | Naming | Verbal Fluency FAS | AAT Token | Repetition | Written | Naming | Comprehension | Type Aphasia |
|------|-----|-----|-------------------|-----------------------------|------------|--------|--------------------|-----------|------------|---------|--------|---------------|--------------|
| C.L. | F | 73 | 7 | 4 | 100 | - | - | 9 | **115** | **69** | 112 | **51** | **Conduction** |
| D.F. | M | 55 | 13 | 0.5 | 100 | 30 | **8.8** | - | - | - | - | - | No aphasia |
| G.D. | M | 67 | - | 2 | 100 | - | - | **25** | **47** | **38** | **94** | **85** | **Broca** |
| G.P. | M | 49 | 17 | 2.5 | 100 | - | - | **35** | **86** | **35** | **50** | **96** | **Wernicke** |
| P.C. | F | 75 | 8 | 0.5 | 100 | 27 | 15.6 | - | - | - | - | - | No aphasia |
| S.S. | M | 50 | 12 | 1 | 100 | - | - | 1 | 141 | 84 | **87** | 97 | **Amnesic** |
| T.S. | M | 65 | 8 | 1.5 | 100 | - | **4.2** | **11** | **129** | **42** | **95** | **90** | **Amnesic** |

| | Memory | | | | | Attention | | | Executive-logical | | Visuo-perceptual | | | Praxis | |
| | LTM | | STM | | | TMT | | | | | VOSP | | | | |
| Case | Word List - Imm Recall | Word List - Late Recall | Digit Span | Digit Span Backward | Corsi | A | B | Attentive Matrix | Wiegl | Raven's CPM | Screening | Object d. | BORB | IMA | IA |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| C.L. | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| D.F. | **23.2** | 5.7 | 5.75 | 4 | **3.75** | 27 | 163 | - | **6.75** | 32.3 | - | 15 | - | 69 | - |
| G.D. | - | - | - | - | - | - | - | - | - | - | - | - | - | 70 | 14 |
| G.P. | - | - | - | - | 4.5 | **73** | p.u. | 20 | 9.75 | 31.1 | - | - | 25 | 68 | - |
| P.C. | 57.3 | 9.3 | 4.25 | **2** | 3.25 | **170** | - | - | 9.25 | **20.3** | - | 16 | - | **55** | 14 |
| S.S. | - | - | 4.75 | 5 | **3.5** | - | - | 32 | 8 | 35.3 | - | 20 | 20 | 68 | 14 |
| T.S. | - | - | 4.25 | **3** | 5 | - | - | 42.3 | **2.75** | 28 | - | 18 | - | 65 | 14 |

Note: Abbreviations and list of tests used in the neuropsychological assessment: F=female; M=male; Handedness=Oldfield (1971); Naming=clinical test developed by our group, max score 30; FAS=phonemic fluency (Carlesimo et al., 1995); AAT= Aaachener Aphasie Test, Italian norms (Luzzatti, Willmes, De Bleser, 1996); LTM=long term memory; Word list= Mauri et al. (1997), Imm recall=immediate recall; STM=short term memory; Digit span= Orsini et al. (1987); Digit span backward= De Beni et al. (2008); Corsi=Corsi test, spatial short term memory (Spinnler & Tognoni, 1987); TMT=trial making test, (Giovagnoli et al., 1996), part A and part B; Attentive Matrix=Spinnler & Tognoni (1987); Weigl= Spinnler & Tognoni (1987); Raven's CPM= Raven Coloured Progressive Matrices (Carlesimo et al., 1995); VOSP= Visual Object and Space Perception battery (Warrington & James, 1991), Screening and Object decision subtests; BORB= Birmingham Object Recognition Battery, (Riddoch &Humphreys, 1993); IMA= test for ideomotor apraxia (Tessari et al., in press); IA=test for ideational apraxia (De Renzi & Lucchelli, 1988).

Table 5.2 Demographic data and results of the neuropsychological evaluation for RBD patients.

| | | | | | | Language | | Visuo-spatial | | | | | | |
| | | | | | | | | BIT | | | | | | |
| Case | Sex | Age | Education (years) | Testing post onset (months) | Handedness | Naming | Verbal Fluency - FAS | Line cross | Line Bisect | Star Cancel | Letter Cancel | Figure copying | Drawing | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| B.E. | M | 64 | 5 | 3 | - | 29 | **20.9** | 36 | **5** | **18** | **12** | 3 | **2** | **76** |
| C.F. | M | 65 | 11 | 1 | 100 | 30 | 24 | **18** | **0** | **22** | **14** | **3** | **2** | **59** |
| C.P. | F | 71 | 11 | 0.5 | - | 30 | 31.9 | 36 | **7** | 52 | 37 | 4 | 3 | 139 |
| G.L. | F | 79 | 5 | 2 | 100 | - | - | 36 | **7** | **31** | **16** | 2 | 2 | **94** |
| H.B. | F | 42 | 5 | 1 | 100 | 26 | 43.9 | **34** | 9 | **46** | 33 | 3 | 3 | **128** |
| M.M. | F | 73 | 8 | 0.5 | 100 | - | **16.9** | **30** | **4** | 25 | - | 2 | 2 | **63** |
| M.R. | M | 42 | 5 | 1.5 | - | 30 | 27.4 | 35 | **6** | 54 | 35 | **0** | 2 | 134 |
| V.L. | F | 74 | 5 | 0.5 | 100 | **20** | 24 | **30** | **5** | 17 | 17 | **0** | 2 | **71** |

| | Memory | | | | | Attention | | | Executive-logical | | Visuo-perceptual | | Praxis | |
| | LTM | | STM | | | TMT | | | | | VOSP | | BORB | |
| Case | Word list - immediate recall | Word List - late recall | Digit Span | Digit Span Backward | Corsi | A | B | Attentive matrix | Wiegl | Raven's CPM | Screening | Object d. | IMA | IA |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| B.E. | - | - | 6.5 | **3** | **4** | - | - | - | 13.75 | 27.9 | 19 | 17 | - | - |
| C.F. | 46.1 | 6.3 | 5.25 | p.u. | 4 | - | - | - | 8.75 | - | - | - | - | - |
| C.P. | 48.8 | 11.8 | 5.25 | 4 | 4.25 | 57 | **436** | 50 | 12 | 25.6 | - | - | 56 | 14 |
| G.L. | - | - | 5.5 | 4 | **3.5** | - | - | **25.3** | - | **17** | - | - | - | - |
| H.B. | 34.7 | 6.1 | 5.5 | **3** | **3.25** | 43 | **382** | - | 13.75 | 25.9 | - | - | - | - |
| M.M. | - | - | **3.25** | **2** | 4.25 | - | - | **23** | **4** | - | - | - | - | - |
| M.R. | 50.8 | 10.2 | 5.25 | 4 | **1.5** | - | - | - | - | 27.3 | - | - | - | - |
| V.L. | 30.4 | 3.5 | 5.5 | **3** | **3.25** | - | - | - | 10 | - | - | **13** | 23 | **50** | 12 |

Note: Abbreviations and list of tests used in the neuropsychological assessment: F=female; M=male; F=female; M=male; Handedness=Oldfield (1971); ); Naming=clinical test developed by our group, max score 30; FAS=phonemic fluency (Carlesimo et al., 1995); BIT= Behavioural Inattention Test (Wilson et al., 1987); LTM=long term memory; Word list= Mauri et al. (1997), Imm recall=immediate recall; STM=short term memory; Digit span= Orsini et al. (1987); Digit span backward= De Beni et al. (2008); Corsi=Corsi test, spatial short term memory (Spinnler & Tognoni, 1987); TMT=trial making test, (Giovagnoli et al., 1996), part A and part B; Attentive Matrix=Spinnler & Tognoni (1987); Weigl= Spinnler & Tognoni (1987); Raven's CPM= Raven Coloured Progressive Matrices (Carlesimo et al., 1995); VOSP= Visual Object and Space Perception battery (Warrington & James, 1991), Screening and Object decision subtests; BORB= Birmingham Object Recognition Battery, (Riddoch &Humphreys, 1993); IMA= test for ideomotor apraxia (Tessari et al., in press); IA=test for ideational apraxia (De Renzi & Lucchelli, 1988).

### 5.2.3 Experimental procedure

The tasks were administered to the patients in two separated session within the same week and the order of the tasks were randomized across sessions and between patients. Prior to the experimental tasks, patients performed a simple left-right judgment task, to assure that they were able to perform left-right discrimination. No deficits in this sense were detected.

Due to the hemiparesis contralateral to the lesion, right brain damaged patients performed the imitation tasks with the right hand and the left brain damage patients with the left hand. To match the control subjects' hand used for performing the tasks with the patients' hand, eight controls performed the experimental tasks with their right hand (hereafter called CNa) whereas seven controls performed the tasks with their left hand (hereafter called CNb). We performed and ANOVA between CNa and CNb to compare the performance of the automatic imitation, action imitation and body rotation tasks. No difference was found in the results between the two groups of controls that performed the tasks with their right hand and those who used their left hand.$F_{(1,13)}$=0.56, p=0.47; for action imitation, $F_{(1,13)}$=0.36, p=0.57; for body rotation, $F_{(1,13)}$=0.003, p=0.96).

*Automatic imitation.* On each trial, five-frame video sequences were presented on a black background on a computer screen, depicting a single tapping movement that could be performed either by a left (50% of the trials) or a right hand with the index (50% of the trials) or the ring finger. In each trial, the first frame was presented for 1000 ms, followed by three frames for 40 ms each depicting the intermediate positions of the finger and a final frame depicting the end position for 2000 ms. Each trial was followed by an inter-trial interval of 3000 ms in which a black background was displayed. E-Prime 2 software (Psychology Software Tools, Pittsburgh, PA) was used for stimulus presentation and data collection. Reaction times (RTs) and accuracy data were collected, RTs being measured from the first 40 ms frame that followed the presentation of the first frame of 1000 ms.

Participants were asked to perform two tasks, in which they had to produce tapping movements similar to those performed by the hand stimulus. In the Anatomical Task, they were asked to tap with their assigned hand (left or right, according to the group) the finger that was anatomically compatible with the one moving on the screen: e.g., when the video displayed an index finger movement, they had to tap their index finger, irrespective of whether the observed hand was a left or a right hand, thus whether the moved finger occupied the same or a different position in space relative to the observed moving finger. In the Spatial Task, they had to tap with their assigned hand the finger that was spatially compatible with the one moving on the screen: e.g., when the observed finger movement occurred closer to the right side of the screen (as in case of a right hand tapping with its index finger), they had to tap using the finger closest to the same side, irrespective of its anatomical identity (i.e. the ring finger). Thus, this task is suitable to detect the tendency to imitate according to anatomical or spatial coordinates.

*Action imitation.* We used a test developed in our lab (Tessari et al., in press) that requires participants to imitate, one after the other, 18 MF intransitive gestures and 18 ML gestures, derived from the MF ones by modifying the spatial relationship between the effector and the main body axis. Gestures were always repeated two times. For each gesture a score of 0, 1, 2 is given according to the performance (0 = no imitation, 1 =

correct imitation in the one of the two trials, 2 = correct imitation in both trials), with the cutoff varying according to age and years of education, for a total score of 72 maximum. Participants' performance was videotaped and analyzed offline by one of the authors (P.M.) and two experienced neuropsychologists unaware of the experimental hypotheses. Raters judged the performance for each trial as "correct" or "incorrect", if two out of three judges rated the performance on a trial as "correct", 1 point was assigned to that trial, otherwise the trial was considered as "incorrect" and 0 points were assigned.

The test was repeated two times, one for each testing session for the patients, to allow the experimental manipulation of the imitation, following anatomical or spatial coordinates. In one session, the experimenter performed the gestures with the arm that was anatomically compatible with the participants' arm, i.e. the Anatomical task. In this case, if the participant was asked to perform the task with his/her right arm, the experimenter showed the gestures with his/her right arm. In another session, the experimenter performed the gestures with the arm that was spatially compatible with the participants' arm, i.e. the Spatial task. In this case, if the participant was asked to perform the task with his/her right arm, the experimenter showed the gestures with his/her left arm, in a mirror-like way.

