

UNIVERSITA' DEGLI STUDI DI PARMA

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DOTTORATO DI RICERCA IN NEUROSCIENZE

CICLO XXIII

**The Bodily Self and  
The Role of its Disruption in Schizophrenia**

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## Chapter 1

## 1. General Introduction

### 1.1 Minimal Self and Bodily Self: Looking for the Minimalist Experience of One's Own Body.

“Self” is a complex, multileveled and multifaceted notion. From a phenomenological perspective (Parnas 2000; 2003) three levels of selfhood have been identified. First, there is the implicit awareness that this is ‘my’ experience. Such pre-reflective level of selfhood is sometimes referred to as the ‘basic’ or ‘minimal’ self or as ‘ipseity’. Second, there is the more explicit awareness of self as an invariant subject of experience and action. Such reflective level of self-awareness assumes the ‘minimal’ self. Finally, there is the social or narrative self, which refers to personality, habits, style and other characteristics of an individual.

The concept of minimal, pre-reflective, or “core self” (Rochat 2004) is currently under debate in cognitive science, developmental psychology and philosophy of mind. However, it is not clear which empirical features such a self is presumed to possess and which kind of experience concurs in shaping this implicit sense of being oneself. In particular, in the ongoing debate about the definition of the notion of self, as the minimalist level of subjective experience, one of the central issues is the contribution of bodily experience to its constitution. For instance, some aspects of the minimal self proposed by contemporary philosophical and empirical research are: the notion of perspective and first-person perspective, the ‘mineness’ of the phenomenal field, the question of transparency, embodiment of point of view, and the issues of agency and ownership (Cermolacce et al. 2007). What is important to note here is that, on the philosophical side, phenomenology emphasizes the necessity of embodiment of the self for all the above cited aspects of self experience. Furthermore, as argued by Cermolacce and colleagues (2007), in phenomenology “the field of experience is not yet considered to be *subjective* because this predicate already implies that there is a subject. For phenomenology, the very idea of the *subject* articulates itself in experience. In

this sense, the manifestation and appearing of experience are the *conditions for* the experience of the subject in question”. This philosophical standpoint should have important implications for the empirical studies, especially for those investigating the neural correlates of self-consciousness or self-representations. Rather than searching for the neural correlates of a pre-defined, explicit and reflective self-knowledge, the first aim of empirical research should be to investigate which kind of experience (and how) allows an implicit and pre-reflective self-knowledge to emerge. For example, reminding the importance of embodiment of the self for self experience, an interesting question to be answered would be: “What is the basic experience of ourselves as bodily selves? What enables us to implicitly distinguish ourselves, as bodily selves, from other human bodies?” Contemporary research answers this question by focusing mostly on the notions of body ownership, sense of agency and first person perspective.

Body ownership refers to “the perceptual status of one’s own body, which makes bodily sensations seem unique to oneself” (Tsakiris et al. 2007a). Different studies on Rubber Hand Illusion (RHI, Botvinick and Cohen 1998) suggested that multisensory integration is the crucial mechanism leading to the experience of our body as our own. The RHI consists in watching a rubber hand being stroked together with one’s own unseen hand. If the stroking of the rubber and real hands occurs synchronously, the position sense of the real hand shifts towards the location of the dummy hand. Participants report that they feel the dummy hand to be part of their body. However, as it has been recently argued (see Gallese and Sinigaglia 2010, 2011), there is a lot of evidence showing that the multisensory integration leading to the experience of our body as our own, far from being the outcome of a mere visual–proprioceptive perceptual association (Costantini and Haggard 2007), is conditioned by the possibility – or not – to perform actions with a given body part (Tsakiris and Haggard 2005; Tsakiris et al. 2006; Tsakiris et al. 2007b).

Sense of agency refers to the sense of being the one who generates an action. We recognize ourselves as agents on the basis of the congruence between self-generated movements and their

expected consequences. This dominant role of action over other possible cues for self-identification is accounted for by the hypothesis of the Central Monitoring Theory of action recognition. In its simplest form, this model holds that each time the motor centers generate an outflow signal for producing a movement, a copy of this command (the “efference copy”, Von Holst and Mittelstedt 1950) is retained and then compared with the reafferent inflow signals generated by the movement (e.g., visual, kinesthetic). A predictive component of the model anticipating the sensory consequences of the movement, is such that, in the case of a self-produced movement, the actual sensory feedback will match the prediction. Otherwise, sensory signals will be referred to an external event (Frith et al. 2000).

However, as argued by Marc Jeannerod (2007), the Central Monitoring Theory “cannot explain the fact that sense of agency also arises in many situations where action representation is formed, but no movement is executed”. Because circumstances where actions remain covert are frequent in our daily life, “the existence of an overt behaviour should not be a prerequisite for self-identification”. Such circumstances occurs, for example, in the case of motor imagery (Jeannerod 1995) or motor simulation, which is a functional mechanism taking place during the observation of others’ actions and having the mirror neuron system as its neural counterpart (Gallese 2000; Gallese 2006; Gallese 2009; Gallese and Sinigaglia 2011). Starting from the concept of shared representations (Georgieff and Jeannerod 1998), Jeannerod (2007) proposed “the model of self/other differentiation as a rotate/simulate model: I first rotate myself at the location of the person I observe in order to specify her location in space. Then, I simulate the action I observe from that person in order to understand what she is doing.”

Finally, first-person perspective may be referred to the phenomenological idea that the world *appears* as constrained by a mobile bodily self, that is, by the spatially located point of view, the orientation and the attitudes relative to the subject’s sensorimotor background capacities (Cermolacce et al. 2007).

In sum, all the notions adopted by contemporary research to answer the question of how we distinguish ourselves, as bodily selves, from other human bodies refer to a crucial role of the motor system.

In the same vein, and more radically, it has been recently proposed (Gallese and Sinigaglia 2010, 2011) that there is a sense of body that is enactive in nature and that enables to capture the most primitive sense of self as bodily self. According to this perspective, “the body is primarily given to us as “source” or “power” for action, that is, as the variety of motor potentialities that define the horizon of how we can interact with the world we live in” (Gallese and Sinigaglia 2010). Such primitive sense of self as bodily self is conceived of as being antecedent the distinction between sense of agency and sense of ownership. Accordingly, Smith (2007) explained the concept of bodily self as follows: “The bodily self is a physical agent. Knowledge of oneself as bodily is fundamentally knowledge of oneself as agentive; such knowledge is grounded in both experience of oneself as instantiating a bodily structure that affords a limited range of actions, and experience of oneself as a physical agent that tries to perform a limited range of actions over time” (Smith 2007).

The existence of such motor experience-based representation of the bodily self has been investigated at the behavioural level in the first study here presented (chapter 2). In that study, we employed the hand laterality judgment task, because it relies upon the visuomotor representation of one’s own body (Cooper and Shepard 1975; Parsons 1987; 1994).

In the following fMRI study (chapter 3), we tested the hypothesis that the sensorimotor system plays a pivotal role in the implicit and pre-conscious self/other distinction during the laterality judgment task. Neuroimaging results associated with this task, showed activation in several dominant spatial-motor processing regions, including the posterior parietal (superior parietal and the intraparietal sulcus), premotor and primary motor cortices, the supplementary motor area and the cerebellum (Parsons et al. 1995; Cohen et al. 1996; Alivisatos and Petrides 1997; Kosslyn et al. 1998; Vingerhoets et al. 2002; Seurinck et al. 2004; Podzbenko et al. 2005). However, given the

higher specificity of the premotor cortex for the mental rotation of body-related stimuli (Kosslyn et al. 1998; Arzy et al. 2006), than non corporeal stimuli, and considering its role in body awareness (Ehrsson et al. 2004; Berti et al. 2005; Arzy et al. 2006), we hypothesized that this brain area may represent one of the essential anatomical and functional basis for the motor aspect of bodily selfhood.

### **1.2 Bodily Self-Advantage Effect and its Loss in Schizophrenia.**

Studies using different methods (behavioral, fMRI, TMS studies) have shown that the recognition of one's own body is independent from the recognition of other people's bodies. Recent evidence suggests that a specific neural network is dedicated to "self-body" recognition. This brain network seems to be, at least partially, distinct from that responsible for general body-related information processing (Sugiura et al. 2006; Myers and Sowden 2008; Hodzic et al. 2009). As argued by Myers and Sowden (2008), from our own body, we combine visual information with, at least, somatosensory, proprioceptive, and motor information, in order to guide our interpretation of sensory events and our actions upon the world. For others' bodies, we have mostly visual information available to us.

According to this remark, previous behavioural studies (Frassinetti et al. 2008; 2009; 2010) have demonstrated the human ability to implicitly recognize one's own body. When submitted to a visual matching task, participants showed the so-called *self-advantage effect*, that is, a better performance with one's own rather than others' body-parts (Frassinetti et al. 2008; 2009; 2010). Moreover, it has been shown that such self-advantage effect is stronger for dynamic than for static stimuli (Frassinetti et al. 2009). Indeed, participants performed better with dynamic than with static images depicting self than others' body-parts, even if the dynamic condition was more difficult than the static one. The mechanism supporting the bodily self-advantage effect is still under debate.

However, this evidence holds for the hypothesis that bodily self recognition is based on a sensorimotor representation (for a review, see Tsakiris 2010).

In a previous study from our group (Frassinetti et al. 2011), we tested the hypothesis that the bodily self-advantage is the expression of an implicit, rather than explicit, and body-specific knowledge, based mainly on the sensorimotor representation of one's own body-effectors. Alternatively, the bodily self-advantage could rely on visual recognition of pictorial cues. According to the first hypothesis, the bodily self-advantage should emerge when self-body recognition is implicitly required and should be specific for body-effectors and not for inanimate objects. In contrast, if the self-advantage is due to a mere visual-perceptual facilitation, it should be independent of the implicit or explicit request (and could be extended also to objects).

To disentangle these hypotheses, healthy participants were implicitly (visual matching task) or explicitly (self/other discrimination task) required to recognize either their own body-effectors or inanimate-objects. They showed the bodily self-advantage effect in the implicit task, but not in the explicit task. Such data supported the idea that this effect relies upon a sensorimotor, rather than a mere visual representation of one's own body. Moreover, the absence of both self/other and implicit/explicit effects, when processing inanimate-objects, underlined the differences between the body and other objects.

The idea of a dissociation between implicit and explicit self body processing is in agreement with the large amount of neuropsychological studies showing that brain damaged patients can be impaired in explicit while sparing implicit processing. Typical clinical conditions in which implicit and explicit processes are dissociated are, for example, neglect (Berti and Rizzolatti 1992; Berti et al. 1994) and the blindsight phenomenon (Tamietto et al. 2010). Regarding the bodily self, such dissociation is in agreement with the independence of implicit from explicit self-body processing reported by infancy research. Indeed, during development an implicit sense of self and the ability to

discriminate self from others appears to emerge earlier than the ability to explicitly self-recognize (Rochat 2003; 2010).

What is important here is that the sensorimotor representation of oneself, as bodily self, can emerge when implicitly, rather than explicitly accessed, even when tested i) by a not proper motor task (like the laterality judgment task) and ii) by using static, rather than dynamic body stimuli. On the other hand, the explicit self-recognition probably requires attention and memory abilities not required in the implicit task. In this case, the recognition of one's own body parts seems to be more vulnerable to errors than the sensorimotor knowledge we implicitly hold about the same body parts.

In the study described in chapter 4, we used the same tasks as in Frassinetti and colleagues (2011) with first-episode schizophrenia (FES) patients, in order to test whether a specific bodily self-advantage effect is either preserved or lost in these patients. Indeed, schizophrenia spectrum has been described as a psychiatric condition associated with disorders that affect the functioning of the "minimal self" (Zahavi 2005), also referred to as "ipseity" (Parnas 2000; Sass and Parnas 2003; Sass and Parnas 2007). Such "self-disorder" in schizophrenia has been illustrated as a disembodiment of the self (Fuchs 2005; Stanghellini 2009), mainly consisting of a loss of the "implicit structure of the body" (Fuchs 2005, p. 95). According to this perspective, we expected the bodily self-advantage effect, supposed to be based on the minimalist level of self experience, namely the sensorimotor experience of one's own body, not to be found in FES patients.

Previous studies investigated the bodily self knowledge in schizophrenia by testing patients' sense of agency and body ownership. For example, Daprati and colleagues (1997) examined the abilities of schizophrenic patients to attribute an action to its proper agent. Schizophrenic patients were more impaired in discriminating their own hand from the alien one than the non-hallucinating ones, and tended to misattribute the alien hand to themselves.

Other empirical evidence supporting the idea of a weaker or more flexible sense of bodily self in schizophrenia comes from the literature on the rubber hand illusion (RHI; Peled et al. 2000).

A recent study (Thakkar et al. 2011) demonstrated that patients with schizophrenia experience a stronger RHI than healthy controls, indexed by self-report and mislocalization of their own hand.

All in all, these data clearly suggest that both agency and body ownership are disturbed in schizophrenia. However, in both the above reported studies (Daprati et al. 1997; Thakkar et al. 2011) schizophrenic patients' bodily self-knowledge was investigated by tasks in which self-body recognition or executed/observed action attribution were explicitly required. Differently, in our study (chapter 4) we wanted to test whether a more basic impairment of the sensorimotor bodily self-knowledge, namely a lack of the self-advantage effect, i) is already present at an implicit level, that is, in absence of an explicit requirement to make a self/other distinction or attribution, ii) is revealed by a task not requiring to overtly execute or observe actions, iii) is already present in first episode schizophrenia patients.

### **1.3 Bodily Self, Self/Other Boundary and Intersubjectivity: What is the Root of Social Deficits in Schizophrenia?**

Along with the loss of a coherent sense of self, in schizophrenia also the relationship and the distinction between self and other may blur (Sass and Parnas 2003). Social dysfunction has been recognized as an elementary feature of schizophrenia, but it remains a crucial issue whether social deficits in schizophrenia concern the intersubjective domain or primarily have their roots in disturbances of bodily self-experience. It has been argued (Stanghellini 2001) that analyses of schizophrenia disorders emphasizing the importance of "lack of ipseity" (the weakening of the feeling of being embedded in oneself and of distinctiveness between the self and the external world) and "hyper-reflexivity" (the monitoring of one's own life entailing the tendency to objectify parts of one's own self in an outer space) consider the person as an isolated self and may ignore the fact that

the self is not merely individual. Indeed, our existence is essentially tied to the phenomenon of intersubjectivity.

Specifically, according to phenomenologists, understanding others does not rely on an inference of mental states, but on a pre-cognitive, intuitive experience (Husserl 1977), a direct perception of the others' emotional life (Scheler 1973). One explanation of intersubjectivity refers to a crucial role of the lived body (Merleau-Ponty 1964; Dillon 1997). Intersubjectivity is based on my identification with my partner's body as like my own, through an immediate perceptual linkage with his body. This primitive phenomenon is antecedent to the self-other distinction. Intersubjectivity is based on this transfer of corporeal schema (Merleau-Ponty 1964). A more proper word to account for intersubjectivity would then be "intercorporeality".

Empirical evidence suggests that social perception comprises vicarious processes grounding an experiential interrelationship with others as well as self-regulation processes allowing to maintain a coherent sense of self. On the one hand, it has been suggested that multimodal brain regions underlying bodily self-experiences are also involved with the pre-reflective understanding of the feelings and behaviours of other individuals, establishing an intersubjective ("intercorporeal") link between self and other during social perception (Gallese 2003; Gallese et al. 2004; Keysers and Gazzola 2009). On the other hand, specific brain regions involved with self-experiences and awareness (Craig 2002; Tsakiris et al. 2007a; Karnath and Baier 2010) rather appear to differentiate between self and other (Ebisch et al. 2011).

Concerning social deficits in schizophrenia, this postulates the question of whether patients with schizophrenia may show altered vicarious neural activations or rather aberrant neural processes underlying multisensory integration and differentiation between self and others' bodily experiences during social perception. To tackle this question, we investigated the perception of social touch in FES.

In healthy people skin-to-skin contact between individuals has a pivotal role in social interactions. Somatosensation is considered a crucial component of social perception and empathy (for a review see Keysers et al. 2010). Moreover, touch constitutes an elementary aspect of self awareness (Tsakiris et al. 2007a).

In a previous study (Ebisch et al. 2011) we investigated whether cortical regions involved with the elementary stages of touch processing are also involved in the automatic coding of the affective consequences of observed touch. In the same study, we investigated also to which extent the same cortical regions show overlapping activation for somatosensory experiences of self and others.

On the one hand, we found a specific negative modulation in the posterior insula by the mere visual perception of other individuals' social or affective cutaneous experiences, compared to neutral inanimate touch. On the other hand, activation in secondary somatosensory and posterior superior temporal regions seemed more dependent on the observed physical stimulus characteristics. In contrast to the detected vicarious activation in somatosensory regions, opposite activation patterns for the experience (positive modulation) and observation (negative modulation) of touch suggested that the posterior insula does not reflect a shared representation of self and others' experiences. It rather appears to differentiate between self and other conditions when affective experiences are implicated.

In order to understand whether social deficits in schizophrenia concern the intersubjective domain (vicarious processes) or rather disturbances of bodily self-experience (self-regulation processes), in the functional magnetic resonance imaging study described in chapter 5, we used the same social task as in Ebisch and colleagues (2011). According to the first hypothesis, we expected FES patients observing others' tactile experiences to show aberrant activation in brain regions involved with first-person tactile experiences (e.g., the somatosensory cortices). Alternatively, FES

patients may show altered activation patterns in brain regions differentiating between self and other conditions, or in multisensory regions grounding a coherent self-experience.

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## Chapter 2

## **2. Motor simulation and the bodily self**

### **2.1 Introduction**

Neuropsychological and neuroimaging studies show that the body is a “unique” object. Indeed, specific brain structures are involved in the visual processing of the human body (Downing et al. 2001; Moro et al. 2008; Peelen and Downing 2007). Viewing non-facial body parts selectively activates a lateral occipito-temporal cortex (OTC), called extrastriate body area (EBA), and an area located in the fusiform gyrus, known as fusiform body area (FBA) (Peelen and Downing 2007; Peelen and Downing 2005; Schwarzlose et al. 2005). Moreover, a topographically organized body part map has been described within the OTC, with distinct clusters of voxels showing clear preference for different visually presented body parts (Orlov et al. 2010). In line with this evidence, a hand-selective region has been recently revealed in the left lateral occipital sulcus, partially overlapping with EBA, which could be functionally and anatomically dissociated from it (Bracci et al. 2010).

When processing a human body, a critical distinction can be made between one’s own body and the body of others (Devue et al. 2007; Sugiura et al. 2006). Studies using different methods (behavioral, fMRI, TMS studies) have shown that the recognition of “self body” is independent from the recognition of other people’s bodies. Interestingly, self-related body stimuli are processed faster and more accurately compared to other-related body stimuli (self-advantage, see (Frassinetti et al. 2008; 2009). This advantage for self body processing was revealed by a visual task in which an explicit self body recognition was not required. Participants were submitted to a matching task in which three pictures, representing a body part (hand, foot, arm and leg), were presented vertically aligned at the centre of the computer screen. They were asked which of the two stimuli, the upper or the lower one, matched with the central target.

Participants' performance was more accurate when one of the stimuli belonged to them compared to when they belonged to someone else.

The mechanism supporting the bodily self-advantage is still under debate. One hypothesis is that bodily self recognition is based on a sensory-motor representation (for a review, see Tsakiris 2010).

The main aim of the present study is to shed new light on the implicit bodily self-advantage. To this purpose, we investigated the contribution of visuo-motor body representation with two different tasks. In a first experiment (Experiment 1) healthy participants were submitted to a laterality judgment task with either self or others' hands as body stimuli. In a second experiment (Experiment 2) we employed the same stimuli as in Experiment 1, but asked participants to explicitly recognize their own hand. Finally, in a third control experiment (Experiment 3) we ruled out the possibility that the results of the first experiment were simply driven by any sort of familiarity of "priming" effects.

In the laterality judgment task (Experiments 1 and 3) participants were requested to report the laterality (left or right) of depicted body parts presented in different angular orientations. We adopted this task because it is well known that in order to perform it participants simulate a motor rotation of *their own body parts* so as to match that of the *observed stimulus* (Parsons 1994; Ionta et al. 2007). Mental motor rotation of body parts shares the same temporal and kinematic properties with actual body rotation in space (Parsons 1994; Decety et al. 1991; Decety et al. 1994; Jeannerod 2004; Parsons et al. 1998; Porro et al. 1996). This idea is further corroborated by evidence showing that longer mental rotation times are needed for stimuli orientations corresponding to body part positions difficult to be maintained (Parsons 1994; Petit et al. 2003; Thayer et al. 2001). Since previous studies (Parsons 1987; Cooper and Shepard 1975) suggest that the left-right judgment of body parts relies upon the visuo-motor representation of one's own body, we hypothesize that the laterality judgment in Experiments 1 and 3 should be easier when

the displayed stimulus is one's own hand. Indeed, only in this case, the displayed stimulus matches with the mentally rotated hand (self-advantage). If this is true, the visuo-motor representation of one's own body is crucial for the self-advantage.

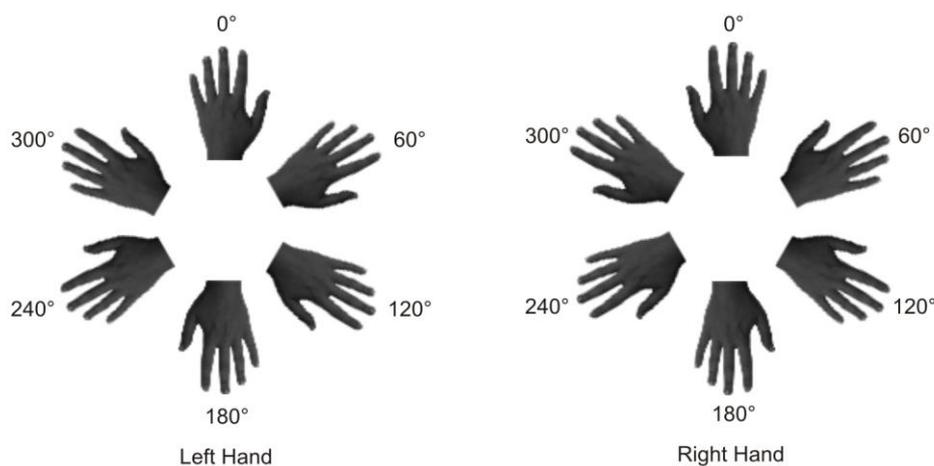
Interestingly, the self-advantage described in previous studies (Frassinetti et al. 2008; 2009; 2010) has been found without requiring an explicit self body recognition, as it emerged on the basis of a mere implicit self-body recognition. As a consequence, the explicit recognition of one's own body does not seem to be necessary for the emergence of the self-advantage. To address the question of whether the requirement of explicitly recognizing one's own body is a sufficient condition for the emergence of the self-advantage, we ran a second experiment using the very same stimuli of the Experiment 1. Here (Experiment 2), participants were asked to explicitly recognize the identity of the displayed hand, that could be either the participants' or other people's hands. If the requirement of explicit self recognition is a sufficient condition for the self-advantage, this should be found also in the Experiment 2. Alternatively, a dissociation between implicit and explicit self body processing should be found.

## **2.2 Methods**

*Participants.* Twenty-four right-handed healthy participants (mean age = 37,5 years; range 20-55), naive as to the purpose of the study, participated in each experiment. The same participants (12 men and 12 women) took part in Experiment 1 and Experiment 2. A different group of participants (14 men and 10 women) took part in Experiment 3. Participants had no history of neurological diseases as self reported. All participants gave their written informed consent for participation in the study. The experimental protocol was approved by the Ethics Committee of the University of Parma.

*Stimuli and Procedure.* The experimental stimuli consisted of grey-scale pictures of the dorsal view of right and left hands (see Figure 1). The hands of each participant were photographed with a digital camera in a session prior to the experiments (1 week before). This session took place in a controlled environment with constant artificial light and a fixed distance between the camera lens and the hands (40 cm), which were always photographed in the same position. Subsequently, photographs were modified with Adobe Photoshop software: they were cut from the original picture, pasted on a white background, and reoriented into the different rotated positions. Other people's hands were selected from this database as the best match for size, skin color, age, and gender, in comparison with each participant's hands. The sizes of the hands were compared in the pictures, in order to minimize the differences between matched hands both in length and in width. In addition, the ages of the people whose hands were matched with the participants' hands varied within 0 to 3 years of the participants' ages.