*Body rotation task.* On each trial, two horizontally aligned black and white pictures were presented on a white background on a computer screen. The pictures showed a human arm, placed to the right (25% of the trials) or left (25% of the trials) of an upright human body whose arms had been removed. The human body was facing away from the observer and the arms were shown always with the palm towards the participant. The arms and could be right or left and could appear rotated, either clockwise or counterclockwise, at one of four possible orientations, namely, at 36°, 72°, 108°, 144°, from their upright canonical orientation. E-Prime 2 software (Psychology Software Tools, Pittsburgh, PA) was used for stimulus presentation and data collection. Reaction times (RTs) and accuracy data were collected. For each experimental trial, the stimuli were presented as long as a participants responded, followed by an inter-trial interval of 3000 ms. Participants were asked to perform a handedness task: if the stimulus was a

right arm they had to press with one of two fingers of their assigned hand (left or right, according to the group) the corresponding button, whereas if the stimulus was a left arm they had to press with one of two fingers of their assigned hand a different button. They were asked to perform the handedness task according two different strategies. In one condition, they had to imagine rotating their own arm until this reached the position depicted in the screen, this is called Egocentric strategy. In another condition, they had to imagine the arm stimulus rotating until this could be wedged in the human photograph, this is called Allocentric strategy. The experiment was built so that those orientations that were closer to the position of the participants' arm (namely, 108° and 144°) were apart from the position that the arm would have if wedged in the visual model of the body. Conversely, those orientations that were close to the position that the arm would have if wedged in the visual model of the body (namely, 36° and 72°) were as well apart from the position of the participants' arm.

Previous studies showed that when participants accomplish the task by relying on the Egocentric strategy, the rotations performed towards the medial line of the body are easier to perform with respect to those towards the lateral line of the body (Parsons, 1987a,b; Tomasino and Rumiati, 2004), whereas when they perform it using the Allocentric strategy this difference is not found (see also Corradi-Dell'Acqua, Tomasino and Fink, 2009). Previous evidences (Corradi-Dell'Acqua, Tomasino and Fink, 2009) showed that these Egocentric and Allocentric strategies tap the body schema and the body structural description respectively.

### 5.2.4 Behavioral analysis

To analyze participants' performance at group level, ANOVAs between LBD vs. CNa, RBD vs. CNb, LBD vs. RBD were performed for each task. To analyze participants' performance at single patient level, the Revised Standardized Difference Test (RSDT) was computed to detect dissociations, as suggested by Crawford and Garthwaite (2006), using the software released with the article by Crawford and Garthwaite (2005). Data for each participant were entered as percentage of correct responses. The software provides a *t* score for each individual performance and estimates the abnormality of the individual

score with respect to the mean performance of the correspondent control sample (CNa or CNb). Dissociations between tasks are reported, based on the significance values of the t scores, and by taking into account the correlation within controls across the two tasks considered. The RSDT method is suitable to detect classical dissociation, in which a patient was impaired compared to controls on Task A, but within the normal range on Task B, and strong dissociations, in which a patient was impaired on both Tasks A and B compared to controls, but relatively more impaired on Task A (revised criteria for dissociations, see Crawford and Garthwaite, 2005).

### 5.2.5 Lesions analysis

Computed tomography scans (CT) were available for 13 out of 15 patients (six LBD and seven RBD). For each of the patients with available imaging data, the CT scan that was closer in time to the neuropsychological evaluation was chosen for the lesion mapping procedure.

Lesions were mapped from the CT scan on the axial plane into the standard single-subject brain template in MRIcro (Rordern and Brett, 2000) following the procedure described by Luzzatti, Scotti & Gattoni (1979). First, we calculated the inclination of the scan on the orbito-meatal plane. Then, the correspondence between orbito-meatal plane and bicommissural plane inclination (used as reference in MRIcro's MNI template) was obtained to allow the correct reproduction of the inclination of the MRIcro's ch2 template. After rotating the ch2 template around the LR axis (i.e. changing the pitch) the rotated image is saved and the lesion is mapped for each slice of the axial plane. The lesion map is saved as region of interest file (ROI). Following this procedure, a more precise match is obtained between the CT scan images and the MRIcro template. Finally, the ROI can be re-rotated back into the standard MNI space.

*5.3 Results*

*5.3.1 Group level*

For each of the three tasks of interest (i.e. automatic imitation, action imitation, body rotation) we performed three separated ANOVA analysis comparing the performance of i) LBD vs. CNa; ii) RBD vs. CNb; iii) LBD vs. RBD.

Concerning automatic imitation, no significant differences were found between LBD and CNs, neither between the two groups nor within the two different tasks (AN vs. SP). RBD were significantly impaired with respect to CNb (main factor of Group, $F_{(1,14)}$ = 15.5, p = 0.001), however no effect of Task was found, suggesting that at group level there is no difference in the automatic tendency to imitate according to anatomical or spatial coordinates. A significant difference in the performance between LBD and RBD patients was found in the ANOVA comparing the two groups (main factor of Group, $F_{(1,13)}$ = 7.7, p = 0.016), with RBD patients more impaired with respect to LBD (79% vs. 94% mean accuracy). See Figure 5.1.
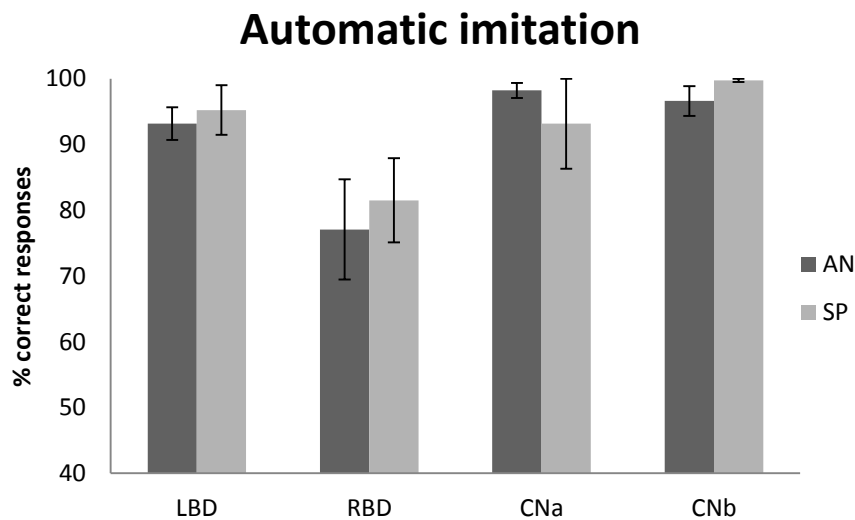


Figure 5.1 Performance as percentage of correct responses for LBD, RBD and controls for the automatic imitation. Vertical bars show the standard error of the mean.

As for action imitation, LBD were significantly impaired in imitating gestures compared with CNa (main factor of Group, $F_{(1,12)}$ = 16.96, p = 0.01). No significant

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effect of Task (AN vs. SP) was found, suggesting that at group level there is no difference in explicitly imitating gestures according to anatomical or spatial coordinates. RBD patients as well were impaired in performing action imitation with respect to CNb (main factor of Group, $F_{(1,14)} = 22.9$, $p < 0.001$) and moreover a significant effect of Task (AN vs. SP) was found ($F_{(1,14)} = 5.65$, $p = 0.03$), suggesting that when RBD and CNb are considered together the action imitation following anatomical coordinates in more difficult to performed compared with the spatial imitation (87% vs. 90%). A significant difference in the performance between LBD and RBD patients was found in the ANOVA comparing the two groups (main factor of Group, $F_{(1,13)} = 5.5$, $p = 0.036$), with RBD patients more impaired with respect to LBD (81% vs. 90% mean accuracy). Moreover, a significant effect of Task (AN vs. SP) was found ($F_{(1,13)} = 6.3$, $p = 0.026$), suggesting that when RBD and LBD are considered together the action imitation following anatomical coordinates in more difficult to performed compared with the spatial imitation (83% vs. 87%). See Figure 5.2.
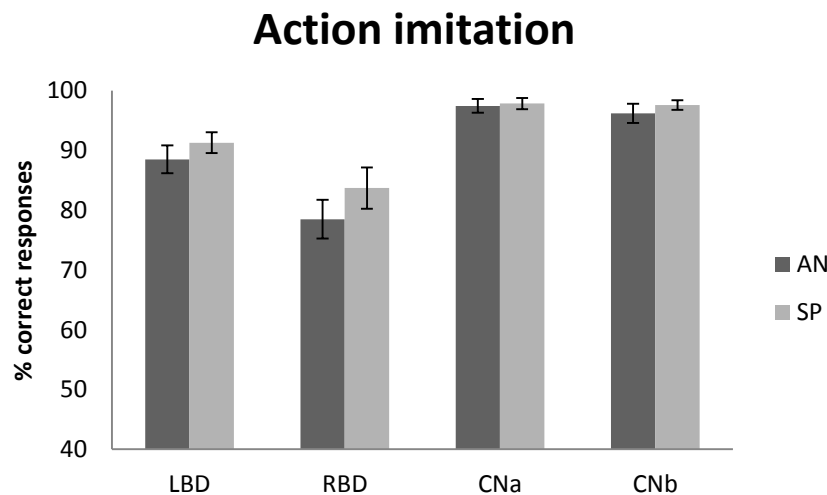


Figure 5.2 Performance as percentage of correct responses for LBD, RBD and controls for the action imitation. Vertical bars show the standard error of the mean.

Concerning the body rotation task, held to tap two of the body representations, the body schema and the body structural description, only a significant effect of Group was found in the ANOVA testing RBD patients vs. CNb ($F_{(1,14)} = 6.3$, $p = 0.025$). No significant effects were found for the two ANOVAs testing for differences between LDB vs. CNa and LBD vs. RBD. See Figure 5.3.
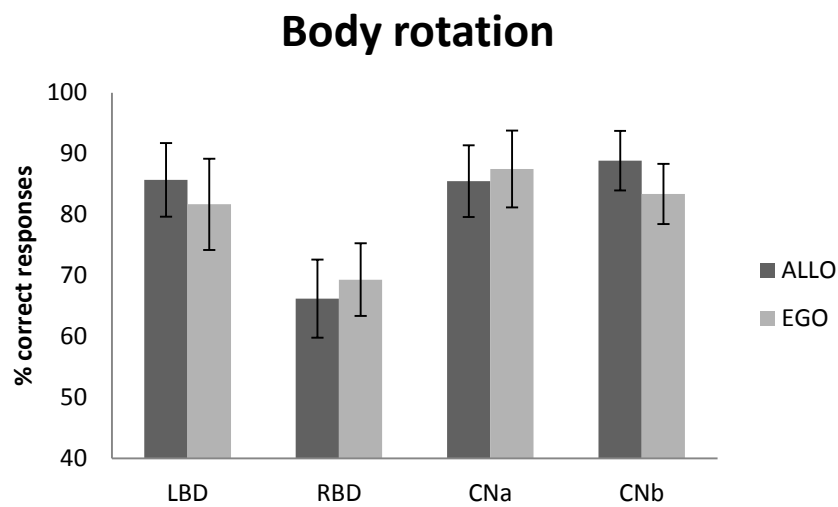
## Body rotation



Figure 5.3 Performance as percentage of correct responses for LBD, RBD and controls for the action imitation. Vertical bars show the standard error of the mean.

*5.3.2 Single cases*

Table 5.3 provides a summary of the individual performance of all patients across the experimental tasks.

Table 5.3 Individual performance of all patients across all experimental tasks.

| Cases | Automatic imitation | | | | Action imitation | | | | Body rotation | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | AN | | SP | | AN | | SP | | ALLO | | EGO | |
| | % corr | *t* score | % corr | *t* score | % corr | *t* score | % corr | *t* score | % corr | *t* score | % corr | *t* score |
| **LBD** | | | | | | | | | | | | |
| C.L. | 98 | -0.09 | 100 | 0.36 | 79 | **-5.67** | 87 | **-4** | 72 | -0.81 | 56 | -1.75 |
| D.F. | 96 | -0.75 | 96 | 0.14 | 83 | **-4.4** | 86 | **-4.53** | 97 | 0.68 | 100 | 0.7 |
| G.D. | 100 | 0.56 | 100 | 0.36 | 96 | -0.5 | 94 | -1.42 | 100 | 0.87 | 92 | 0.26 |
| G.P. | 94 | -1.4 | 100 | 0.36 | 90 | -2.21 | 86 | **-4.53** | 83 | -0.16 | 72 | -0.87 |
| P.C. | 96 | -0.75 | 73 | -1.05 | 89 | -2.65 | 94 | -1.42 | 58 | -1.66 | 57 | -1.75 |
| S.S. | 87 | **-3.34** | 98 | 0.25 | 96 | -0.5 | 93 | -1.91 | 100 | 0.87 | 95 | 0.44 |
| T.S. | 81 | **-5.36** | 100 | 0.36 | 86 | **-3.52** | 97 | -0.37 | 91 | 0.31 | 100 | 0.7 |
| | | | | | | | | | | | | |
| **RBD** | | | | | | | | | | | | |
| B.E. | 94 | -0.46 | 96 | **-5.25** | 72 | **-5.66** | 74 | **-11.31** | 69 | -0.3 | 67 | 0.8 |
| C.F. | 46 | **-7.98** | 79 | **-27.6** | 65 | **-7.3** | 80 | **-8.06** | 42 | **-3.14** | 58 | -1.72 |
| C.P. | 100 | 0.53 | 75 | **-33.27** | 86 | **-2.38** | 86 | **-5.42** | 64 | -1.67 | 77 | -0.46 |
| G.L. | 69 | **-4.38** | 69 | **-41.75** | 83 | **-3.04** | 86 | **-5.42** | 86 | -0.2 | 84 | 0.06 |
| H.B. | 100 | 0.53 | 96 | **-5.25** | 93 | -0.75 | 97 | -0.19 | 86 | -0.2 | 73 | -0.67 |
| M.M. | 90 | -1.1 | 46 | **-72.6** | 72 | **-5.66** | 72 | **-11.97** | 52 | **-2.51** | 42 | **-2.77** |
| M.R. | 67 | **-4.7** | 96 | **-5.25** | 82 | **-3.37** | 97 | -0.19 | 47 | **-2.83** | 58 | -1.72 |
| V.L. | 52 | **-6.99** | 96 | **-5.25** | 74 | **-5.33** | 76 | **-9.99** | 69 | -1.36 | 67 | -1.09 |

Note: Patients are ordered divided into LBD and RBD groups and ordered alphabetically by their initials. Numbers in bold denote t scores (Crawford & Garthwaite, 2005) significantly below the controls' mean.

*Comparisons within automatic imitation.* Overall six patients out of 15 were impaired in performing the Anatomical task with respect to the controls, two of them were LBD whereas four were RBD. All eight RBD patients performed below controls in the Spatial task, whereas performance of all LBD patients was comparable to controls.

One LBD patient (T.S.) showed a classical dissociation between the two tasks, performing pathologically in Anatomical task, but normally in Spatial task. Six RBD patients showed the reverse dissociation, with better performance on Anatomical than Spatial task. Four of them exhibited a classical dissociation (B.E, C.P., H.B., M.M.) with

performance within normal range for Anatomical task and pathological performance for Spatial task. Two RBD patients showed a strong dissociation (C.F., G.L.), as performance on both tasks was worse than that of controls but Anatomical task was more impaired than Spatial task. See Figure 5.4.
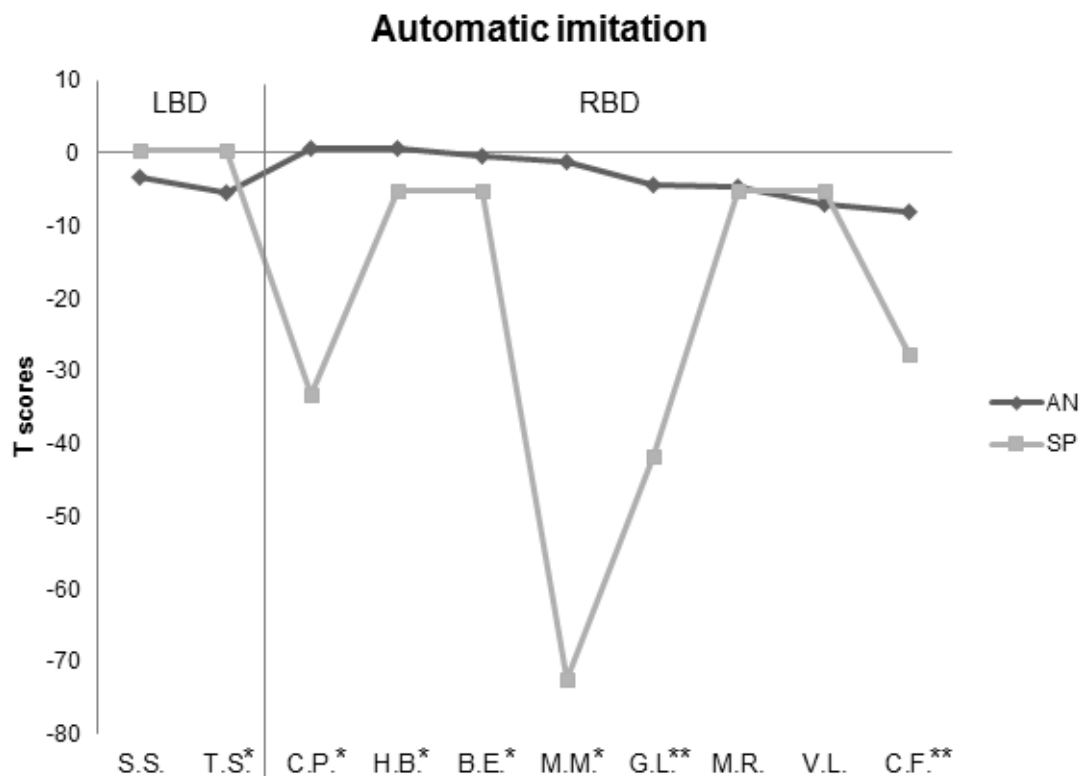
**Automatic imitation**



Figure 5.4 Dissociations between Anatomical and Spatial task in automatic imitation. Patients whose performance was below controls' in at least one of the two tasks are shown. Beside patients' initials: * indicates classical dissociation, ** indicates strong dissociation.

*Comparisons within action imitation.* Overall 10 out of 15 patients were impaired in performing the Anatomical task for action imitation, three of them were LBD whereas seven were RBD. Nine patients were impaired in performing the Spatial task for action imitation, three of them were LBD whereas six were RBD. Four RBD patients (B.E., C.P., M.M., V.L.) exhibited a strong dissociation, with performance on both tasks worse

than that of controls, but Spatial task was more impaired than Anatomical task. See
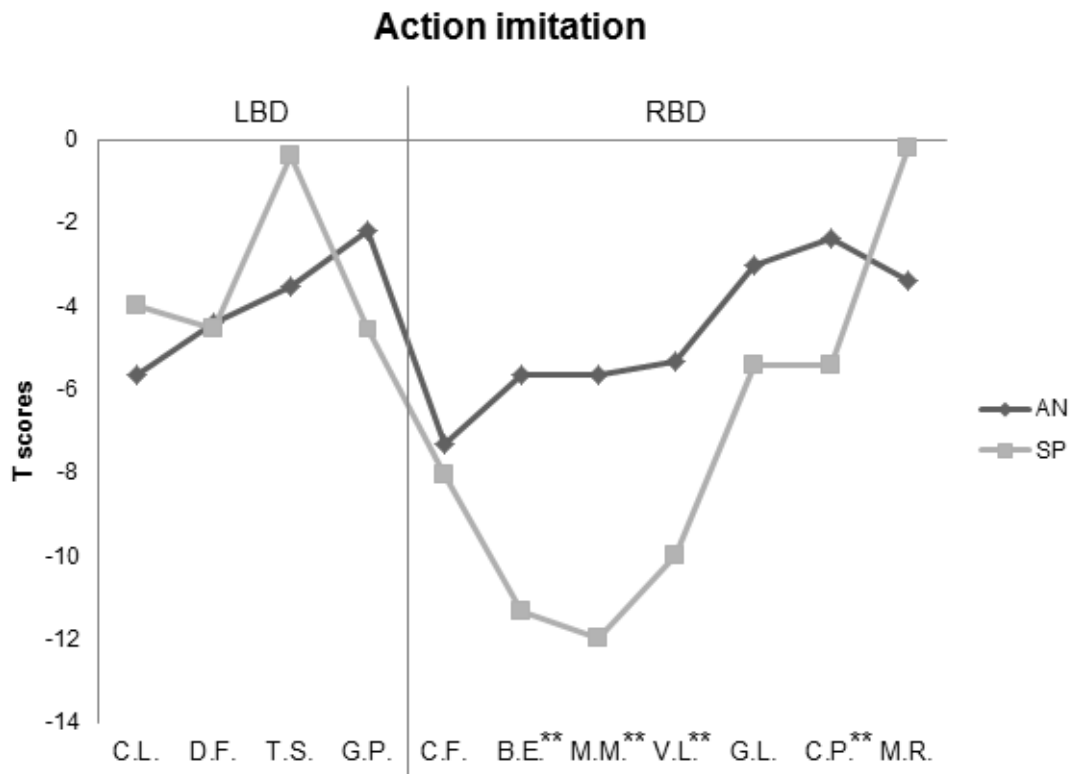Figure 5.5.

**Action imitation**



Figure 5.5 Dissociations between Anatomical and Spatial task in action imitation. Patients whose performance was below controls' in at least one of the two tasks are shown. Beside patients' initials: ** indicates strong dissociation.

*Comparisons within body rotation.* Significant results were restricted to the RBD patients for body rotation, with three patients (C.F., M.M., M.R.) whose performance was impaired with respect to controls in the Allocentric strategy and one patient (M.M.) whose performance was impaired also in the Egocentric strategy. None of them reached significance for dissociating pattern.

*Comparisons between automatic and action imitation.* We compared the two imitation tasks in order to find differences within Anatomical or Spatial task in the two imitative modalities. As for the Anatomical task, we failed to find a double dissociation, however

two dissociating cases were found. One LBD patient (C.L.) and one RBD patient (B.E.) showed a classical dissociation, performing pathologically on action imitation, but normally on automatic imitation. See Figure 5.6.
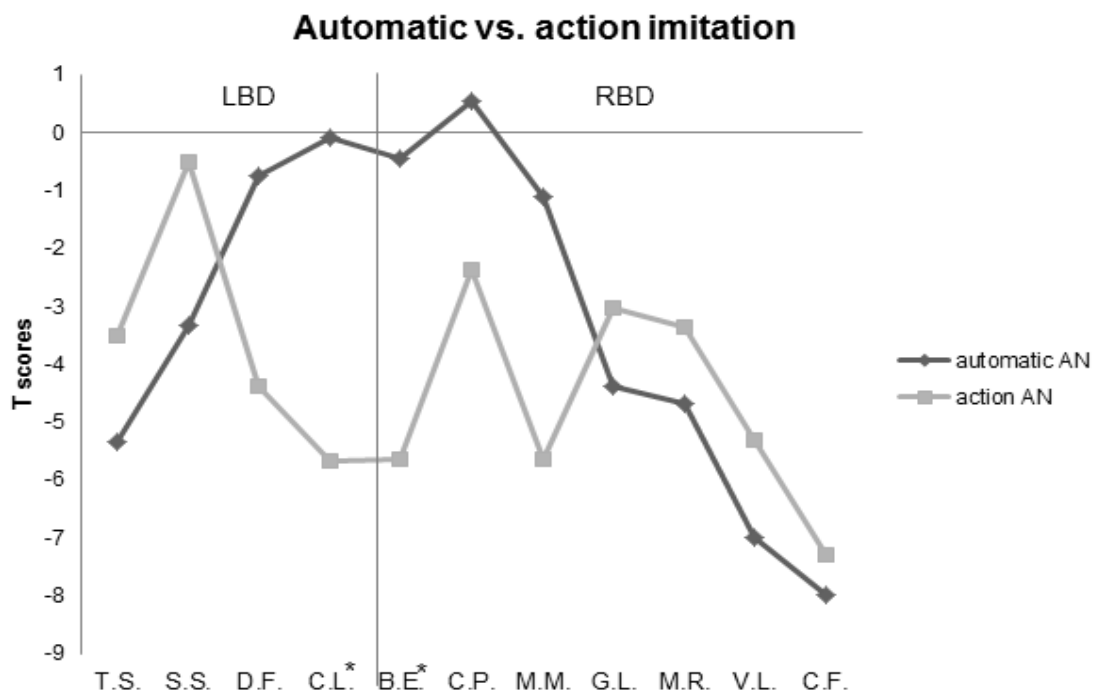


Figure 5.6 Dissociations between automatic and action imitation in Anatomical task. Patients whose performance was below controls' in at least one of the two conditions are shown. Beside patients' initials: * indicates classical dissociation.