Images of hands were presented one at a time at the centre of the computer screen in six different clockwise orientations from the upright ( $0^\circ$ ,  $60^\circ$ ,  $120^\circ$ ,  $180^\circ$ ,  $240^\circ$ ,  $300^\circ$ ). The upright orientation was defined as fingers pointing upwards (figure 1).



**Figure 1- Stimuli.** Experimental stimuli consisted of pictures depicting the dorsal view of right and left hands in six different clockwise orientations. Images of participant's hands or of three other people's hands were presented one at a time in 'self' trials and 'other' trials, respectively.

Stimuli depicted the participant's own left or right hand in half of the trials ('self' trials). In the other half of the trials, stimuli depicted the right or left hand of other three people ('other' trials, Experiments 1 and 2). In Experiment 3 stimuli presented in the 'other' trials depicted the right or left hand of only one other individual. This methodological change was done to control for "priming" or familiarity effects that might occur in the laterality judgment task.

Participants sat in front of a PC screen, at a distance of about 30 cm. Stimuli presentation was controlled by E-Prime (Psychology Software Tools Inc., Schneider et al. 2002b; 2002a). Each trial started with a central fixation cross (500 ms duration), followed by stimulus presentation. The trial was timed-out as soon as participants responded (up to 4000 ms).

In Experiment 1 and 3 participants were required to judge the laterality (left or right) of observed digital images of hands by pressing as accurately as possible and within the allowed time interval, a left or a right response key, with their left and right index fingers, respectively.

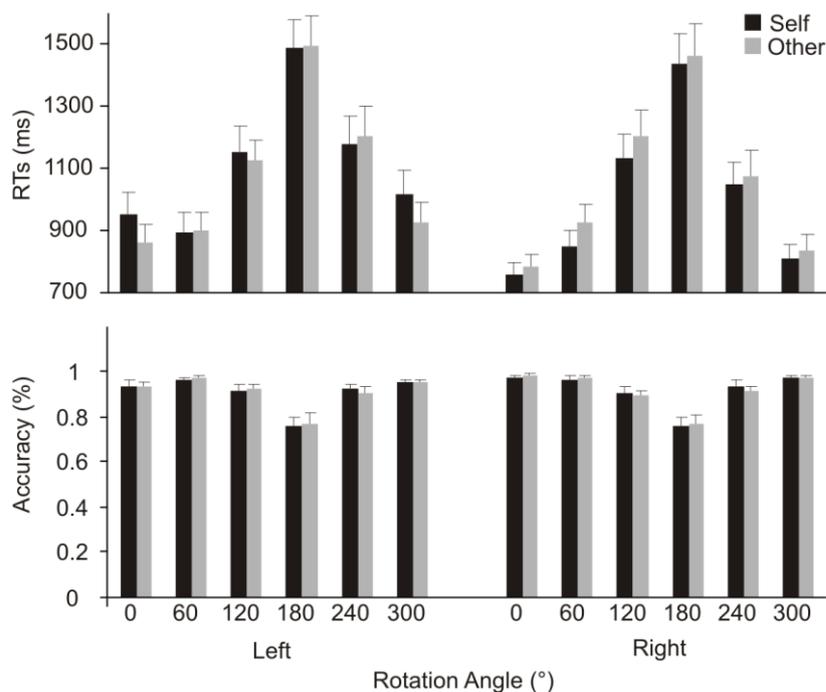
In Experiment 2, participants were required to explicitly judge whether the displayed hand corresponded or not to their own hand by pressing as accurately as possible and within the allowed time interval, a left or a right previously assigned response key, with their left and right index fingers, respectively. The response keys were counterbalanced between subjects.

Each Experiment consisted of 288 trials, 72 trials for each of the four conditions: self-right, self-left, other-right, other-left. In particular, in Experiment 1 and 2 the self right and left hand stimuli were shown to participants 72 times each; others' right and left hand stimuli were shown only 24 times. To rule out the possibility that higher repetition rates of self, compared to others' stimuli led to a "priming" effect during the laterality judgment task, a control Experiment 3 was performed. In this experiment others' right and left hands belonged to only one "other" individual. Thus, self and others' right and left hands were shown 72 times each. In all the three experiments, each orientation was randomly depicted 12 times per condition. Experiments were always preceded by a task-specific practice block.

Since Experiment 1 investigated the implicit and Experiment 2 the explicit self-bodily recognition, Experiment 1 was always conducted before Experiment 2. The same group of participants performed both Experiments in one single session. Experiment 3 was administered in a separate session to a different group of participants.

### 2.3 Results

*Results of Experiment 1.* Data are shown in Figure 2. To test the presence of self-advantage with the laterality judgment task, an ANOVA was conducted on participants' reaction times (RTs), with Owner (one's own and other people's stimuli), Laterality (left and right), and Orientation ( $0^\circ$ ,  $60^\circ$ ,  $120^\circ$ ,  $180^\circ$ ,  $240^\circ$  and  $300^\circ$ ) as within-subject factors. The Newman-Keuls test was used for all post-hoc comparisons.



**Figure 2- Experiment 1.** Mean response times (upper panel) and accuracy (bottom panel) at the different self' and others' hands stimuli orientations in the Implicit task. Error bars depict the standard error of the mean.

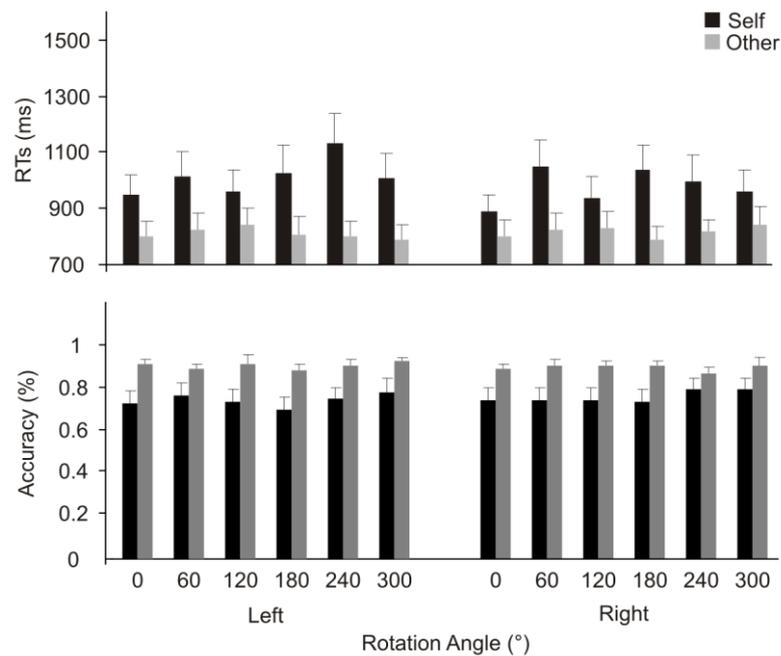
The ANOVA revealed the significance of the main effect of Laterality [ $F(1,23) = 9.28$ ,  $p < .006$ ,  $\eta_p^2 = .29$ ], since RTs to right stimuli were faster than RTs to left stimuli (1028 ms vs 1100 ms). The factor Orientation was also significant [ $F(5,115) = 57.74$ ,  $p < .001$ ,  $\eta_p^2 = .72$ ]. This effect was accounted for by faster RTs at  $0^\circ$ ,  $60^\circ$  and  $300^\circ$  (839, 893, 898 ms, respectively) compared to RTs at  $120^\circ$ ,  $180^\circ$ ,  $240^\circ$  (1155, 1472, 1128 ms, respectively;  $p < .001$  in all cases). The Laterality by Orientation interaction was also significant [ $F(5,115) = 4.01$ ,  $p < .002$ ,  $\eta_p^2 = .15$ ], because of the faster performance with right than left stimuli at  $0^\circ$  (771 ms vs. 908 ms),  $240^\circ$  (1064 ms vs. 1192 ms), and  $300^\circ$  (822 ms vs. 974 ms,  $p < .01$  for all comparisons). Relevant to the main goal of the study, the interaction Owner by Laterality was also significant [ $F(1,23) = 5.82$ ,  $p < .02$ ,  $\eta_p^2 = .20$ ]. The interaction was explained by faster RTs to right self stimuli compared to right others' stimuli (1007 ms vs. 1048 ms,  $p < .05$ , see Figure 2). No significant difference was observed for left hands between self and others' stimuli (1114 ms vs. 1087 ms,  $p = .19$ ). Moreover, RTs to self-right stimuli were faster than RTs to self-left ones (and other-left;  $p < .002$  for all comparisons), whereas only a trend to significance was found between other-right and other-left stimuli ( $p = .07$ ).

When the same analysis was conducted on accuracy (percentage of correct responses), only the factor Orientation was significant [ $F(5,115) = 20.2$ ,  $p < .0003$ ,  $\eta_p^2 = .47$ ], being subjects less accurate at  $180^\circ$  (76%) than at all other orientations ( $0^\circ = 96\%$ ,  $60^\circ = 97\%$ ,  $120^\circ = 91\%$ ,  $240^\circ = 92\%$ ,  $300^\circ = 96\%$ ,  $p < .0001$  for all comparisons). The other orientations were not significantly different.

*Results of Experiment 2.* Data are shown in Figure 3. An ANOVA similar to that of Experiment 1 and 2 was conducted on participants' reaction times (RTs), with Owner, Laterality and Orientation as within-subject factors.

The factor Owner was significant  $F[(1,23) = 18.66, p < .001, \eta_p^2 = .45]$ , since participants responded faster to others' than to self stimuli (814 vs 997 ms, see Figure 3). No other significant effects were found.

The same analysis conducted on accuracy (percentage of correct responses) confirmed a worse performance with self than with others' stimuli (76% vs 91%,  $F[(1,23) = 11.29, p < .001, \eta_p^2 = .33]$ ).



**Figure 3- Experiment 2.** Mean response times (upper panel) and accuracy (bottom panel) at the different self' and others' hands stimuli orientations in the Explicit task. Error bars depict the standard error of the mean.

*Results of Experiment 3.* To rule out the possibility that the presence of the self-advantage for right hands with the laterality judgment task was due to any sort of familiarity or “priming” effect, we asked a new group of participants to perform the same task in the control Experiment 3. In this experiment, each self and other's stimulus was shown the same number of times. An ANOVA was conducted on participants' reaction times (RTs), with Owner (one's own and other

people's stimuli), Laterality (left and right), and Orientation (0°, 60°, 120°, 180°, 240° and 300°) as within-subject factors. The Newman-Keuls test was used for all post-hoc comparisons.

The ANOVA revealed the significance of the main effect of Laterality [ $F(1,23) = 6.1$ ,  $p < .05$ ,  $\eta_p^2 = .21$ ], since RTs to right stimuli were faster than RTs to left stimuli (838 ms vs 867 ms). The factor Orientation was also significant [ $F(5,115) = 23.9$ ,  $p < .001$ ,  $\eta_p^2 = .86$ ]. This effect was accounted for by faster RTs at 0°, 60° and 300° (704, 755, 732 ms, respectively) compared to RTs at 120°, 180°, 240° (888, 1165, 870 ms, respectively;  $p < .001$  in all cases). Most interestingly, the significance of the interaction Owner by Laterality, found in Experiment 1, was confirmed in the present control experiment [ $F(1,23) = 4.5$ ,  $p < .05$ ,  $\eta_p^2 = .16$ ]. Once again this interaction was explained by faster RTs to right self stimuli compared to right others' stimuli (831 ms vs. 844 ms,  $p < .05$ ). No significant difference was observed for left hands between self and others' stimuli (868 ms vs. 865 ms,  $p = .55$ ). Moreover, RTs to self-right stimuli were faster than RTs to self-left ones (and other-left;  $p < .0002$  for all comparisons). Similarly, RTs to other-right stimuli were faster than RTs to other-left ones (and self-left;  $p < .002$  for all comparisons).

When the same analysis was conducted on accuracy (percentage of correct responses), only the factor Orientation was significant [ $F(5,115) = 14.8$ ,  $p < .001$ ,  $\eta_p^2 = .60$ ], being participants less accurate at 180° (86%) than at all other orientations (0°=97%, 60°=97%, 120°=95%, 240°=96%, 300°=97%,  $p < .001$  for all comparisons). The other orientations were not significantly different.