As for the Spatial task, a double dissociation was found. In three LBD patients (C.L., G.P., D.F.) and six RBD patients (C.F., C.P., G.L., H.B., M.M., M.R.) the performance was worse for the action imitation rather than automatic imitation. All three LBD patients exhibited a classical dissociation, performing pathologically on action imitation, but normally on automatic imitation. Concerning the RBD dissociating patients, four out of six (C.F., C.P., G.L., M.M.) exhibited a strong dissociation, whereas two of them (H.B., M.R.) showed a classical dissociation. See Figure 5.7.
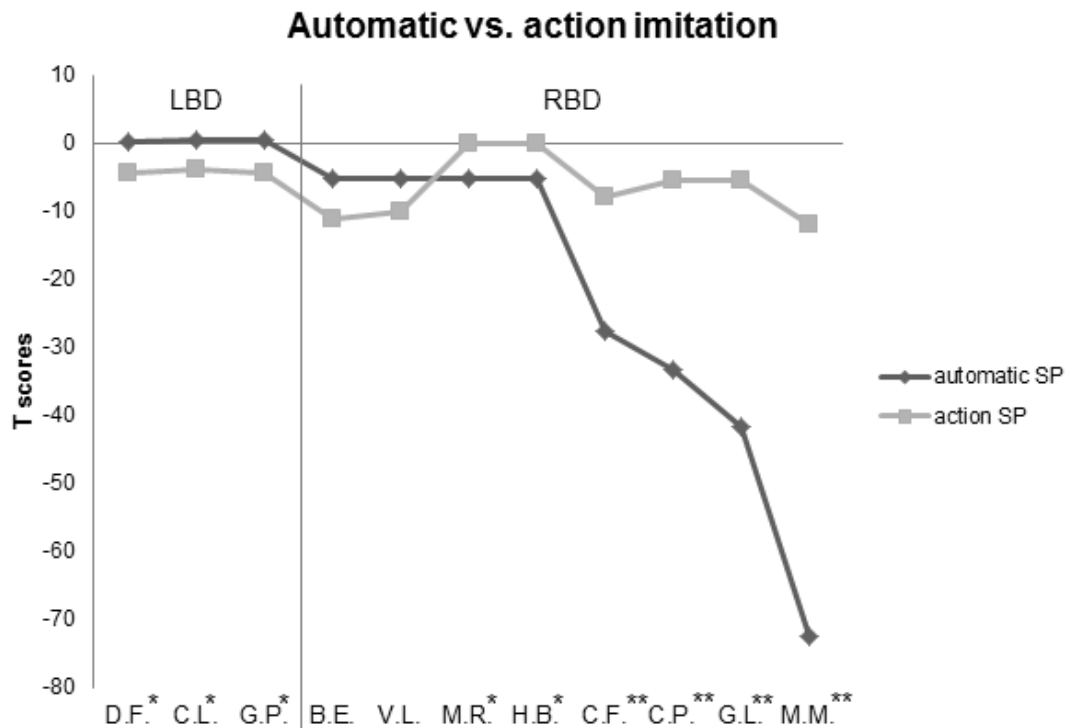
Figure 5.7 Dissociations between automatic and action imitation in Spatial task. Patients whose performance was below controls' in at least one of the two conditions are shown. Beside patients' initials: * indicates classical dissociation, ** indicates strong dissociation.

*Comparisons between imitation and body rotation.* To investigate the connection between imitation and body rotation we tested whether patients with impaired performance on one of the two body rotation tasks showed dissociations with performance on imitation tasks. Three RBD patients (C.F., M.M., M.R.) were impaired compared to controls in the Allocentric strategy, and one of them (M.M.) was impaired also in the Egocentric strategy. One patient (M.R.) did not show dissociations between performances on body rotation and imitation tasks. Patient C.F. exhibited strong dissociations between Allocentric strategy and all imitation tasks, however performance on imitation tasks was in all cases worse than performance on body rotation task. Patient M.M. exhibited strong dissociations between Allocentric strategy and all imitation tasks and between Egocentric strategy and Spatial task both for automatic and action imitation,

however performance on imitation tasks was in all cases worse than performance on body rotation task.

### 5.3.3 Lesion results

Limited by the size of our sample, we performed a simple overlay of all LBD and RBD patients. Therefore, results have to be considered as descriptive. See Table 5.4 and Figure 5.8.

As for LBD group, the regions most commonly damaged (in four patients out of six) were the insular cortex, extending to the parietal operculum and the putamen. Similar regions were most commonly damaged in RBD patients (in six out of seven).

Table 5.4 Results of the lesions overlay.

|  | MNI coordinates | | | Region |
|---|---|---|---|---|
|  | x | y | z |  |
| **LBD** | 41 | -8 | -1 | Insula |
|  | 34 | -11 | 14 | OP |
|  | 36 | -7 | 2 | Putamen |
| **RBD** | -33 | -12 | 21 | Insula/OP |
|  | -27 | -13 | 4 | Putamen |

Note: OP=parietal operculum. MNI coordinates are shown according to the neurological convention.
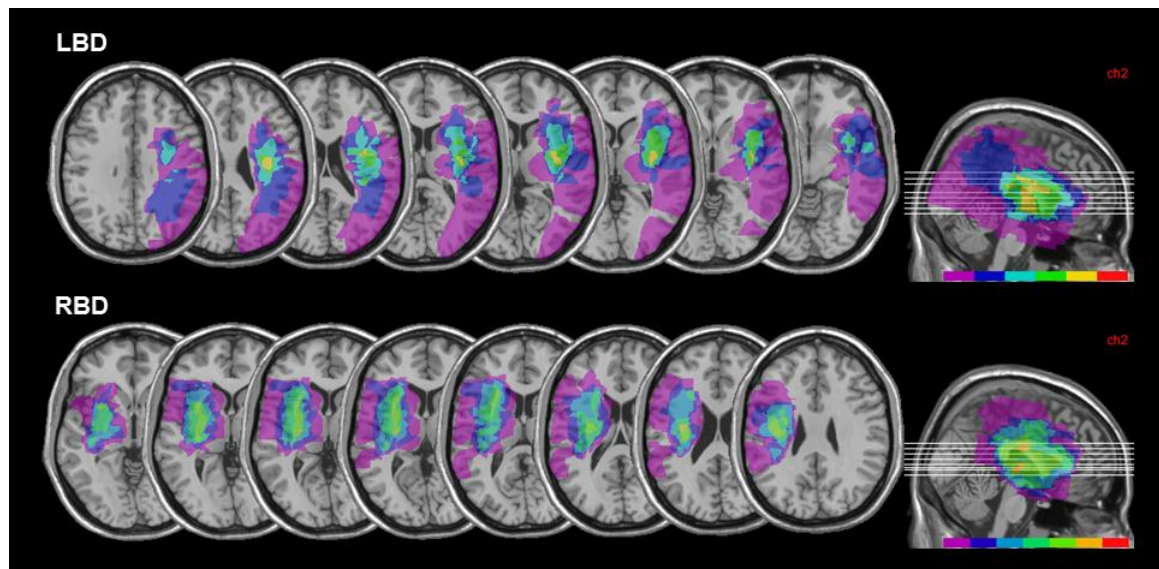
Figure 5.8 The lesion overlay of all LBD and RBD patients. In each figure, the number of overlapping lesions is illustrated by different colors coding increasing frequencies from a violet (n=1) to red (indicating the maximum number of subjects in each group) color.

Note: Images are shown in the neurological convention, with the right hemisphere on the left side of the picture and vice versa.

## 5.4 Discussion

The first aim of the study was to address eventual differences between the different ways in which individuals may reproduce actions, whether automatically or voluntarily, and whether there are differences when imitation is performed according to anatomical and specular perspectives. Indeed, while neuroimaging studies on automatic imitation suggests that different neural substrates could serve imitation performed following anatomical or spatial coordinates, direct evidence based on neuropsychological patients is missing.

This issue is important also for the clinical implications, as the ideomotor apraxia showed by brain damaged patients is tested using imitation tests that are normally administered according to the specular perspective, in which the model is like the mirror-image of the imitator. The second, related aim of this study was to assess how body

representations interact with imitative behaviors. To this end, I have employed a new body part rotation task that is suitable to disentangle two putative body representations: the body schema and the body structural description.

We studied left and right brain damaged patients to investigate the contribution of each hemisphere in performing imitation tasks and in processing body related information. So far, I have tested seven LBD and eight RBD patients. Due to current limitations of the study mostly concerning the sample size of the patient groups, the data presented cannot be taken as conclusive.

Overall, performance on the experimental tasks administered to RBD patients was worse than that of LBD patients; RBD patients were found to be significantly impaired with respect to controls in automatic imitation, action imitation and body rotation tasks, whereas LBD patients were significantly impaired only in action imitation. Moreover, RBD patients were more impaired in imitation tasks than LBD patients. Even keeping in mind the differences in the overall severity of the cognitive impairment between the two groups, what is interesting here is that LBD patients performed differently on automatic imitation and action imitation tasks. Given that a deficit on action imitation task is typically referred to as ideomotor apraxia, the present results suggest that automatic imitation tasks are not sufficiently sensitive to detect imitative deficits. This can be simply due to differences in the level of difficulty of the two tasks, rather than different cognitive processes implied.

Single-case results are in line with data at the group level, with three LBD patients showing a dissociation between automatic imitation and action imitation, and performance on action imitation being more impaired than that on automatic imitation (one patient showed the dissociation both for Anatomical and Spatial task, whereas two patients showed the dissociation only for the Spatial task). The reverse dissociation was found for RBD patients, with six patients being more impaired in automatic that action imitation (for the Spatial task). However, one RBD patient showed the same pattern of LBD patients, with better performance on automatic than action imitation (only in the Anatomical task). The dissociating cases imply that different mechanisms are operating in automatic and action imitation. We can hypothesize that the main difference could

concern the complexity of the motor schemes required to perform a complete action or gesture reproduction, as in action imitation, rather than to perform a pre-determined simple finger movement as in automatic imitation. The incorrect execution of motor plans or the disruption of the motor plan itself is one of the basics concepts of theoretical accounts used to explain apraxic deficits (Liepmann, 1920; Ochipa, Rothi, Heilman, 1991; Rumiati, Carmo, Corradi-Dell'Acqua, 2009). On the contrary, automatic imitation tasks typically involve simple movements and do not imply planning complex action but a careful selection of the finger performing the action or of the movement direction, suggesting that different processes, more related to attention or response selection of action rather than motor planning, are more likely to be necessary to successfully accomplish the task (see Brass, Derrfuss, Matthes-von Cramon, von Cramon, 2003 for a study on frontal patients). This can partially explain why there are discrepancies between neuroimaging studies and patients' studies, as most of the neuroimaging studies on imitation employed automatic imitation tasks (Iacoboni et al. 1999; Brass, Zysset, von Cramon, 2001; Koski et al. 2003; Bien, Roebroeck, Goebel, Sack, 2009; Mengotti, Corradi-Dell'Acqua, Rumiati, 2012) and patients' studies used action imitation as measure of apraxia (De Renzi, Motti, Nichelli, 1980; Papagno, Della Sala, Basso, 1993; Goldenberg 1995; Haaland, Harrington, Knight, 2000; Tessari, Canessa, Ukmar, Rumiati, 2007).

As to the components of imitation (anatomical and specular), we found a double dissociation between LBD and RBD patients in their automatic tendency to imitate, with one LBD patient's performance being impaired on the Anatomical task, but not in the Spatial task, and the reverse pattern for six RBD patients (two of them had a strong dissociation, with performance below control's in both tasks, but the Spatial task was more impaired than the Anatomical task). We failed to find a double dissociation within LBD or RBD patients, suggesting that mechanisms of automatic tendency to imitate according to anatomical or spatial coordinates may be discretely grounded in the two hemispheres. The automatic imitation paradigm used implies, for the two tasks, not only the activation of the mechanisms necessary to imitate in anatomical or specular way, but

also inhibitory mechanisms to suppress the tendency to imitate anatomically when the Spatial task is performed and vice versa. This is due to the particular structure of the paradigm. For instance, when the Spatial task is performed and a non-mirror hand is shown to the participant (i.e. when the participant is moving his/her right hand and a right hand is shown on the screen), the correct answer requires to move the finger that is in the same spatial position of that moved by the stimulus hand and to ignore the identity of the finger, in this case incongruent between stimulus' and participant's hand. The poor performance of the RBD patients on the Spatial task, compared to the Anatomical task, suggests that a disruption of the mechanisms underlying an automatic response following spatial coordinates, i.e. specular imitation, occurred.

While previous neuroimaging studies showed that the middle frontal gyrus plays a role in detecting spatial incompatibility between model's and performer's movements (Brass, Zysset, von Cramon, 2001; Bien, Roebroeck, Goebel, Sack, 2009; Mengotti, Corradi-Dell'Acqua, Rumiati, 2012), the lateralization of this components is less clear as conflicting findings have been reported (bilateral (Brass, Zysset, von Cramon, 2001), more lateralized on the left (Mengotti, Corradi-Dell'Acqua, Rumiati, 2012), or on the right (Bien, Roebroeck, Goebel, Sack, 2009)). However, the present results are in line with a general competence of the right hemisphere for visuospatial abilities and in particular for the visuospatial analysis of gestures (Goldenberg, 1999).

As for the LBD patients, one patient showed the reverse dissociation, with normal performance on Spatial task and impaired performance on Anatomical task, suggesting the presence of mechanisms for coding anatomical correspondence between model's and performer's movements that are independent from those abovementioned that respond to spatial information.

A similar pattern of results is showed in the analysis of single cases in the action imitation, for differences between Anatomical and Spatial task. So far, results are restricted to the RBD patients, four of them showed a strong dissociation between Anatomical and Spatial task, with performance on Spatial task more impaired than performance on Anatomical task. These results are in favor of the hypothesis that mechanisms underlying anatomical and spatial imitation are different and processes

recruited by each type of imitation can be compared whether participants' performed automatic or action imitation tasks.

As results were mainly restricted to RBD patients, it is inevitable to discuss the possible influence of the unilateral neglect in the present data. Even if we cannot completely rule out the possibility that unilateral neglect could directly be responsible of the observed performance in imitation tasks, this is unlikely because for automatic imitation stimuli are the same in both tasks; thus if the contralateral side of the space is neglected in RBD patients, performance should be impaired not only in Spatial task, but in the Anatomical task as well. For action imitation, the Spatial task of RBD patients is performed with the experimenter's left hand in the right visual field, whereas the Anatomical task is performed in the left visual field, thus results are completely reversed with respect to those that could be predicted from the influence of unilateral neglect. Moreover, one of the patients that showed a dissociation between Anatomical and Spatial task both for automatic and action imitation did not present neglect.

Present results enrich the current literature on the differences between anatomical and specular imitation, suggesting the existence of independent mechanisms underlying these two types of imitation. Previous studies were restricted on children and showed a general preference towards specular imitation (Wapner & Cirillo, 1968; Schofield, 1976; Bekkering, Wohlschläger, Gattis, 2000; Gleissner, Melzoff, Bekkering, 2000), suggesting only that specular imitation was easier to accomplish. However, a systematical investigation on the mechanisms serving the two types of imitation was missing. Present data showed that for action imitation the anatomical imitation is more difficult to perform rather than specular one, but also that different cognitive mechanisms underlie these two types of imitation.

As to the interaction between imitation and body representations, only two RBD patients presented with a strong dissociation between body rotation and imitation tasks, but with worst performance on imitation task than on body rotation. Thus, the present data cannot clarify which of the body representations is necessary in performing imitation. As abovementioned, the present data cannot be considered as conclusive

because of the small sample size and of a slightly greater severity of the RBD patients compared with the LBD patients. Further work will be required to fully clarify the connections between automatic imitation, action imitation and body representations.

# Chapter 6

## GENERAL DISCUSSION

On the very first page of this thesis I listed some questions concerning imitation that have not yet found a satisfactory answer. These questions include what we mean by imitation, but also how the observed actions are mapped onto the motor system of the observer and whether can we talk about imitation even when we reproduce movements performed by abstract or robotic models. In the following chapters, I then tried to provide some answers to these questions based on my own empirical work. In the present chapter, I will sum up the main results, how they modify the theoretical characterization of imitation and sketch some further directions for future work.

What is imitation then? There is a large consensus that the perception of an action produced by a model influences the performer's executed action. The existence of this basic mechanism is acknowledged and supported by the two main theories of imitation: the ideomotor theory (Prinz, 1997; Hommel, Müsseler, Aschersleben, Prinz, 2001; Massen & Prinz, 2009) and the associative learning theory (Heyes & Ray, 2000). Demonstrations of this basic mechanism of imitation have been provided and widely replicated using automatic imitation paradigms (e.g. Brass, Bekkering, Wohlschläger, Prinz, 2000; Brass, Bekkering, Prinz, 2001; Brass, Derrfuss, Matthes-von Cramon, von Cramon, 2003; Bertenthal, Longo, Kosobud, 2006; Longo, Kosobud A, Bertenthal, 2008; Longo & Bertenthal, 2009; Boyer, Longo, Bertenthal, 2012). In these studies, participants are typically asked to observe a finger movement and produce a finger movement that can be the same or different with respect to the one observed. Results showed a compatibility effect, thus if observed and executed movements are the same,

participants are faster to produce the movement than when the two movements are different.

Even though sharing this fundamental principle, the two theoretical frameworks were stretched in different directions, with the ideomotor theory focusing on the cognitive mechanisms underlying the link between action and perception, and the associative learning theory emphasizing the manner in which these associations are acquired. However, in my view these two theories are more similar than it was first thought, as they represent two sides of the same coin (Hommel, personal communication).

In my dissertation, the assumption that perception and action are connected through a basic ideomotor mechanism has been further developed in two main directions. On one hand, I further investigated how this principle works and what are the cues that are used by the imitator to match the model's movements with his/her own movements; on the other hand I have also investigated some external factors that may influence automatic imitation and what is the relationship of these simple mechanisms with the more complex "real life" imitation.

*6.1 Matching mechanisms between model and performer*

One of the open questions I raised in the chapter 1 concerned the correspondence problem whereby the actions performed by the model are mapped from observation onto the motor systems of the performer. The two main theories dealt with this issue by proposing that the correspondence between model and performer movements can be achieved through *similarity* for the ideomotor theory and *contiguity* for the associative learning theory. According to the former account, actions that are more similar are easier to reproduce, whereas according to the latter account, actions that were performed together in the past are easier to reproduce. However, neither of the two theories provides any insight as to which cues or coordinates the imitator relies on in reproducing the model's actions.

In everyday life, when we want to reproduce a gesture performed by a model in front of us, we can select one of two types of imitation: specular or anatomical. When I

replicate a gesture as if the model were my mirror-image, I rely on spatial coordinates, as the spatial position of the model's actions will be the most important cue for imitation (specular imitation). Instead, I can choose to move the very same effector that the model also moved (if the model moves his/her left hand I will move my left hand). This is called anatomical imitation and the anatomical matching between the body of the model and my body will be the most important cue for imitation.

In chapters 2 and 3 of my dissertation, I investigated the model-imitator matching problem using an automatic imitation paradigm. In the first study (see chapter 2), using the fMRI we were able to show that a particular region of the brain, i.e. the parietal opercula, was active whenever the matching between model and imitator was anatomical. Moreover, the left middle frontal gyrus was active when task instructions required participants to refrain from imitate according to spatial coordinates. We found evidence of different neural substrates for imitation depending on whether participants selected the anatomical cue or spatial cue. Behaviorally two different compatibility effects were found, the spatial compatibility in which participants were faster to perform the action when the observed and executed action occurred on the same side of the space, and the imitative compatibility (or anatomical compatibility) in which participants were faster to perform the action when the observed action and executed action were performed by the same finger. Some of the early studies on automatic imitation, which did not distinguish between these two types of compatibility (Brass, Bekkering, Wohlschläger, Prinz, 2000; Brass, Bekkering, Prinz, 2001), suggested that automatic imitation shared some basic principles with the stimulus-response compatibility (SRC). However, further studies showed that automatic imitation is something more than SRC; Thus, these studies successfully disentangled between spatial compatibility - an effect more in line with SRC accounts - and imitative compatibility (Boyer, Longo, Bertenthal, 2012; Catmur & Heyes, 2011), based on the anatomical correspondence between model and performer and hence especially human.

In chapter 3, I addressed more in depth the role of the parietal opercula in coding for the anatomical matching between the model and the performer. The hypothesis was that if the activity of this region was temporarily disrupted using double-pulse TMS, we

should have observed a reduction of the imitative compatibility. This is what it was found, thus suggesting that the spatial compatibility and imitative compatibility are two different processes that rely on different neural structures.

Thus in this first part of my dissertation, I have investigated how the model-performer matching mechanism works, and I showed that, depending on the cues on which imitators rely, the processes and neural substrates differ. The main focus has been on the imitative compatibility, as it is a process specific to imitation and, in particular, to imitation of a human model. This aspect will be addressed specifically in the following part of this chapter.

*6.2 Factors modulating imitative behaviors and real-life imitation*

The second part of my thesis was dedicated to explore the factors that may modulate automatic imitation. In chapter 4, I reported an fMRI study in which we investigated the role of the model identity and of the emotional context on automatic imitation. Since as for the effect spatial compatibility the most important factor is the spatial position or direction of the movement, in principle such effect can be replicated not only with a human model, but also with abstract shapes as model. On the contrary, if the model is human the matching mechanisms do not rely only on the spatial cues but also on the imitative compatibility or anatomical matching. The effect of the two types of compatibilities (or cues) can be present at the same time like, for example, when, in a simplified version of the automatic imitation paradigm, only one finger is moved but in two different directions, that is when a tapping and a lifting movement is performed. Using fMRI, we found that fronto-parietal regions that are traditionally considered to support imitative behaviors are more active when both types of compatibility are combined, thus when the model is human and when the model's gesture and imitator's gesture are performed in the same direction, i.e. when both are tapping movements. Moreover, we also found that emotions can influence automatic imitation, as the activations of fronto-parietal regions were found to promote affiliative tendencies in an emotional context, for instance when a sad face is shown. These activations were not

present when the action to be imitated was preceded by a different emotional context as, for instance, when an angry face was shown.

This study clearly suggests that automatic imitation can be modulated by changing some external parameters, such as the emotional context or the model identity. However, what remains to be explained is, for instance, the exact role played by the factors that contribute in this increased activation of fronto-parietal regions when a human model is shown. Is it all about the anatomical matching? Some studies suggest that this is not the case. Longo, Kosobud and Bertenthal (2008) showed that even with the same human model, if they manipulated the movement of the hand, that in one condition it showed a normal movement whereas in another condition it showed an impossible movement, the compatibility effect was reduced. However, this occurred only if participants were aware of the differences between the two movements.

In the last study of my thesis, described in chapter 5, I investigated the connections between automatic imitation and the more complex action imitation. Moreover, I addressed the issue of how body representations subserve imitative behaviors. To this end I have carried out a neuropsychological study in which I tested some hypotheses derived from the combination of neuropsychological and neuroimaging studies (De Renzi, Motti, Nichelli, 1980; Papagno, Della Sala, Basso, 1993; Goldenberg 1995; Iacoboni et al. 1999; Haaland, Harrington, Knight, 2000; Brass, Zysset, von Cramon, 2001; Koski et al. 2003; Rumiati et al. 2005; Tessari, Canessa, Ukmar, Rumiati, 2007; Bien, Roebroeck, Goebel, Sack, 2009; Menz, McNamara, Klemen, Binkofski, 2009; Mengotti, Corradi-Dell'Acqua, Rumiati, 2012). To date, there is no agreement between neuropsychological reports on patients with apraxia caused by left hemisphere damage, and neuroimaging studies, that highlighted bilateral activations associated with imitation. Furthermore, imitation has been studied using different tasks, with automatic imitation paradigms or with gesture imitation, relying on the fact that the basic mechanism that links perception and action is shared by all types of imitation. However, no study directly investigated whether automatic and action imitation can be comparable, or whether some differences can be found. Our data show that some differences are present between automatic and action imitation, with some patients double dissociating

between the two types of imitation, as well as a tendency towards a different lateralization of the underlying processes. However, as mentioned in chapter 5, these observations should not be considered as conclusive.