## **2.4 Discussion**

In this study we investigated whether and to what extent the so-called self-advantage (Frassinetti et al. 2008; 2009; 2010) is based on a motor simulation. To this aim healthy participants were submitted to a hand laterality judgment task. Crucially, the hand to be judged could be either the participants' own hand or other people's hand. Results showed an advantage

when judging one's own right compared to others' hands. Such an advantage was reflected by faster reaction times when responding to the former stimulus compared to the latter ones (Experiment 1 and 3). It is worth noting that this advantage was present in a task in which explicit self recognition was not required. By contrast, the self-advantage was lacking in the second experiment where self recognition was explicitly required. Indeed, a worse performance with self-related stimuli compared to other-related stimuli was observed.

Experiments 1 and 3 differed from Experiment 2 with respect to two main variables. The first one is the motor strategy required to solve the task, present in the laterality judgment task (Experiment 1 and 3), but not in the self-body recognition task (Experiment 2). In order to perform the laterality judgment task a mental motor rotation of body parts is required (Parsons 1987; 1994; 1998; Ionta et al. 2007). Coherently, the classical bell-shaped function of RTs found for this task (see Figure 2) constitutes the behavioral signature of mental rotation. On the other hand, the absence of such a function in the RTs of the self-body recognition task (see Figure 3) shows that a motor simulation is not required to accomplish the explicit task. For these reasons the presence of the self-advantage in Experiment 1 and 3, and its absence in Experiment 2 suggest that the bodily self is ultimately linked to a motor representation.

The second variable is the requirement to explicitly recognize self stimuli, which characterizes the second, but not the first and the third experiments. Our data demonstrate that the request of an explicit recognition of one's own body does not lead to the emergence of the self-advantage. Thus, explicit body processing is *per se* neither necessary nor sufficient to grant the bodily self-advantage.

We are aware the two tasks required two different responses, thus they cannot be directly compared to each other. However, to the best of our knowledge, this is the first study investigating the implicit and explicit self bodily knowledge by means of the very same stimuli and the same experimental procedure. The idea of a dissociation between implicit and explicit

self body processing is in agreement with the large amount of neuropsychological studies showing that brain damaged patients can be impaired in explicit while sparing implicit processing. A typical clinical condition in which implicit and explicit processes are dissociated is neglect. Neglect patients fail to explicitly detect stimuli presented in the contralesional affected field. However, they can implicitly process the same stimuli up to the semantic level (Berti et al. 1994; Berti and Rizzolatti 1992). Regarding the bodily self, such dissociation is in agreement with the independence of implicit from explicit self-body processing reported by infancy research. Indeed, during development an implicit sense of self and the ability to discriminate self from others appears to emerge earlier than the ability to explicitly self-recognize (Rochat 2003; 2010).

Taken together, data from Experiments 1 (confirmed by Experiment 3) and 2, although not directly comparable to each other, suggest that the crucial element for the self-advantage to emerge is the recruitment of a motor simulation. This interpretation is in agreement with and provides a coherent explanation to a variety of previous studies. Tsakiris et al. (2006) carried out a study in which participants had to decide whether they viewed their own right hand or someone else's right hand covered with identical gloves, while experiencing a passive displacement of their own right index finger, either generated by the experimenter or by participants' own left hand. The results showed that the performance was significantly better when the displacement of participants' right index finger was self-generated. As argued by Tsakiris, Schutz-Bosbach, & Gallagher (2007), this shows that "Self recognition was significantly more accurate when subjects themselves were the authors of the action" (p. 654-655). Coherently, visual and motor related information converge within the OTC in a body part specific manner (Devue et al. 2007), and the feeling of ownership of the hand positively correlates with activity in the premotor cortex (Ehrsson et al. 2004).

In a behavioral study Loula, Prasad, Harber, & Shiffrar (2005) asked participants to perform a self identification task while observing sagittal displays of point-light depictions of themselves, their friends, and strangers while performing various actions. They found higher sensitivity to one's own motion. Since everyone has little experience of viewing her own body moving, such self-advantage can be easily explained by the activation of observers' own action motor representation. Similarly, a self-advantage was demonstrated by Casile & Giese (2006) in a behavioral task, in which only non-visual motor training was available to participants.

The last point to be addressed is the presence of the self-advantage only for participants' right hand. Such selectivity is a further argument in favor of our motor hypothesis of the self-advantage. The presence of the "self-advantage" only for the right hand can be explained by the greater lateralization in hand motor skills observed in right-handers compared to left-handers (e.g., Gentilucci et al. 1998). Neuroimaging studies have shown hemispheric asymmetries in cortical areas associated with body representation in right-handed people, but not in left-handed people. Indeed, right-handed individuals have a greater cortical surface area in the left sensory cortex and stronger activation in the left sensory-motor cortex while performing right hand movements than in the corresponding areas of the right hemisphere. In contrast, left-handed individuals seem to have near-symmetrical surface areas and activations (Amunts et al. 1996; Kawashima et al. 1997; Zilles et al. 1997). Similar results have been observed with electroencephalographic (EEG) studies (Buchner et al. 1995; Jung et al. 2003). Furthermore, it was recently shown that right-handers perceive their own right arm and hand as being longer than their left ones, whereas left-handers perceive both arms and hands accurately (Linkenauger et al. 2009). Thus, it appears that the conscious perception of the body is grounded on its motor potentialities (Gallese and Sinigaglia 2010).

Since according to our data the self-advantage relies upon a sensory-motor representation, the presence of the self-advantage only for self right hand stimuli is likely the consequence of the

greater involvement of the left, rather than the right, sensory-motor areas in right-handers during a mental motor task. Given such a near-symmetrical cortical representation in left-handers, future studies on this population might help us to shed new light on this phenomenon. Recent data seem to support our hypothesis. Conson and colleagues (2010) asked right-handed and left-handed healthy participants to categorize full-colored pictures of hands, presented according to the egocentric or the allocentric perspective, as belonging to themselves or to other people. They found that both right- and left-handers were faster in recognizing dominant hands (right and left hand, respectively) in egocentric perspective, and others' non-dominant hands in allocentric perspective.

Possibly one may argue that the self advantage we found in Experiment 1 can be construed in terms of “priming” effect or any sort of visual familiarity. Indeed, in this experiment self stimuli were presented 72 times while each of the three others' stimuli was presented only 24 times. To deal with this possible concern, we run a third control experiment in which we used the hands of only one other individual, thus matching the number of occurrences of each stimulus in terms of identity. We found the same results as in Experiment 1. This rules out the possibility that the self-advantage is exclusively due to “priming” effects. Regarding visual familiarity, we believe something different might underpin our behavioral effect. Indeed, out of the total of self-related trials, one half involved the presentation of the right hand while the other half involved the presentation of the left hand. It follows that if perceptual familiarity could fully explain our results, it is not clear why our effect was visible only for right hand stimuli. Our idea is also corroborated by a recent study (Aranda et al. 2010) exploring whether symbolic cues, predicting the appearance of one's own or another person's hand could optimize the processing of these stimuli. Results showed a selective attentional effect with one's own hand, but not with someone else's hand. More relevant for the purpose of our study, in a control experiment the authors tested whether this selective attentional effect could be due to the higher perceptual familiarity. Results

showed that participants could use the cues to anticipate the appearance of both stimuli, since a behavioral advantage was observed for all valid stimuli, regardless of their degree of familiarity.

In conclusion, our data demonstrate that implicit and explicit recognition of the bodily self dissociate and that, only when bodily self recognition is implicit, a self-advantage does emerge. Since the implicit mechanism recruits a motor simulation, it follows that the bodily self is primarily mapped in motor terms. Indeed, when explicit self recognition is required and different cognitive and/or perceptually-based mechanisms are likely involved, the self-advantage is lacking. The idea of the motor nature of the bodily self is in agreement with previous philosophical intuitions. Merleau-Ponty posited that our body appears to us as an attitude directed towards a certain existing or possible tasks. When referring to the spatiality of the body he claimed: “[...] my body appears to me as an attitude directed towards a certain existing or possible task. And indeed its spatiality is not, like that of external objects [...], a spatiality of position, but a spatiality of situation”.

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## Chapter 3

### **3. A sensorimotor network for the bodily self**

#### **3.1 Introduction**

In everyday life, we move, see and feel our body, and have no doubt that it is our own. Any experience of our body provides us with a variety of information related to it, such as visual, tactile and, more generally, concerning its physiological state. Beyond the distinction between exteroceptive, interoceptive and proprioceptive awareness, what is the basic experience of our body as a bodily self: what enables us to implicitly distinguish our body from other human bodies (Frassinetti et al. 2008; 2009; 2010; 2011; Ferri et al. 2011;)? Recently, it has been proposed that the bodily self can be conceived as motor in nature (Legrand 2006; Gallese and Sinigaglia 2010), that is, based on our experience of our own body parts according to their motor potentialities, as they are represented in a motor bodily format (see Gallese and Sinigaglia 2011). In this vein, Smith explained the concept of bodily self as follows: “The bodily self is a physical agent. Knowledge of oneself as bodily is fundamentally knowledge of oneself as agentive; such knowledge is grounded in both experience of oneself as instantiating a bodily structure that affords a limited range of actions, and experience of oneself as a physical agent that tries to perform a limited range of actions over time.” (Smith 2007)

The existence of such motor experience based representation of the bodily self has been investigated at the behavioural level in a previous study from our group (Ferri et al. 2011). In that study, right-handed participants underwent a laterality judgment task using rotated hand stimuli. Crucially, the hand to be judged could be either the participant’s own hand or another person’s hand. The results showed faster reaction times (RTs) when judging one’s right hand compared to all the other hand stimuli, regardless of the magnitude of the rotation. According to previous studies (Frassinetti et al. 2008; 2009; 2010), we named such an effect as a “self-advantage”. Moreover, Ferri and colleagues (2011) found that the self-advantage does not emerge when participants are

asked to explicitly recognize the owner of the observed hand. Based on these empirical data, we argued in favour of the assumption that an implicit motor representation of the bodily self exists and that it might help us in distinguishing one's own from others' body, thus leading to the self-advantage.

In this fMRI study we tested the hypothesis that the sensorimotor system plays a pivotal role in the implicit self/other distinction during the laterality judgment task and, more specifically, in the self-advantage for right hand in right-handed participants.

We adopted the laterality judgment task because it is now accepted that in order to perform it one simulates a motor rotation of her own hand. Such simulation shares the same temporal and kinematic properties with actual body rotation in space (Parsons 1994). The linear increases in both RTs (Cooper and Shepard 1973) and the BOLD signal (Milivojevic et al. 2009) as a function of angular displacement of the stimulus are “hallmarks” of this mental process. Furthermore, slope and intercept of the described linear regressions are thought to reflect the efficiency on the task (Shepard and Cooper 1982; Christova et al. 2008), depending upon the actual mental rotation process (rotational factor) and more general processes (non-rotational factors) occurring before or after mental rotation proper (Shepard and Cooper 1982), respectively.

If a motor experience based representation of the bodily self does exist, likely leading to the self-advantage, measures of the rotational factor in right-handed participants should reveal higher efficiency for the actual mental rotation of one's own right hand compared to all the other hand-stimuli. Such modulation should be found within the sensorimotor nodes of the network recruited during the laterality judgment task.

Neuroimaging results associated with this task, using both corporeal and non-corporeal stimuli, showed activation in several dominant spatial-motor processing regions, including the posterior parietal (superior parietal and the intraparietal sulcus), premotor and primary motor cortices, the supplementary motor area and the cerebellum (Parsons et al. 1995; Cohen et al. 1996;

Alivisatos and Petrides 1997; Kosslyn et al. 1998; Vingerhoets et al. 2002; Seurinck et al. 2004; Podzebenko et al. 2005).

As far as parietal activations are concerned, Bonda and colleagues (1995) proposed that areas of the superior and the inferior parietal cortex are components of a neural system underlying a constantly updated representation of the body in space. This interpretation is supported by evidence that parietal lesions are associated with disorders of body schema, personal space and left/right orientation (DeRenzi 1982).

And as far as premotor regions are concerned, a dissociation has been found between mental rotation of body parts and mental rotation of non-corporeal objects (Kosslyn et al. 1998; Arzy et al. 2006). The selectivity of premotor regions for the mental rotation of corporeal stimuli has been shown by Arzy and colleagues (2006). They investigated the performance of a patient with a lesion centred on the right premotor cortex suffering from asomatognosia, a deficit of corporeal awareness, in two tasks requiring the mental rotation of hands and letters, respectively. They found an impairment in the mental rotation of body parts while the mental rotation of letters was preserved. These data suggest a pivotal role of the premotor cortex in corporeal awareness. Given the higher specificity of the premotor cortex for the mental rotation of body-related stimuli, and considering its role in body awareness (Ehrsson et al. 2004; Berti et al. 2005; Arzy et al. 2006), it is plausible to hypothesize that this brain area may represent one of the essential anatomical and functional basis for the motor aspect of bodily selfhood.

### **3.2 Methods**

#### *Participants*

Eighteen volunteers (9 females and 9 males; mean age = 24 years, range 21-34) took part in this study after giving written informed consent. All were right-handed as defined by the Italian version of the Edinburgh Inventory (Oldfield 1971). They had normal or corrected-to-normal visual

acuity and were naïve as to the purposes of the experiment. The experimental protocol was approved by the Ethics Committee of the University of Parma.

### *Apparatus*

All images were collected with a 3T GE scanner operating at the University of Parma. Participants lay supine in the scanner with the response buttons (Resonance Technology, Inc.) under their index fingers. Visual stimuli were presented by means of a head mounted display with a resolution of 800 horizontal pixels by 600 vertical pixels (Resonance Technology, Inc.). Sound-attenuating headphones were used to muffle scanner noise. The presentation of the stimuli and the recording of the participants' responses were controlled by E-Prime software (Psychology Software Tools Inc.).

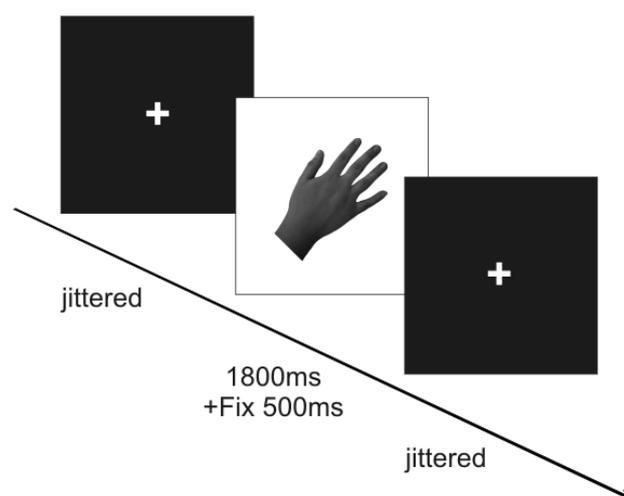
### *fMRI Data Acquisition*

Functional images were collected with a gradient echo EPI sequence. Each subject underwent 4 acquisition runs. Each run included 245 consecutive volumes comprising 40 consecutive 3-mm-thick slices oriented parallel to the anterior-posterior commissure and covering the whole brain (TR = 2.3 s, TE = 60 ms, 64 x 64 image matrix, 3 x 3 mm in-plane resolution). T1-weighted anatomical images were collected using a multiplanar rapid acquisition gradient-echo sequence (156 sagittal slices, voxel size: 1 x 1 x 1 mm, TR = 8.08 ms, TE = 3.7 ms).

### *Stimuli and Procedure*

The experimental paradigm was modelled on a previous behavioural study (Ferri et al. 2011) with appropriate modification for fMRI scanning. The experimental stimuli consisted of grey-scale pictures of the dorsal view of right and left hands. The hands of each participant were photographed with a digital camera in a session prior to the experiment (1 week before). This session took place in

a controlled environment with constant artificial light and a fixed distance between the camera lens and the hands (40 cm), which were always photographed in the same position. Subsequently, photographs were modified with Adobe Photoshop software: they were cut from the original picture, pasted on a white background, and reoriented into the different rotated positions. Other people's hands were selected from this database as the best match for size, skin colour, age, and gender, in comparison with each participant's hands. Images of hands were presented one at a time at the centre of the visual field in six different clockwise orientations (0°, 60°, 120°, 180°, 240°, 300°). 0 degrees orientation (upright) was defined as fingers pointing upwards. 0 degrees was also the angle identical to the orientation of participants' hands in the moment of responding while in the scanner. Indeed, before starting a scanning session, we always checked that participants held the button box at some comfortable angle centred around 0 degrees. Thus, the design was a 2x2x6 factorial with owner (self, other), laterality (left, right) and orientation (0°, 60°, 120°, 180°, 240°, 300°) as main factors. Each trial lasted 2300 ms, starting with a central fixation cross for 500 ms followed by stimulus presentation for 1800 ms or timed-out as soon as participants responded (see figure 1). If a response was given before, the fixation cross was presented for the rest of the remaining trial time.



**Figure 1:** A typical experimental trial. Participants were required to judge the laterality of the presented hand. The shown image is either the participant's own hand or another person's hand. Hands were presented in six different clockwise orientations (0°, 60°, 120°, 180°, 240°, 300°).

Participants were required to judge the laterality (left or right) of observed digital images of hands by pressing as accurately as possible and within the allowed time interval a left or a right response key, with their left and right index fingers, respectively. Each participant provided us with 40 trials per condition. The trial order was determined using the program *optseq2* (Dale 1999). *Optseq2* arranges trials in an order that appears random to participants while trying to jitter the trial onset times so that the overlaps of the hemodynamic response course are removed from the image-processing estimate of the induced hemodynamic response. The overall result is a trial order where trials from every condition are intermixed along with variable fixation times. This method allows a maximum number of trials presented while eliminating possible behavioural effects of expectation of upcoming trials by participants. At the end of the fMRI session, we investigated, at the behavioural level, how well participants could discriminate between their own hands and those of others. We employed the same stimuli and the same experimental paradigm as in the laterality judgment task. However, in this case, participants were required to explicitly judge whether or not the displayed hand corresponded to their own hand by pressing, within the allowed time interval (1800 ms), a left or a right (previously assigned) response key, with their left and right index fingers, respectively. The response keys were counterbalanced across subjects.

### *Data Analysis*

fMRI data were analyzed using SPM8 (Wellcome Department of Cognitive Neurology, Institute of Neurology, London) according to the following procedure. For each subject, functional images were first corrected for head movement using a least-squares approach and a six-parameter rigid body spatial transformation (Friston et al. 1995) and for difference in acquisition timing between slices. The high-resolution anatomical image and the functional images were then stereotactically normalized to the Montreal Neurological Institute (MNI) brain template used in SPM8 (Mazziotta et al. 1995). Functional images were resampled with a voxel size of  $3 \times 3 \times 3$  mm

and spatially smoothed with a three-dimensional Gaussian filter of 6 mm full width at half maximum to accommodate anatomical variations between subjects (Friston et al., 1995). The time series of functional MR images obtained from each participant were analyzed on a voxel-by-voxel basis using the principles of the general linear model extended to allow the analysis of fMRI data as a time series (Worsley and Friston 1995). The onset of each stimulus constituted a neural event, that was modelled through a canonical hemodynamic response function, chosen to represent the relationship between neuronal activation and BOLD signal changes (Friston et al. 1998).

We analyzed the fMRI data in 2 ways. First, we used a 2x2 factorial design to investigate the neural correlates of the self-advantage for one's dominant hand (see Ferri et al. 2011) and behavioural results of the present study regardless of the different orientation. The neuronal correlates of the interaction term, namely, owner (self, other) by laterality (right, left) was assessed using the contrast [(self-right hand, SR > self-left hand, SL)-(other-right hand, OR > other-left hand, OL)], 0.05 FDR corrected.

A second analysis was performed in order to tease apart different components of the mental rotation process and see how they are related to the self/other distinction and self-advantage. We used a 2x2x6 factorial design to assess the neuronal correlates of the main effect of different orientation, 0.01 FWE corrected ([www.fil.ion.ucl.ac.uk/~wpenny/publications/rik\\_anova.pdf](http://www.fil.ion.ucl.ac.uk/~wpenny/publications/rik_anova.pdf)). Then, for each brain region resulting from the above main effect and for each participant, we performed four linear regression analyses, one per stimulus category (SR, SL, OR, OL). BOLD response (Beta values extracted by each cluster) and RTs at different orientations were included in the regression analyses as dependent and predictor variables, respectively (Richter et al. 1997; Richter et al. 2000). Then we computed slopes and intercepts. The slope would reflect the efficiency of the neural mechanism underlying the actual mental rotation process (BOLD signal per RT at each degree of rotated angle): the smaller the slope, the higher the efficiency of neural mental rotation (Christova et al. 2008). The intercept would reflect the efficiency of the neural mechanism

underlying more general processes occurring before (e.g., stimulus encoding) or after (e.g., response preparation) mental rotation proper (Shepard and Cooper 1982): the smaller the intercept, the higher the efficiency of processing hand stimuli unrelated to the actual mental rotation. Slopes and intercepts were compared by means of two separate two-ways ANOVAs, each including owner (self, other) and laterality (right, left) as main factors. These analyses were carried out to assess whether any cortical regions among those involved in the motor task also i) specifically contributed to the self-advantage for right hand and/or ii) generally supported an implicit discrimination between one's own and other people hands, either for rotational or non-rotational processes, or both.

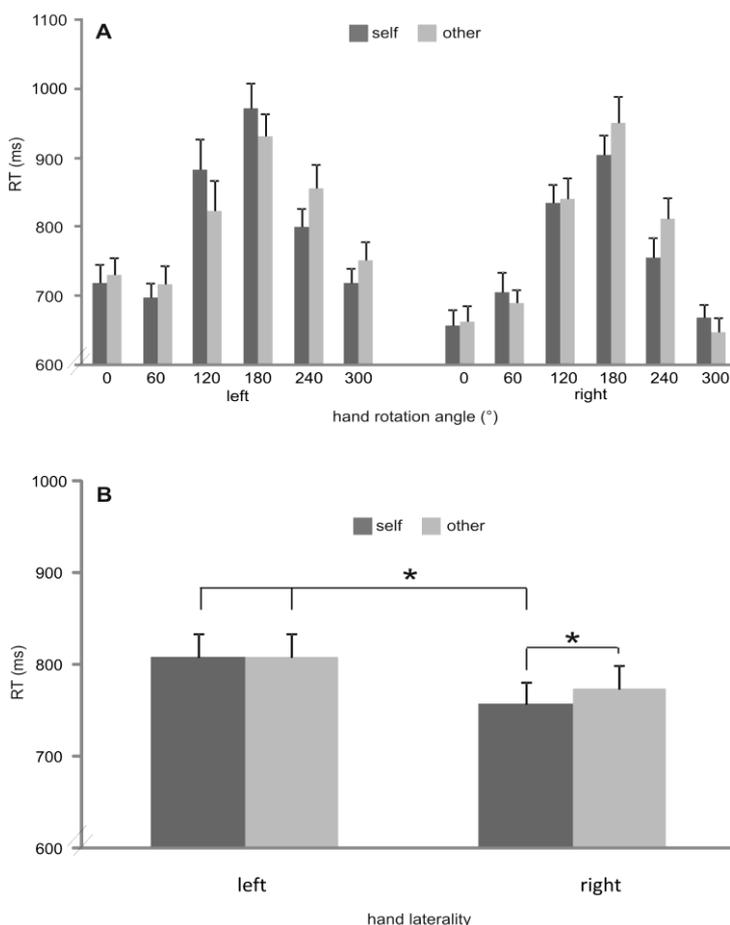
### **3.3 Results**

#### *Behavioural results*

Trials in which participants did not respond (5.8%) or failed to respond (6%) were discarded from the analysis. The mean reaction time (RT) of the correct responses was calculated for each condition; responses longer than 2 standard deviations from the individual mean were treated as outliers and not considered (3,2% of the data set).