*6.3 Concluding remarks and future directions*

With my thesis I tried to fill the gaps between theories on imitation and behavior. However, more work is needed, especially when considering the role of body representations in imitation, and the comparison between automatic and action imitation. These two behavioral patterns seem to rely on the same cognitive mechanism of common coding between perception and action; however, the correct reproduction of a gesture or the production of the correct action in an automatic imitation task requires the activation of some additional processes.

Thus, the take-home message of my thesis is that complex behaviors such as imitation have to be studied from different perspectives. First, it is necessary to investigate in depth the basic mechanisms underlying a given behavior by breaking down the behavior itself into functional components. This is what my studies on automatic imitation have contributed to, by investigating imitative phenomena with very simple paradigms, based on the assumptions that some basic mechanisms, such as perception and action common coding processes, are shared by all types of imitation. Second, as it is important to pay attention also to the whole forest and not only to the single tree, in the second part of my dissertation, I have analyzed the influence of some external factors on automatic imitation and I studied the differences between different types of imitation.

One advantage of using different research methods to investigate the components of imitation is that we can obtain converging evidence on the phenomenon under scrutiny. However, as it has been discussed also in other cognitive domains, such as reading (Coltheart, 2006), sometimes different techniques may lead to apparently inconsistent results. My dissertation is an attempt towards this reconciliation.

# REFERENCES

Agnew, Z., Wise, R.J.S. (2008). Separate areas for mirror responses and agency within the parietal operculum. *Journal of Neuroscience*, 28, 12268-12273.

Alaerts, K., Swinnen, S. P., Wenderoth, N. (2009). Is the human primary motor cortex activated by muscular or direction-dependent features of observed movements? *Cortex,* 45(10), 1148-1155.

Arrington, C.M., Carr, T.H., Mayer, A.R., Rao, S.M. (2000). Neural mechanisms of visual attention: object-based selection of a region in space. *The Journal of Cognitive Neuroscience,* 12, 106-117.

Ashburner, J., Friston, K.J. (2003). Rigid body registration. In: Frackowiak RS, Friston KJ, Frith CD, Dolan RJ, Price CJ, Zeki S, Ashburner JT, Penny WD, editors. Human brain function. London: Academic. pp. 653–655.

Avikainen, S., Forss, N., Hari, R. (2002). Modulated activation of the human SI and SII cortices during observation of hand actions. *NeuroImage*, 15, 640-646.

Bekkering, H., Wohlschläger, A., Gattis, M. (2000) Imitation of gestures in children is goal-directed. *The Quarterly Journal of Experimental Psychology,* 53A(1), 153-164.

Belopolsky, A.V., Olivers, C.N.L., Theeuwes, J. (2008). To point a finger: Attentional and motor consequences of observing pointing movements. *Acta Psychologica,* 128(1), 56–62.

Bertenthal, B.I., Longo, M.R., Kosobud, A. (2006). Imitative response tendencies following observation of intransitive actions. *The Journal of Experimental Psychology: Human Perception and Performance*, 32, 210-225.

Bien, N., Roebroeck, A., Goebel, R., Sack, A.T. (2009). The brain's intention to imitate: the neurobiology of intentional versus automatic imitation. *Cerebral Cortex*, 19, 2338-2351.

Bird, G., Leighton, J., Press, C., Heyes, C. (2007). Intact automatic imitation of human and robot actions in autism spectrum disorders. *Proceedings of the Royal Society B*, 274, 3027–3031.

Blair, R.J.R., Morris, J.S., Frith, C.D., Perrett, D.I., Dolan, R. (1999). Dissociable neural responses to facial expressions of sadness and anger. *Brain*, 122, 883–893.

Blair, R.J.R. (2003). Facial expressions, their communicatory functions and neuro-cognitive substrates. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 358, 561–572.

Blair, R.J. (2007). Dissociable systems for empathy. Novartis Found Symp, 278, 134-141; discussion 141-145, 216-221.

Boyer, T.W., Longo, M.R., Bertenthal, B.I. (2012). Is automatic imitation a specialized form of stimulus–response compatibility? Dissociating imitative and spatial compatibilities. *Acta Psychologica*, 139(3), 440-448.

Brass, M., Bekkering, H., Wohlschläger, A., Prinz, W. (2000). Compatibility between observed and executed finger movements: comparing symbolic, spatial, and imitative cues. *Brain and Cognition*, 44, 124-143.

Brass, M., Bekkering, H., Prinz, W. (2001). Movement observation affects movement execution in a simple response task. *Acta Psychologica*, 106, 3-22.

Brass, M., Zysset, S., von Cramon, D.Y. (2001). The inhibition of imitative response tendencies. *NeuroImage*, 14, 1416-1423.

Brass, M., Derrfuss, J., Matthes-von Cramon, G., von Cramon, D.Y. (2003). Imitative response tendencies in patients with frontal brain lesions. *Neuropsychology,* 17(2), 265-271.

Brass, M., Derrfuss, J., von Cramon, D.Y. (2005). The inhibition of imitative and overlearned responses: a functional double dissociation. *Neuropsychologia,* 43, 89–98.

Brass, M. Heyes, C. (2005). Imitation: Is cognitive neuroscience solving the correspondence problem? *Trends in Cognitive Sciences*, 9, 489–495.

Brebner, J., Shephard, M., Cairney, P. (1972). Spatial relationships and S-R compatibility. Acta Psychologica, 36, 1-15.

Bremmer, F., Schlack, A., Shah, N., Zafiris, O., Kubischik, M., Hoffmann, K., Zilles, K., Fink, G.R. (2001) Polymodal motion processing in posterior parietal and premotor cortex: a human fMRI study strongly implies equivalencies between humans and monkeys. *Neuron*, 29, 287-296.

Burton, H., Fabri, M., Alloway, K. (1995). Cortical areas within the lateral sulcus connected to cutaneous representations in areas 3b and 1: a revised interpretation of the second somatosensory area in macaque monkeys. *The Journal of Comparative Neurology*, 355, 539-562.

Buxbaum, L.J., Giovannetti, T., Libon, D. (2000). The role of the dynamic body schema in praxis: evidence from primary progressive apraxia. *Brain and Cognition*, 44, 166–191.

Buxbaum, L.J., Coslett, H.B. (2001). Specialised structural descriptions for human body parts: Evidence from autotopagnosia. *Cognitive Neuropsychology,* 18(4), 289–306.

Cabeza, R., Nyberg, L. (2000). Imaging cognition II: an empirical review of 275 PET and fMRI studies. *The Journal of Cognitive Neuroscience,* 12, 1-47.

Carlesimo, G.A., Caltagirone, C., Gainotti, G., Nocentini, U. (1995). Batteria per la valutazione del deterioramento mentale (parte II): standardizzazione e affidabilità diagnostica nell'identificazione di pazienti affetti da sindrome demenziale. *Archivio di Psicologia, Neurologia e Psichiatria*, 56 (4), 471- 488.

Carr, L., Iacoboni, M., Dubeau, M.C., Mazziotta, J.C., Lenzi, G.L. (2003). Neural mechanisms of empathy in humans: A relay from neural systems for imitation to limbic areas. *Proceedings of the National Academy of Sciences USA*, 100, 5497–5502.

Caspers, S., Zilles, K., Laird, A.R., Eickhoff, S.B. (2010). ALE meta-analysis of actionobservation and imitation in the human brain. *NeuroImage,* 50(3), 1148–1167.

Castiello, U., Lusher, D., Mari, M., Edwards, M., Humphreys, G. (2002). Observing a human or a robotic hand grasping an object: Differential motor priming effects. In W. Prinz & B. Hommel (Eds.), Common mechanisms in perception and action: Attention and performance XIX (pp. 315–333). New York: Oxford University Press.

Catmur, C., Walsh, V., Heyes, C. (2007). Sensorimotor learning configures the human mirror system. *Current Biology,* 17(17), 1527–1531.

Catmur, C., Walsh, V., Heyes, C. (2009). Associative sequence learning: the role of experience in the development of imitation and the mirror system. *Philosophical Transactions of the Royal Society B: Biological Sciences,* 364(1528), 2369 -2380.

Catmur, C., Heyes, C. (2011). Time course analyses confirm independence of imitative and spatial compatibility. *Journal of Experimental Psychology: Human Perception and Performance*, 37(2), 409-421.

Chakrabarti, B., Bullmore, E., Baron-Cohen, S. (2006). Empathizing with basic emotions: common and discrete neural substrates. *Social Neuroscience*, 1, 364-384.

Chaminade, T., Meltzoff, A.N., Decety, J. (2005). An fMRI study of imitation: action representation and body schema. *Neuropsychologia,* 43(1), 115-127.

Chartrand, T.L., Bargh, J.A. (1999). The chameleon effect: The perception-behavior link and social interaction. *Journal of Personality and Social Psychology*, 76, 893-910.

Chen, R., Wassermann, E.M., Caños, M., Hallett, M. (1997). Impaired inhibition in writer's cramp during voluntary muscle activation. *Neurology,* 49(4), 1054-1059.

Cieslik, E.C., Zilles, K., Kurth, F., Eickhoff, S.B. (2010). Dissociating bottom-up and top-down processes in a manual stimulus–response compatibility task. *Journal of Neurophysiology*, 104(3), 1472-1483.

Coltheart, M. (2006). What has functional neuroimaging told us about the mind (so far)? *Cortex*, 42(3), 323-31.

Cook, R., Press, C., Dickinson, A., Heyes, C. (2010). Acquisition of automatic imitation is sensitive to sensorimotor contingency. *Journal of Experimental Psychology: Human Perception and Performance*, 36(4), 840-852.

Corbetta, M., Kincade, J.M., Ollinger, J.M., McAvoy, M.P., Shulman, G.L. (2000). Voluntary orienting is dissociated from target detection in human posterior parietal cortex. *Nature Neuroscience,* 3, 292-297.

Corbetta, M., Kincade, J.M., Shulman, G.L. (2002). Neural systems for visual orienting and their relationships to spatial working memory. *The Journal of Cognitive Neuroscience*, 14, 508-523.

Corbetta, M., Patel, G., Shulman, G.L. (2008). The reorienting system of the human brain: from environment to theory of mind. *Neuron,* 58, 306-324.

Corradi-Dell'Acqua, C., Tomasino, B., Fink, G.R. (2009). What is the position of an arm relative to the body? Neural correlates of body schema and body structural description. *The Journal of Neuroscience*, 29, 4162-4171.

Cunnington, R., Windischberger, C., Robinson, S., Moser, E. (2006). The selection of intended actions and the observation of others' actions: A time-resolved fMRI study. *NeuroImage,* 29(4), 1294-1302.

Dapretto, M., Davies, M.S., Pfeifer, J.H., Scott, A.A., Sigman, M., Bookheimer, S.Y., Iacoboni, M. (2005). Understanding emotions in others: mirror neuron dysfunction in children with autism spectrum disorders. *Nature Neuroscience,* 9, 28-30.

Dassonville, P., Lewis, S.M., Zhu, X.H., Ugurbil, K., Kim, S.G., Ashe, J. (2001). The effect of stimulus-response compatibility on cortical motor activation. *NeuroImage,* 13(1), 1-14.

De Beni, R., Borella, E., Carretti, B., Indiano, A., Cornoldi, C. (2008). Riattivare la memoria nell'invecchiamento: l'intervento strategico-metacognitivo. *Rassegne di Psicologia,* 1-2, 167-180.

De Renzi, E., Motti, F., Nichelli, P. (1980). Imitating Gestures: A Quantitative approach to ideomotor apraxia. *Archives of Neurology*, 37, 6-10.

De Renzi, E., Lucchelli, F. (1988). Ideational apraxia. *Brain*, 111, 1173–1185.

Dinstein, I., Gardner, J.L., Jazayeri, M., Heeger, D.J. (2008). Executed and observed movements have different distributed representations in human aIPS. *The Journal of Neuroscience,* 28(44), 11231–11239.

di Pellegrino, G., Fadiga, L., Fogassi, L., Gallese, V., Rizzolatti, G. (1992). Understanding motor events: a neurophysiological study. *Experimental Brain Research*, 91(1), 176-180.