Visual inspection of behavioural data suggested that for each stimulus category (SR, SL, OR, OL) we obtained the classic response time function of a bell-shaped curve, constituting the behavioural signature of mental rotation (figure 2, panel A). Tests on trends indicated that the three-way quadratic interaction (owner by laterality by orientation) was significant ( $F_{1,17}=18.6$ ,  $p<0.001$ ), whereas the three-way linear interaction was not significant ( $F_{1,17}=1.01$ ,  $p=0.33$ ). As the aim of the present work was to investigate the role played by the sensorimotor system in the self/other distinction and the self-advantage, we limited the ANOVA to the factors owner (self, other) and laterality (left, right), while the levels of the factor orientation were collapsed. Mean RTs of the correct responses were calculated for each condition entered in the above described two-ways

ANOVA. The Tukey's test was used for all post-hoc comparisons. Statistical analysis of RTs recorded from participants lying in the scanner showed significant main effects of owner ( $F_{1,17}=5.2$ ,  $p<0.05$ ) and laterality ( $F_{1,17}=14.1$ ,  $p<0.005$ ). Also, the two-way interaction owner by laterality ( $F_{1,17}=4.4$ ,  $p=0.05$ ) was significant. The owner main effect was accounted for by faster performance for self-related stimuli ( $M= 783$  ms) with respect to other-related stimuli ( $M= 791$  ms). The laterality main effect was accounted for by faster performance for right stimuli ( $M= 766$  ms) with respect to left stimuli ( $M= 808$  ms). Finally, the interaction owner by laterality was accounted for by faster performance to self-right stimuli ( $M= 758$  ms) compared to all the other conditions (other-right:  $M=774$  ms; self-left:  $M=809$  ms; other-left:  $M=808$  ms;  $p<0.05$  in all cases, see figure 2, panel B). By contrast, RTs for self-left and other-left stimuli did not differ ( $p=1$ ) from each other. In conclusion, behavioural data confirmed the self-advantage for one's dominant hand we previously described (Ferri et al. 2011).

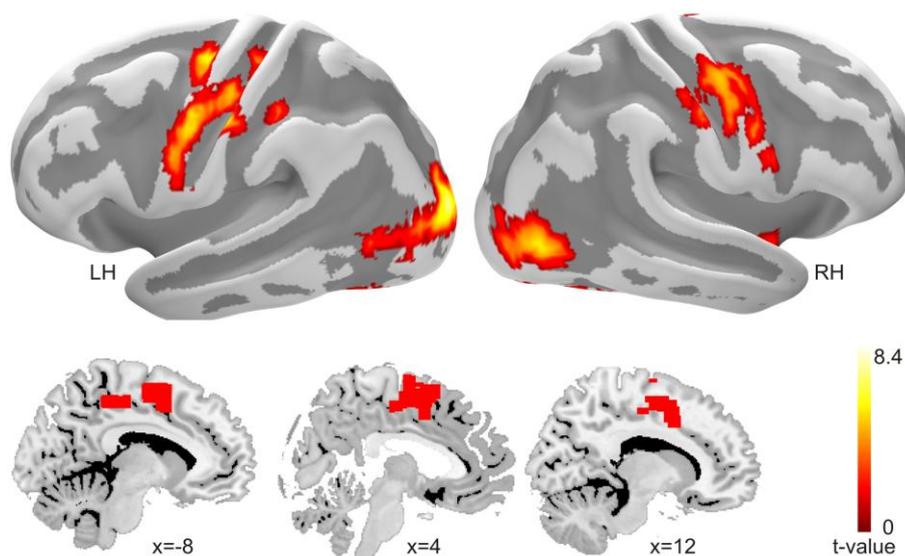


**Figure 2:** Mean response times at the self-left, self-right, other-left and other-right hand stimuli as a function of the angular orientation (panel A). Mean response times at the self and other hand stimuli, regardless of the stimulus orientation (panel B). Error bars depict the standard error of the mean.

Strikingly, the self-advantage effect was not due to the fact that participants can better recognize their own right hand with respect to all the others' hand stimuli. Indeed, participants were quite accurate in categorizing all hand stimuli. The mean accuracy was 89.2% (SR= 88.2%; SL= 86.5%; OR=91.5%; OL= 90.7%). ANOVA on these values did not reveal any significant difference. Importantly, when comparing the sensitivity of our participants in making an explicit self/other discrimination between right ( $d' = 2.59$ ) and left ( $d' = 2.43$ ) hands, we found that  $d'$  scores did not differ from each other ( $T_{17}=0,41$ ;  $p=0.69$ ).

*Neural correlates of the self-advantage for right hands.*

The owner by laterality interaction term (see method for the contrast definition), i.e., the superior performance when judging the laterality of one's right hand (self-advantage) revealed activation in the precentral gyrus bilaterally, the supplementary and pre-supplementary motor areas extending to the middle cingulate cortex, the left postcentral gyrus, the right hippocampus, the right temporal cortex encompassing the extrastriate body area (EBA; Downing et al. 2001), the right fusiform gyrus, the occipital cortex and the cerebellum bilaterally (see figure 3 and table 1).



**Figure 3:** Regions showing higher activation during the mental rotation of one's own right hand as compared to the mental rotation of one's own left and other's hand. Group activation data are rendered on the cortical surface of a "canonical" brain (Mazziotta et al. 1995).

Brain Region	side	Cluster size (voxels)	Local maxima (MNI)			Brodmann Area
			x	y	z	
middle frontal gyrus	R	97	48	3	57	6
supplementary motor area	L	289	-3	3	57	6
	R		9	3	51	6
precentral gyrus	L	175	-54	-3	48	6
	R	124	60	9	21	6
	R		51	-3	36	4
middle cingulate cortex	L	75	-9	-36	48	na
	R	51	12	9	36	32
postcentral gyrus	L	64	-27	-33	48	3
hippocampus	R	184	30	-12	-18	20
temporal cortex	R	161	48	-72	3	37
	R		42	-54	-15	37
fusiform gyrus	R	152	27	-78	-15	19
occipital cortex		1895				
	L		-12	-75	12	17
	R		15	-72	15	18
	L		-27	-93	12	18
	L		-21	-57	-9	19
	R		24	-51	-6	37
cerebellum	L	431	-36	-66	-21	19
	R	437	27	-48	-30	37

**Table 1:** Montreal Neurological Institute (MNI) coordinates of peaks of relative activation in the cortical regions where BOLD signal was higher during the mental rotation of one's own right hand as compared to the mental rotation of one's own left and other's hand. Table shows local maxima more than 4 mm apart.

### *Correlation of Neuroimaging and Psychophysical data*

The standard BOLD analyses carried out so far clearly indicated a stronger involvement of sensorimotor regions while judging the laterality of one's own right hand as compared to others' right hand. Nevertheless, they do not reveal whether and to what extent regions specifically involved in our motor task also participate to the behavioural self-advantage effect. Indeed, the facilitation in judging the laterality of one's own right hand could be triggered by a higher efficiency of either the neural mental rotation process or by more general, non-rotational processes, or both. To tackle this issue, we firstly isolated all the brain regions involved in the task,

irrespectively of the variables owner and laterality ( $p < 0.01$  FWE corrected, see methods). These regions were localized in the left insula, the right insula encompassing the pars orbitalis of the inferior frontal gyrus, the supplementary and pre-supplementary motor areas, the left premotor cortex, the right middle frontal gyrus, the superior frontal gyrus bilaterally, the left inferior parietal lobe, the left precuneus, the superior parietal lobule and the calcarine cortex bilaterally (see figure 4 and table 2). Then, we performed two ANOVAs for each cluster; one to assess reliable differences between slopes; the other to assess reliable differences between intercepts for the different stimulus categories (SR, SL, OR, OL). Such differences would be due to effects of owner, laterality and their interaction on regression lines on BOLD response for RTs at different orientations. We can make the following predictions:

1. If sensorimotor resources involved in the laterality judgment task also contribute to self-advantage for right hand due to higher neural efficiency when rotating one's own compared to another's hand, then slopes should be lower (higher efficiency) for self- than for other- right hand. The same difference should not be found for left hands.

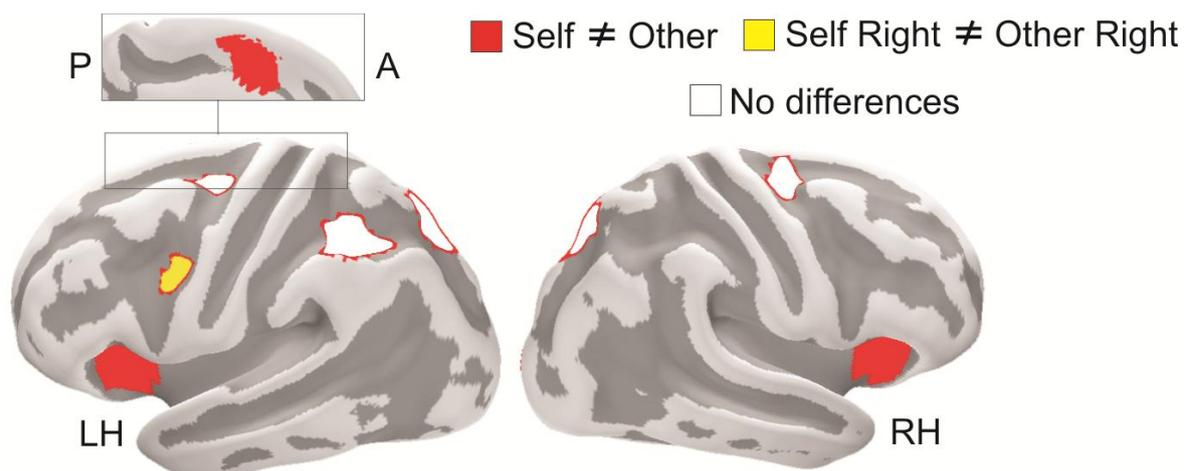
2. If the recruitment of sensorimotor resources involved in the task is optimized for distinguishing one's own from another's right hand based on more general, non-rotational processes, such as those occurring before or after actual mental rotation, then intercepts should be lower (higher efficiency) for self- than for other- right hand. The same difference should not be found for left hands.

As far as slopes are concerned, a significant main effect of owner was found in the left insula ( $F_{1,17} = 11.8$ ,  $p < .005$ ), the right insula ( $F_{1,17} = 9.3$ ,  $p < .01$ ), the supplementary and pre-supplementary motor areas ( $F_{1,17} = 11.4$ ,  $p < .005$ ), the left premotor cortex ( $F_{1,17} = 13.8$ ,  $p < .005$ ) and the calcarine cortex ( $F_{1,17} = 10.3$ ,  $p < .005$ ). In all the above listed regions, the owner main effect was accounted for by lower slopes (higher efficiency of actual motor process) for self hands as compared to others' hands (see table 2). Strikingly, the interaction of owner and laterality was

significant only in the left premotor cortex ( $F_{1,17}=5.4$ ,  $p<.05$ ). Post-hoc comparisons (Tukey's test) showed that slope was lower ( $p<.001$ ) for self-right stimuli compared to other-right stimuli, whereas slopes of self-left and other-left stimuli did not differ from each other ( $p=.33$ ). As far as intercepts are concerned, a significant main effect of owner was found in the left insula ( $F_{1,17}=17.6$ ,  $p<.001$ ), the right insula ( $F_{1,17}=15.3$ ,  $p<.005$ ), the supplementary and pre-supplementary motor areas ( $F_{1,17}=17.3$ ,  $p<.001$ ), the left premotor cortex ( $F_{1,17}=19.9$ ,  $p<.001$ ) and the calcarine cortex ( $F_{1,17}=13.1$ ,  $p<.005$ ). In all the above listed regions, the owner main effect was accounted for by lower intercepts (higher efficiency of non-rotational processes) for others' hands as compared to self hands (see table 2). Again, the interaction of owner and laterality was significant only in the left premotor cortex ( $F_{1,17}=6.3$ ,  $p<.05$ ). Post-hoc comparisons (Tukey's test) showed that intercepts were lower ( $p<.001$ ) for other-right stimuli compared to self-right stimuli, whereas intercepts of other-left and self-left stimuli did not differ from each other ( $p=.32$ ). The main effect of laterality was never significant. In sum, these results suggest that among regions involved in the mental rotation task the left premotor cortex' activity is likely to be related also to self-advantage for right hand. Such a relation between the local neural activity and the behavioural effect seems to be specifically explained by a higher neural efficiency during the actual mental rotation process, and not by neural efficiency for more general, non-rotational processes. Also, our results indicate that (for similar reasons) bilateral insula, supplementary and pre-supplementary motor areas, and calcarine cortex are engaged in general self/other distinction.