Disbrow, E., Roberts, T., Krubitzer, L. (2000). Somatotopic organization of cortical fields in the lateral sulcus of homo sapiens: evidence for SII and PV. *Journal of Comparative Neurology,* 418, 1–21.

Disbrow, E., Litinas, E., Recanzone, G.H., Padberg, J., Krubitzer, L. (2003). Cortical connections of the second somatosensory area and the parietal ventral area in macaque monkeys. *Journal of Comparative Neurology,* 462, 382-399.

Eickhoff, S.B., Stephan, K.E., Mohlberg, H., Grefkes, C., Fink, G.R., Amunts, K., Zilles, K. (2005). A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. *NeuroImage,* 25, 1325-1335.

Eickhoff, S.B., Schleicher, A., Zilles, K., Amunts, K. (2006). The human parietal operculum. I. Cytoarchitectonic mapping of subdivisions. *Cerebral Cortex*, 16, 254-267.

Eickhoff, S.B., Amunts, K., Mohlberg, H., Zilles, K. (2006). The Human Parietal Operculum. II. Stereotaxic Maps and Correlation with Functional Imaging Results. *Cerebral Cortex*, 16, 268-279.

Eickhoff, S.B., Grefkes, C., Zilles, K., Fink, G.R. (2007). The somatotopic organization of cytoarchitectonic areas on the human parietal operculum. *Cerebral Cortex*, 17, 1800-1811.

Eickhoff, S.B., Jbabdi, S., Caspers, S., Laird, A.R., Fox, P.T., Zilles, K., Behrens, T.E.J. (2010). Anatomical and functional connectivity of cytoarchitectonic areas within the human parietal operculum. *The Journal of Neuroscience*, 30, 6409-6421.

Fadiga, L., Fogassi, L., Pavesi, G., Rizzolatti, G. (1995). Motor facilitation during action observation: a magnetic stimulation study. *Journal of Neurophysiology,* 73(6), 2608-2611.

Fiorio, M., Haggard, P. (2005) Viewing the body prepares the brain for touch: effects of TMS over somatosensory cortex. *European Journal of Neuroscience, 22*, 773–777.

Fitzgerald, P.J., Lane, J.W., Thakur, P.H., Hsiao, S.S. (2004). Receptive field properties of the macaque second somatosensory cortex: evidence for multiple functional representations. *The Journal of Neuroscience, 24*, 11193-11204.

Fitzgerald, P.J., Lane, J.W., Thakur, P.H., Hsiao, S.S. (2006a). Receptive field properties of the macaque second somatosensory cortex: representation of orientation on different finger pads. *The Journal of Neuroscience, 26*, 6473-6484.

Fitzgerald, P.J., Lane, J.W., Thakur, P.H., Hsiao, S.S. (2006b). Receptive field (RF) properties of the macaque second somatosensory cortex: RF size, shape, and somatotopic organization. *The Journal of Neuroscience, 26*, 6485-6495.

Fogassi, L., Ferrari, P.F., Gesierich, B., Rozzi, S., Chersi, F., Rizzolatti, G. (2005). Parietal lobe: from action organization to intention understanding. *Science, 308*, 662-667.

Folstein, M.F., Folstein, S.E., McHugh, P.R. (1975). "Mini-Mental State": A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, 12, 189-198.

Forss, N., Mustanoja, S., Roiha, K., Kirveskari, E., Mäkelä, J. P., Salonen, O., et al. (2012). Activation in parietal operculum parallels motor recovery in stroke. *Human Brain Mapping, 33*(3), 534-541.

Fox, M.D., Snyder, A.Z., Vincent, J.L., Corbetta, M., Van Essen, D.C., Raichle, M.E. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proceedings of the National Academy of Sciences USA*, 102, 9673-9678.

Friston, K.J., Jezzard, P., Turner, R. (1994). Analysis of Functional MRI Time-Series. *Human Brain Mapping*, 1, 153-171.

Friston, K.J., Glaser, D.E., Henson, R.N., Kiebel, S., Phillips, C., Ashburner, J. (2002). Classical and Bayesian inference in neuroimaging: Applications. *NeuroImage*, 16, 484–512.

Gallese, V., Fadiga, L., Fogassi, L., Rizzolatti, G. (1996). Action recognition in the premotor cortex. *Brain,* 119, 593-609.

Gazzola, V., Rizzolatti, G., Wicker, B., Keysers, C. (2007). The anthropomorphic brain: The mirror neuron system responds to human and robotic actions. *NeuroImage*, 35, 1674-1684.

Giovagnoli, A.R., Del Pesce, M., Mascheroni, S., Simoncelli, M., Laiacona, M., Capitani, E. (1996) Trail making test: normative values from 287 normal adult controls. *The Italian Journal of Neurological Sciences*, 17(4), 305-9.

Gleissner, B., Melzoff, A.N., Bekkering, H. (2000). Children's coding of human action: cognitive factors influencing imitation in 3-year-old. *Developmental Science*, 3(4), 405-414.

Goldenberg, G. (1995). Imitating gestures and manipulating a manikkin - The representation of the human body in ideomotor apraxia. *Neuropsychologia*, 33(1), 63-72.

Goldenberg, G. (1999). Matching and imitation of hand and finger postures in patients with damage in the left or right hemispheres. *Neuropsychologia*, 37, 559-566.

Goldenberg, G., Karnath, H.O. (2006). The neural basis of imitation is body part specific. *The Journal of Neuroscience,* 26(23), 6282-6287.

Goldenberg, G., Münsinger, U., Karnath, H.O. (2009). Severity of neglect predicts accuracy of imitation in patients with right hemisphere lesions. *Neuropsychologia,* 47, 2948–2952.

Gowen, E., Poliakoff, E. (2012). How does visuomotor priming differ for biological and non-biological stimuli? A review of the evidence. *Psychological Research*, 76(4), 407-420.

Grecucci, A., Buiatti, T., Balaban, E., Budai, R., Rumiati, RI. (2009). The emotional control of action. ERP evidence. *Archives Italiennes de Biologie*, 147, 37-49.

Grecucci, A., Koch, I., Rumiati, R.I. (2011). The role of emotional context in facilitating imitative actions. *Acta Psychologica*, 138, 311–315.

Greenwald, A.G. (1970). Sensory feedback mechanisms in performance control: with special reference to the ideomotor mechanism. *Psychological Review*, 77, 73-99.

Haaland, K.Y., Harrington, D.L., Knight, R.T. (2000). Neural representations of skilled movement. *Brain,* 123, 2306-2313.

Hari, R., Hänninen, R., Mäkinen, T., Jousmäki, V., Forss, N., Seppä, M., Salonen, O. (1998). Three hands: fragmentation of human bodily awareness. *Neuroscience Letters*, 240, 131-134.

Hein, G., Knight, R.T. (2008). Superior temporal sulcus-it's my area: or is it? *The Journal of Cognitive Neuroscience*, 20(12), 2125-2136.

Heyes, C.M., Ray, E.D. (2000). What Is the Significance of Imitation in Animals? Advances in the Study of Behavior (Vol. Volume 29, pp. 215-245). Academic Press.

Heyes, C., Bird, G., Johnson, H., Haggard, P. (2005). Experience modulates automatic imitation. *Cognitive Brain Research*, 22(2), 233-240.

Heyes, C. (2011). Automatic imitation. *Psychological Bulletin,* 137(3), 463-483.

Hinkley, L.B., Krubitzer, L.A., Nagarajan, S.S., Disbrow, E.A. (2007). Sensorimotor integration in S2, PV, and parietal rostroventral areas of the human sylvian fissure. *Journal of Neurophysiology*, 97, 1288-1297.

Hommel, B., Müsseler, J., Aschersleben, G., Prinz, W. (2001). The theory of event coding (TEC): A framework for perception and action planning. *Behavioral and brain sciences,* 24(5), 849-937.

Iacoboni, M., Woods, R.P., Mazziotta, J.C. (1996). Brain-behavior relationships: evidence from practice effects in spatial stimulus-response compatibility. *Journal of Neurophysiology,* 76(1), 321-331.

Iacoboni, M., Woods, R.P., Brass, M., Bekkering, H., Mazziotta, J.C., Rizzolatti, G. (1999). Cortical mechanisms of human imitation. *Science*, 286, 2526-2528.

Iacoboni, M., Koski, L.M., Brass, M., Bekkering, H., Woods, R.P., Dubeau, M.C., Mazziotta, J.C., Rizzolatti, G. (2001). Reafferent copies of imitated actions in the right superior temporal cortex. *Proceedings of the National Academy of Sciences USA*, 98(24), 13995-13999.

Iacoboni, M., Mazziotta, J.C. (2007). Mirror neuron system: basic findings and clinical applications. *Annals of Neurology,* 62(3), 213–218.

Iacoboni, M. (2009). Imitation, empathy, and mirror neurons. *Annual Review of Psychology*, 60, 653–70.

Jackson, P.L., Meltzoff, A.N., Decety, J. (2006). Neural circuits involved in imitation and perspective-taking. *NeuroImage*, 31, 429-439.

James, W. (1890). Principles of psychology. New York: Holt.

Jellema, T., Baker, C., Oram, M., Perret, D. (2002). Cell populations in the banks of the superior temporal sulcus of the macaque monkey and imitation. In: Meltzoff & Prinz (Eds.), The imitative mind: Development, evolution and brain bases (pp. 143-162). Cambridge, UK: Cambridge University Press.

Jonas, M., Biermann-Ruben, K., Kessler, K., Lange, R., Baumer, T., Siebner, H. R., et al. (2007). Observation of a finger or an object movement primes imitative responses differentially. *Experimental Brain Research*, 177, 255–265.

Kaas, J.H., Collins, C.E. (2003). The organization of somatosensory cortex in anthropoid primates. *Advances in Neurology*, 93, 57-67.

Keysers, C., Wicker, B., Gazzola, V., Anton, J., Fogassi, L., Gallese, V. (2004). A touching sight: SII/PV activation during the observation and experience of touch. *Neuron,* 42, 335-346.

Kiebel, S., Holmes, A.P. (2003). General linear model. In: Frackowiak RS, Friston KJ, Frith CD, Dolan RJ, Price CJ, Zeki S,Ashburner JT, Penny WD, editors. Human brain function London: Academic. p 725–760.

Kilner, J.M., Paulignan, Y., Blakemore, S.J. (2003). An interference effect of observed biological movement on action. *Current Biology*, 13, 522–525.

Kilner, J.M., Hamilton, A.F., Blakemore, S.J. (2007). Interference effect of observed human movement on action is due to velocity profile of biological motion. *Social Neuroscience*, 2, 158-166.

Kilner, J.M., Neal, A., Weiskopf, N., Friston, K.J., Frith, C.D. (2009). Evidence of mirror neurons in human inferior frontal gyrus. *The Journal of Neuroscience*, 29(32), 10153–10159.

Kohler, E., Keysers, C., Umiltà, M.A., Fogassi, L., Gallese, V., Rizzolatti, G. (2002). Hearing sounds, understanding actions: action representation in mirror neurons. *Science,* 297, 846-848.

Koski, L., Iacoboni, M., Dubeau, M., Woods, R.P., Mazziotta, J.C. (2003). Modulation of cortical activity during different imitative behaviors. *Journal of Neurophysiology*, 89, 460-471.

Krubitzer, L., Clarey, J., Tweedale, R., Elston, G., Calford, M. (1995). A redefinition of somatosensory areas in the lateral sulcus of macaque monkeys. *The Journal of Neuroscience,* 15, 3821-3839.

Leiguarda, R.C., Marsden, C.D. (2000). Limb apraxias. *Brain,* 123, 860-879.

Leslie, K.R., Johnson-Frey, S.H., Grafton, S.T. (2004). Functional Imaging of face and hand imitation: towards a motor theory of empathy. *NeuroImage*, 21, 601–607.

Liepelt, R., Brass, M. (2010). Top-down modulation of motor priming by belief about animacy. *Experimental Psychology*, 57, 221–227.

Liepmann, H. (1920). Apraxie. *Ergebnisse der gesamten Medizin*, 1, 516-543.

Longo, M.R., Kosobud, A., Bertenthal, B.I. (2008). Automatic imitation of biomechanically possible and impossible actions: Effects of priming movements versus goals. *Journal of Experimental Psychology: Human Perception and Performance*, 34(2), 489-501.