Brain Region	Side	Cluster size (voxels)	Local maxima (MNI)			Slopes				Intercepts			
			x	z	y	SR	SL	OR	OL	SR	SL	OR	OL
<i>Self ≠ Other</i>													
insula	LH	148	-27	24	-3	<b>3.8</b>	<b>2.4</b>	3.9	5.9	<b>-2.4</b>	<b>-1.3</b>	-2.7	-4.2
insula/inferior frontal gyrus ( <i>pars.orb</i> )	RH	277	42	21	-3	<b>3.8</b>	<b>3.9</b>	3.9	5.9	<b>-2.4</b>	<b>-1.3</b>	-2.7	-4.2
supplementary motor area/ middle cingulate cortex	LH/RH	325	-3	12	48	<b>4.0</b>	<b>3.5</b>	5.7	7.1	<b>-1.7</b>	<b>-1.2</b>	-3.4	-4.1
calcarine cortex	LH/RH	189	-9	-93	-6	<b>4.5</b>	<b>2.4</b>	6.9	6.3	<b>1.8</b>	<b>3.1</b>	-0.5	0.3
<i>Self-Right ≠ Other-Right</i>													
premotor cortex	LH	25	-42	0	33	<b>3.4</b>	3.9	8.2	7.9	<b>-0.5</b>	-0.7	-4.6	-4.0
<i>No differences</i>													
middle/superior frontal gyrus	RH	48	30	-3	54	3.3	3.5	5.4	4.7	-1.0	-1.0	-2.8	-1.9
superior frontal gyrus	LH	27	-24	-6	54	3.7	4.0	5.7	5.3	-1.1	-1.4	-2.9	-2.4
inferior parietal lobe	LH	144	-36	-48	39	5.1	4.5	6.4	5.8	-2.1	-1.8	-3.2	-2.9
precuneus/ superior parietal lobe	LH	63	-12	-69	60	5.6	7.2	7.3	5.0	-2.2	-3.4	-3.3	-1.7
superior parietal lobe	RH	65	18	-72	57	4.9	6.5	5.4	3.5	-1.4	-2.6	-1.8	-0.4

**Table 2:** Montreal Neurological Institute (MNI) coordinates of peaks of relative activation in the cortical regions involved in the mental rotation process (main effect of angular orientation), irrespectively of the variables owner and laterality. Rightmost columns report slopes and intercepts for each region calculated for self-right (SR), other-right (OR), self-left (SL) and other-left (OL) conditions. In bold are slopes and intercepts of self hands significantly different from those of other hands, for both right and left stimuli.



**Figure 4:** Regions involved in the mental rotation process (main effect of angular orientation), irrespectively of the variables owner and laterality. Group activation data are rendered on the cortical surface of a “canonical” brain (Mazziotta et al. 1995). Red clusters identify areas where the slopes and the intercepts were significantly different between self and other conditions, regardless of the laterality. The yellow cluster identifies the cortical region where slope and intercept were significantly different between self right and other right hand stimuli. White clusters identify areas where both slopes and intercepts were not different between self and other conditions.

### 3.4 Discussion

The hand laterality judgment task requires participants to simulate a motor rotation of the observed stimulus. Specifically, when performing this task participants imagine their own hand rotating into the stimulus position to confirm a judgment of handedness (Parsons 1994). This means that the imagined hand is translated into its motor representation, engaging sensorimotor rather than visual processes (Parsons et al. 1995; Kosslyn et al. 1998; Parsons et al. 1998; de Lange et al. 2006). This idea is further corroborated by imaging studies, showing an involvement of sensorimotor areas while performing the task (for a review: Zacks 2008). In the present study we took advantage of this task to investigate whether mental rotation of pictures of participant’s own hand leads to a different activation of sensorimotor areas as compared to the mental rotation of pictures of another’s hand. If this holds, it would be evidence for the existence of a motor representation of the participant’s hand that allows for the efficient differentiation between one’s own hand and another person’s hand.

Empirical data support the existence of a bodily self grounded in the sensorimotor system. For instance, Loula and colleagues (2005) asked participants to identify and discriminate actors during tasks in which the action could be performed either by the participant or by a stranger. They found highest sensitivity to one's own motion in both tasks. These results have been interpreted in light of the fact that the neural mechanism responsible for identity perception is deeply entrenched within the action production system.

In the same vein, during a hand laterality judgement task, we recently found faster reaction times in the implicit processing of one's own hand, compared to others' hands (Ferri et al. 2011). Such self-advantage, likely related to the motor experience based bodily self, was specific for the participant's right dominant hand. Furthermore, it was not observed during a self/other discrimination task, thus suggesting that an explicit recognition of one's own body parts is not mandatory for the self-advantage to emerge.

Here we investigated the neural activity underlying this effect. Behavioural data collected inside the scanner basically replicate our previous findings (Ferri et al. 2011). We will now relate this behaviour to neural activity recorded by fMRI. We found higher activation in bilateral premotor cortex, extending to the postcentral gyrus and the supplementary and pre-supplementary motor areas, besides occipito-temporal cortices, while rotating one's right hand as compared to others' hand stimuli. Strikingly, the second analysis on our data revealed that only in the left premotor cortex a selective higher efficiency for self- right hand was present. Indeed, slope was lower, and intercept higher, for self-right as compared to other-right hand. Conversely, slope and intercept for self-left and other-left hands did not differ from each other. Thus, we speculate that such area is the crucial node for the bodily self-advantage.

Current neuroimaging data (Ehrsson et al. 2004) suggest that the premotor cortex is an ideal candidate for the multisensory representation of one's own body. Indeed, it is anatomically connected to visual and somatosensory areas in the posterior parietal cortex and to frontal motor

areas (Rizzolatti et al. 1998). For this reason it is plausible to assume that the premotor cortex activity reflects the detection of congruent multisensory signals from one's own body and that this could be the mechanism responsible for the feeling of body ownership (Ehrsson et al. 2005). However, different studies on Rubber Hand Illusion, (Botvinick and Cohen 1998) showed that the multisensory integration leading to the experience of our body as our own is conditioned by the possibility – or not – to perform actions with a given body part (Tsakiris and Haggard 2005; Tsakiris et al. 2006; Tsakiris et al. 2007b). Neuropsychological evidence further corroborates the link between motor abilities and self-body recognition. For instance, the patient described by Arzy and colleagues (2006), who suffered from asomatognosia following a lesion in the right motor and premotor cortices, beside being unable to move her contralesional arm, most importantly was unable to recognize it.

Interestingly, the second analysis of the fMRI data not only confirmed a pivotal role of the premotor cortex in the behavioural self-advantage for right hand, but also allowed us to identify another distinct pattern of self-processing neural activity, more generally discriminating between one's own and others' hands (general self/other distinction). Indeed, for both the right and left stimuli, self-hand slopes were lower than other-hand slopes in the SMA/pre-SMA, anterior insula bilaterally and calcarine cortex. This shows that the actual mental rotation process was more efficient for both one's own hands as compared to others' hands, regardless of the laterality of the stimuli. In the same areas, self-hand intercepts were higher than other-hand intercepts for both the right and left stimuli, thus suggesting that non-rotational factors did not play any role in self/other distinction. All in all these data show that the motor experience based bodily self recruited by our motor task is purely linked to the motor skills of our participants, rather than to non-rotational processes such as those occurring before (e.g., stimulus encoding and visual familiarity) or after (e.g., response preparation) mental rotation proper.

Let us now take a deeper look at how the above mentioned areas, recruited by the task, might contribute to the general self/other distinction.

As regards the supplementary and pre-supplementary motor areas, recordings of single neurons from monkeys revealed neurons in the medial frontal cortex, including the pre-supplementary motor area, which selectively encode others' action (Yoshida et al. 2011). The authors suggested that these neural structures might be involved in self/other differentiation in the domain of action. Accordingly, evidence for the supplementary motor cortex playing such a role was provided by Mukamel and colleagues (2010). They recorded extracellular activity from cells in human medial frontal and temporal cortices while patients executed or observed hand grasping actions. A subset of these neurons showed excitation during action execution and inhibition during action observation, thus suggesting a different recruitment of this area while processing self and others' motor acts. Concerning the possible role of anterior insular cortices in self/other distinction, previous studies showed that this area is involved in bodily self-awareness, sense of agency and sense body ownership (Craig 2002; Tsakiris et al. 2007a; Craig 2009). This area is thought to be a convergence zone where interoceptive and exteroceptive self-related information is integrated (Craig 2010). Reduced neural activity during rest periods, particularly in the bilateral anterior insula, was found in patients with major depressive disorder, together with abnormal body perception (Wiebking et al. 2010). Bilateral activation of the anterior insula was observed in a PET study where participants were requested to attribute an action to themselves compared to a condition where they attributed it to another person (Farrer and Frith 2002). Insular lesions, prominently in the right hemisphere, have been reported to be responsible for anosognosia for hemiparesis, asomatognosia or somatoparaphrenia (Baier and Karnath 2008; Karnath and Baier 2010).

Given that the insular cortex deals with both interoceptive (Critchley et al. 2004) and sensorimotor information (Karnath and Baier 2010), one may question whether the self/other

distinction arises from the former or the latter. In particular, the question is whether interoceptive information feeds sensorimotor processes providing them with the sense of self or vice versa. At this stage we are not able to answer this question. According to our data, we can only speculate that sensorimotor processes play a non trivial role in self/other distinction (see also Jeannerod 2007). One may argue that the engagement of sensorimotor regions is strictly related to the task employed in the present study, that is, a motor simulation task. However, evidence coming from literature on visuo-tactile integration goes in the same direction. Recently, Cardini and colleagues (2010) showed that observing one's own face being touched, while experiencing touch on the same anatomical location resulted in a better behavioural performance in a tactile detection task. On the neural side this behavioural advantage was associated to a reduction of BOLD signal in somatosensory and ventral premotor cortices. These data confirm that the sensorimotor system is involved during implicit self-processing, regardless of the motor nature of the task.

Besides sensorimotor regions, we also found stronger activation in the occipito-temporal cortices for self-related with respect to other-related stimuli. This finding expands previous knowledge showing that these cortices not only house a shared topographic representation of seen and moved body parts (Orlov et al. 2010), but would also be involved in the self/other distinction during a motor simulation task. Accordingly, sensorimotor influences on a region in the lateral occipito-temporal cortex, which is selectively activated by non-facial body parts and named extrastriate body area (EBA, Downing et al. 2001), have already been shown by an earlier fMRI study by Astafiev and colleagues (2004). In that study the authors showed that EBA is strongly modulated by limb movements even in the absence of visual feedback from the movement. The evidence that EBA responds to one's own goal-directed body movements suggests that, at least a portion of this region, plays a role in the self/other distinction.

The literature on body representation ascribes a crucial role to the parietal cortices in the assignment of body identity (Uddin et al. 2005; Sugiura et al. 2006; Hodzic et al. 2009) and in the

representation of the position of body parts in space, i.e., body schema (Bonda et al. 1995; Creem-Regehr et al. 2007). Also, right parietal lesions often give rise to a deficit of body identity such as personal neglect (Bisiach et al. 1986; Guariglia and Antonucci 1992); whereas left parietal lesions lead to a deficit in localizing body parts in relation to one's own or others' body such as autotopagnosia and heterotopagnosia, respectively (Ogden 1985; Semenza 1988; Sirigu et al. 1991; Cleret de Langavant et al. 2009). At first glance our results seem at odds with this literature; indeed, we did not find any involvement of parietal regions in the self/other distinctions, either in the first or in the second analysis. A possible explanation for the difference between present and previous findings is that the involvement of the parietal areas in the recognition of body identity has been described in studies in which body identity was explicitly accessed. In contrast, in the present study only implicit access to the self was required, suggesting that partially segregated neural networks may underpin implicit and explicit access to bodily self-representation. The lack of parietal involvement while implicitly processing self and others suggests that the body known in bodily self-knowledge is not necessarily the body conceived as a spatial organization of its parts, as the notion of a body schema might suggest (Berlucchi and Aglioti 1997; Maravita et al. 2003; Peelen and Downing 2007; Medina and Coslett 2010).

To sum up, by using a laterality judgment task with self and other hand stimuli, we highlighted, firstly, the neural correlates of the self-advantage, secondly, a neural network for the more general representation of the bodily self. The former seems to be confined within the left premotor cortex, while the latter encompasses pre-SMA/SMA, the anterior insula and the occipital cortex. We believe the present data enrich the theoretical definition of the bodily self as motor in nature by grounding it in empirical evidence.