Longo, M.R., Bertenthal, B.I. (2009): Attention modulates the specificity of automatic imitation to human actors. *Experimental Brain Research*, 192(4), 739-744.

Luzzatti, C., Willmes, K., De Bleser, R. (1996). Aachener Aphasie Test: Versione Italiana (Seconda edizione). Organizzazioni Speciali, Firenze.

Maeda, F., Kleiner-Fisman, G., Pascual-Leone, A. (2002). Motor facilitation while observing hand actions: specificity of the effect and role of observer's orientation. *Journal Neurophysiology*, 87, 1329-1335.

Mahon, B.Z., Caramazza, A. (2005). The orchestration of the sensory-motor systems: Clues from neuropsychology. *Cognitive Neuropsychology, 22*(3-4), 480-494.

Massen, C., Prinz, W. (2009). Movements, actions and tool-use actions: an ideomotor approach to imitation. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 364(1528), 2349 -2358.

Matsumoto, E., Misaki, M., Miyauchi, S. (2004). Neural mechanisms of spatial stimulus–response compatibility: the effect of crossed-hand position. *Experimental Brain Research*, 158, 9-17.

Mauri, M., Carlesimo, G.A., Graceffa, A.M.S., Loasses, A., Lorusso, S., Sinforiani, E., Bono, G., Caltagirone, C. Standardizzazione di due nuovi test di memoria: apprendimento di liste di parole correlate e non correlate semanticamente. Archivio di Psicologia, Neurologia e Psichiatria, 1997;58:621-45.

Mengotti, P., Corradi-Dell'Acqua, C., Rumiati, R.I. (2012). Imitation components in the human brain: An fMRI study. *NeuroImage, 59*(2), 1622-1630.

Menz, M.M., McNamara, A., Klemen, J., Binkofski, F. (2009). Dissociating networks of imitation. *Human Brain Mapping*, 30, 3339–3350.

Negri, G.A.L., Rumiati, R.I., Zadini, A., Ukmar, M., Mahon, B.Z., Caramazza, A. (2007): What is the role of motor simulation in action and object recognition? Evidence from apraxia. *Cognitive Neuropsychology, 24*(8), 795-816.

Newman-Norlund, R.D., Ondobaka, S., van Schie, H.T., van Elswijk, G., Bekkering, H. (2010). Virtual lesions of the IFG abolish response facilitation for biological and non-biological cues. *Frontiers in Behavioral Neuroscience*, 4-5.

Oldfield, R.C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia*, 9, 97-113.

Orsini, A., Grossi, D., Capitani, E., Laiacona, M., Papagno, C., Vallar, G. (1987). Verbal and Spatial Immediate Memory Span: Normative Data from 1355 Items and 1112 children. *Italian Journal of Neurological Science*, 8.

Oshio, R., Tanaka, S., Sadato, N., Sokabe, M., Hanakawa, T., Honda, M. (2010). Differential effect of double-pulse TMS applied to dorsal premotor cortex and precuneus during internal operation of visuospatial information. *NeuroImage,* 49, 1108–1115.

Papagno, C., Della Sala, S., Basso, A. (1993). Ideomotor apraxia without aphasia and aphasia without apraxia: the anatomical support for a double dissociation. *Journal of Neurology, Neurosurgery & Psychiatry*, 56, 286-289.

Penny, W.D., Holmes, A.P. (2003). Random effects analysis. In: Frackowiak RS, Friston KJ, Frith CD, Dolan RJ, Price CJ, Zeki S, Ashburner JT, Penny WD, editors. Human brain function. London: Academic. pp. 843–850.

Perani, D., Fazio, F., Borghese, N. A., Tettamanti, M., Ferrari, S., Decety, J., Gilardi, M. C. (2001). Different brain correlates for watching real and virtual hand actions. *NeuroImage*, 14, 749-758.

Perrett, D.I., Harries, M.H., Bevan, R., Thomas, S., Benson, P.J., Mistlin, A.J., Chitty, A.J., Hietanen, J.K., Ortega, J.E. (1989). Frameworks of analysis for the neural representation of animate objects and actions. *The Journal of Experimental Biology*, 146, 87-113.

Pessoa, L. (2008). On the relationship between emotion and cognition. *Nature Reviews Neuroscience*, 9, 148-158.

Pichon, S., de Gelder, B., Grèzes, J. (2008). Emotional modulation of visual and motor areas by dynamic body expressions of anger. *Social Neuroscience*, 3, 199-212.

Pichon S, de Gelder B, Grèzes J. (2009). Two different faces of threat. Comparing the neural systems for recognizing fear and anger in dynamic body expressions. *NeuroImage*, 47, 1873-1883.

Press, C., Bird, G., Flach, R., Heyes, C.M. (2005). Robotic movement elicits automatic imitation. *Cognitive Brain Research*, 25, 632–640.

Press, C., Gillmeister, H., Heyes, C. (2006). Bottom-up, not top-down, modulation of imitation by human and robotic models. *European Journal of Neuroscience*, 24, 2415-2419.

Press, C., Gillmeister, H., Heyes, C. (2007). Sensorimotor experience enhances automatic imitation of robotic action. *Proceedings of the Royal Society B Biological Sciences*, 274, 2509-2514.

Press, C., Bird, G., Walsh, E., Heyes, C. (2008). Automatic imitation of intransitive actions. *Brain and Cognition*, 67(1), 44-50.

Preston, S.D., de Waal, F.B. (2002). Empathy: Its ultimate and proximate bases. *Behavioural and Brain Sciences*, 25, 1–20.

Prinz, W. (1997). Perception and action planning. *European Journal of Cognitive Psychology,* 9, 129-154.

Puce, A., Perrett, D. (2003). Electrophysiology and brain imaging of biological motion. *Proceedings of the Royal Society B Biological Sciences*, 358(1431), 435-445.

Qi, H., Lyon, D.C., Kaas, J.H. (2002). Cortical and thalamic connections of the parietal ventral somatosensory area in marmoset monkeys (Callithrix jacchus). *Journal of Comparative Neurology,* 443, 168-182.

Riddoch, M.J., Humphreys, G.W. (1993). Birmingham Object Recognition Battery. Hove, England: Erlbaum.

Rizzolatti, G., Arbib, M.A. (1998). Language within our grasp. *Trends in Neurosciences,* 21(5), 188–194.

Rizzolatti, G., Craighero, L. (2004). The mirror-neuron system. *Annual Review of Neuroscience*, 27, 169-192.

Rizzolatti, G., Sinigaglia, C. (2010). The functional role of the parieto-frontal mirror circuit: interpretations and misinterpretations. *Nature Reviews Neuroscience*, 11, 264-274.

Rothi, L.J.G., Ochipa, C., Heilman, K.M. (1991) A cognitive neuropsychological model of limb praxis. *Cognitive Neuropsychology,* 8(6), 443-458.

Rowe, J.B., Passingham, R.E. (2001). Working memory for location and time: activity in prefrontal area 46 relates to selection rather than maintenance in memory. *NeuroImage*, 14(1), 77-86.

Rumiati, R.I., Weiss, P.H., Tessari, A., Assmus, A., Zilles, K., Herzog, H., Fink, G.R. (2005). Common and differential neural mechanisms supporting imitation of meaningful and meaningless actions. *Journal of Cognitive Neuroscience,* 17(9), 1420–1431.

Rumiati, R.I., Tessari, A. (2007). Automatic and strategic effects in human imitation. In P. Haggard, Kawato, & I. Rossetti (Eds.) Sensorimotor foundations of human cognition: Attention and Performance, Vol. XXII. Oxford: Oxford University Press.

Sauser, E. L., Billard, A. G. (2006). Parallel and distributed neural models of the ideomotor principle: An investigation of imitative cortical pathways. *Neural Networks,* 19(3), 285-298.

Schumacher, E.H., Cole, M.W., D'Esposito, M. (2007). Selection and maintenance of stimulus-response rules during preparation and performance of a spatial choice-reaction task. *Brain Research*, 1136, 77-87.

Schwoebel, J., Buxbaum, L. Coslett, H. B. (2004) Representation of the human body in the production and imitation of complex movements. *Cognitive Neuropsychology*, 21, 285–298.

Schwoebel, J., Coslett, H.B. (2005). Evidence for multiple, distinct representations of the human body. *Journal of Cognitive Neuroscience*, 17(4), 543–553.

Schofield, W.N. (1976). Hand movements which cross the body midline: Findings relating age differences to handedness. *Perceptual and Motor Skills*, 42, 643-646.

Simon, J. R. (1969). Reactions toward the source of stimulation. *Journal of Experimental Psychology*, 81, 174-176.

Simon, J. R., Sly, P. E., Vilapakkam, S. (1981). Effect of compatibility of S-R mapping on reactions toward the stimulus source. *Acta Psychologica,* 47, 63-81.

Sirigu, A., Grafman, J., Bressler, K., Sunderland, T. (1991). Multiple representations contribute to body knowledge processing. *Brain,* 114, 629-642.

Spinnler, H., Tognoni, G. (Eds.) (1987) Standardizzazione e taratura italiana di test neuropsicologici (Gruppo italiano per lo studio neuropsicologico dell'invecchiamento), The Italian Journal of Neurological Sciences S8(6).

Stevens, J.A., Fonlupt, P., Shiffrar, M.A., Decety, J. (2000). New aspects of motion perception: Selective neural encoding of apparent human movements. *NeuroReport*, 11, 109-115.

Stürmer, B., Aschersleben, G., Prinz, W. (2000): Correspondence effects with manual gestures and postures: A study of imitation. *Journal of Experimental Psychology: Human Perception and Performance,* 26(6), 1746-1759.

Tai, Y.F., Scherfler, C., Brooks, D.J., Sawamoto, N., Castiello, U. (2004). The human premotor cortex is ''mirror'' only for biological actions. *Current Biology*, 14, 117-120.

Tessari, A., Canessa, N., Ukmar, M., Rumiati, R.I. (2007). Neuropsychological evidence for a strategic control of multiple routes in imitation. *Brain*, 130 (4), 1111-1126.

Tessari, A., Toraldo, A., Lunardelli, A., Zadini, A., Rumiati, R.I. Prova standardizzata per la diagnosi del disturbo aprassico ideomotorio selettivo per tipo di azione e tipo di effettore. *Ricerche di Psicologia*. In press.

Thiel, C.M., Zilles, K., Fink, G.R. (2004). Cerebral correlates of alerting, orienting and reorienting of visuospatial attention: an event-related fMRI study. *NeuroImage,* 21, 318-328.

Thomas, R., Press, C., Haggard, P. (2006). Shared representations in body perception. *Acta Psychologica,* 121, 317–330.

Thompson, J.C., Clarke, M., Stewart, T., Puce, A. (2005). Configural processing of biological motion in human superior temporal sulcus. *The Journal of Neuroscience*, 25(39), 9059-9066.

Tottenham, N., Tanaka, J., Leon, A.C., McCarry, T., Nurse, M., Hare, T.A. Marcus, D.J., Westerlund, A., Casey, B., Nelson, C. (2009). The NimStim set of facial expressions: judgments from untrained research participants. *Psychiatry Research*, 168, 242-249.

Tsakiris, M., Hesse, M.D., Boy, C., Haggard, P., Fink, G.R. (2007). Neural signatures of body ownership: a sensory network for bodily self-consciousness. *Cerebral Cortex*, 17, 2235-2244.

Umiltà, M.A., Kohler, E., Gallese, V., Fogassi, L., Fadiga, L., Keysers, C., Rizzolatti, G. (2001). I know what you are doing: A neurophysiological study. *Neuron,* 31, 155–165.

Vossel, S., Weidner, R., Thiel, C.M., Fink, G.R. (2009). What is "odd" in Posner's location-cueing paradigm? Neural responses to unexpected location and feature changes compared. *The Journal of Cognitive Neuroscience*, 21, 30-41.

Wapner, S., Cirillo, L. (1968). Imitation of a model's hand movements: Age changes in transposition of left-right relations. *Child Development,* 39(3), 887-894.

Warrington, E.K., James, M. (1991). The Visual Object and Space Perception Battery. Bury St Edmunds, UK: Thames Valley Test Company.

Wilson, B., Cockburn, J., Halligan, P. (1987) Behavioural Inattention Test. Titchfield, UK: Thames Valley Test Company.