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## Chapter 4

## **4. “Bodily Self” and schizophrenia: loss of the implicit self-body knowledge**

### **4.1 Introduction**

There is a large body of evidence for the presence of social cognition deficits in patients with schizophrenia (Penn et al. 1997; Pinkham et al. 2003). Such deficits concern, for example, emotion recognition (Edwards et al. 2001; Edwards et al. 2002), decoding non-verbal social cues (Monti and Fingeret 1987), recognition of familiar social situations (Corrigan et al. 1992) and interpersonal problem solving (Bellack et al. 1994). These social cognition deficits seem to be present also in the first episode of schizophrenia (Edwards et al. 2001; Addington et al. 2006; Bertrand et al. 2007). It has been argued that the poor social functioning (i.e., compromised social relationships and social behaviours) observed in schizophrenic patients may be thought of as a secondary marker of the more basic disturbance of the sense of self in psychotic disorders (Nelson et al. 2009). Self-disturbance (Nelson et al. 2008) is a complex notion including disturbed sense of presence, corporeality, stream of consciousness, self-demarcation and existential reorientation. All of these types of self-experience disturbance are evident in the prodromal period and are closely interrelated (Parnas 2003). Such complexity of the notion of self-disturbance in schizophrenia, however, somehow reflects the multileveled and multifaceted concept of self experience.

From a phenomenological perspective (Parnas 2000; 2003) three levels of selfhood have been identified. First, there is the implicit awareness that this is ‘my’ experience. Such pre-reflective level of selfhood is sometimes referred to as the ‘basic’ or ‘minimal’ self or as ‘ipseity’. Second, there is the more explicit awareness of self as an invariant subject of experience and action. Such reflective level of self-awareness assumes the ‘minimal’ self. Finally, there is the social or narrative self, which refers to personality, habits, style and other characteristics of an individual. According to the phenomenological perspective, the main self–disturbance in patients

with schizophrenia spectrum disorders occurs at the most ‘basic’ level, that pertaining to ipseity (Parnas and Handest 2003).

In this vein, Fuchs and Schlimme (2009) proposed that in schizophrenia the weakening of the basic sense of self, the disruption of implicit bodily functioning and the disconnection from intercorporeality with others are manifestations of a fundamental disturbance of the bodily self, or a disembodiment. How such loss of the implicit structure of the body can lead to compromised social perception and behavior can be exemplified by the following case of a 28-year-old female patient: “For some time I had a feeling as if my clothes did not seem appropriate any more. My gait had changed, I walked stiffly and did not know how to hold my hands. Then I often looked into the mirror and found that my facial expression had changed, and I began to think that I might be regarded as a prostitute. Men looked so strange at me . . . I took passport pictures of myself in order to examine whether I only imagined that. Then I began to feel a kind of charging or tension in my body when others came near to me, as if it were passing over from them. Finally I thought I should be made a prostitute by brain manipulation . . .” (Fuchs 2005, p. 165). In the case reported by Fuchs the patient clearly experiences a progressive alienation from her bodily feelings, a sense of increasing difficulty in recognizing the way she moves or behaves. Such sense of disembodiment leads her to rationalize this state by relying on a delusional explanation (others manipulated her brain). It is clear from this example that one of the first signs of schizophrenia consists in disturbances of the bodily self.

In a previous work from our group, we proposed that the experience we make of ourselves as bodily selves can be dissociated from the explicit recognition of body parts as our own body parts (Ferri et al. 2011). In that study, the results showed that right-handed healthy participants submitted to a hand laterality judgment task were faster when judging one’s right hand compared to all the other hand stimuli (their own left hand and others’ right and left hands). In other words, participants showed the so-called self-advantage effect (Frassinetti et al. 2008; 2009; 2010). Such

effect did not emerge in a second experiment when the same participants were asked to explicitly recognize the owner of the observed hands, which were the same as those they had been presented with in the laterality judgment task. Based on these empirical data, we argued that implicit and explicit recognition of the bodily self can dissociate and only an implicit recognition of the bodily self allows the self-advantage effect to emerge. Such dissociation is in agreement with the independence of implicit from explicit self-body processing reported by infancy research. Indeed, during development an implicit sense of self and the ability to discriminate self from others appears to emerge earlier than the ability to explicitly self-recognize (Rochat 2003; 2010). Four months-old infants show signs of distinguishing between self and others (Rochat and Striano 2002), whereas the ability to recognize oneself in front of a mirror emerges around 2 years of age (Amsterdam 1972).

The different contribution to our sense of self, as bodily self, provided by the representation of our body-effectors, when implicitly or explicitly accessed, was shown for the first time in a study in which we contrasted a visual matching task, as the implicit self-recognition task, with an explicit self/other discrimination task (Frassinetti et al. 2011). Both tasks consisted of two distinct blocks, employing, as stimuli, either participant's own and other people's body-effectors (hands and feet) or participant's own and other people's inanimate objects (shoes and mobile phones). The results showed that participants were more accurate in the implicit task with their own rather than with others' body-effectors. In contrast, the self-advantage was not found when an explicit recognition of one's own body-effectors was required. Moreover, when processing inanimate-objects both self/other and implicit/explicit effects were absent.

In the present study we use the same tasks of Frassinetti et al. (2011) with first-episode schizophrenia (FES) patients, in order to test whether a specific bodily self-advantage effect is either preserved or lost in these patients. According to the phenomenological perspective conceiving of schizophrenia as a disturbance of the basic sense of self, mainly consisting of a loss

of the “implicit structure of the body” (Fuchs 2005, p. 95), we expect the bodily self-advantage effect not to be found in FES patients.

## **4.2 Methods**

### *Participants*

Twenty-one out-patients with a diagnosis of first-episode schizophrenia (FES) according to DSM-IV criteria and 21 matched healthy control (HC) participants were included in the present study (for demographic variables and participant characteristics, see Table 1). Exclusion criteria for all participants included physical health problems and neurological hard signs, a history of severe head trauma, loss of consciousness, drug abuse,  $IQ < 85$ , and, for the HC group, a personal history of Axis I/II disorders or a history of psychosis in first-degree relatives. FES patients were recruited from regional mental health centres. The mean time from psychotic episode was 6.3 ( $\pm 4.7$ ) months. All the FES patients were evaluated six months after the study and the diagnosis of schizophrenia according to DSM-IV criteria was confirmed. They responded well to pharmacological therapy indicated by relatively compensated positive and negative symptoms, and stabilized global functioning in daily living. The patient group had intellectual capacities in the range of the average healthy population ( $IQ$  mean scores =  $100.6 \pm 8.5$ ). The study was approved by the local Ethics Committee. Written informed consent was obtained from all participants after full explanation of the procedure of the study, in line with the Declaration of Helsinki. The participants were given a recompense for participating in the experiment.

**Table 1.** Demographic information about First Episode Schizophrenia patients group and Control group.

	patients (N=21)	Controls (N=21)
Age	27.7 ( $\pm 6.5$ )	29.2 ( $\pm 5.9$ )
Mean time from psychotic episode (months)	6.3 ( $\pm 4.7$ )	n.a.
Handedness score	64.8 ( $\pm 21.2$ )	66.9 ( $\pm 14.3$ )
Male/female	11/10	11/10
Diagnosis	First Episode Schizophrenia	n.a.
SCID-II Cluster A	n.a.	negative
SCID-II Cluster B	n.a.	negative
SCID-II Cluster C	n.a.	negative
PANSS Negative Scale	22 24 16 12 15 10 9 11 8 11 13 9 11 12 14 9 9 8 12 22 (12.9 $\pm$ 4.8)	n.a.
PANSS General Psychopathology Scale	25 37 25 22 26 20 20 23 22 23 24 21 25 22 25 19 20 19 22 35 (23.7 $\pm$ 4.7)	n.a.
Medication	6 Quetiapine, 7 Risperidone, 4 Paliperidone, 3 Aripiprazole, 1 Olanzapine*	n.a.

\*Clorpromazine equivalent mean dose =484 mg/die SD= 412 (calculated on 17 patients because no equivalents are available for paliperidone).

### *Evaluation scales*

FES patients were evaluated by the Structured Clinical Interview for DSM-IV Axis I Disorders (First et al. 1996b), rated for symptom severity with the Positive And Negative Symptom Scale (PANSS; Kay et al. 1987), and for intelligence quotient (IQ) by means of the Wechsler Adult Intelligence Scale – Revised (WAIS-R; (Wechsler 1997)) by trained psychiatrists. HC participants were evaluated by means of the Structured Clinical Interview for DSM-IV for Axis II personality Disorders (First et al. 1996a).

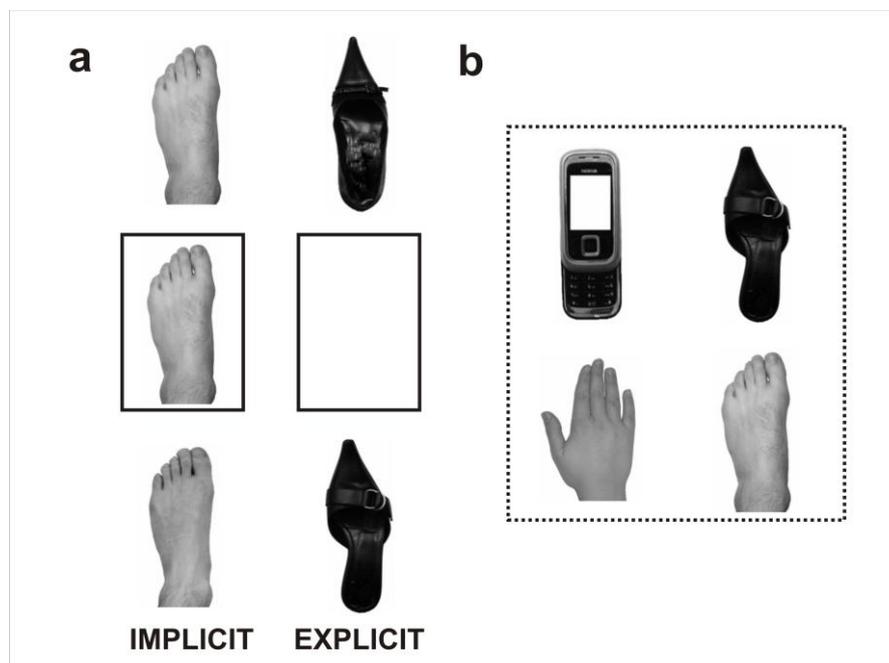
### *Stimuli and Procedure*

Stimuli were grey-scale pictures of participants' body-effectors and objects (fig. 1a). Flash photographs were taken with a digital camera, perpendicular to effectors or objects, one week before the experiments. Participants' pictures were taken in an indirectly illuminated environment while standing against a uniform white background. The pictures were equalized for visual properties such as brightness and contrast and digitally edited (Adobe Photoshop) for extracting the background, equalizing the size across participants, isolating the body-effectors and centering them on a uniform white background. Stimuli represented body-effectors (hands and feet), counterbalanced for gender (male and female) and side of the body (left and right), and objects (mobile phones and shoes) (figure 1b).

In Experiment 1 three stimuli of the same body-effectors (and of the same gender), or of the same inanimate-objects category, were simultaneously presented in each trial. The stimuli were aligned along the vertical meridian of the computer screen. The central stimulus, which corresponded to the target stimulus, was presented in upright position within a black frame. Stimuli presented in each trial were matched for visual similarity. Participants sat in front of the PC screen, at a distance of about 30 cm. They were required to decide whether the upper or the lower stimulus matched the central target stimulus and to press, as fast as possible, an upper or a lower vertically

aligned and previously assigned response keys, with their right index finger. The trial ended as soon as participant pressed a response key. RTs and response accuracy were recorded (figure 1a-implicit task).

In Experiment 2 two stimuli of the same body-effectors (and of the same gender), or of the same inanimate-objects category, were simultaneously presented in each trial. The stimuli were the same as in Experiment 1, except that there was no target stimulus within the central frame. As in Experiment 1, the stimuli were aligned along the vertical meridian of the computer screen. Participants were required to press an upper or a lower, vertically aligned and previously assigned, response key, whether the upper or the lower image corresponded to their own body or object. If none of the stimuli corresponded to their own body-effectors, they were instructed to press a central response key (figure 1a-explicit task).



**Figure 1- Tasks and Stimuli.** a) An example of a single trial. In Experiment 1 (implicit task), participants were required to decide which of the two images (the upper or the lower one) matched the central stimulus target. In Experiment 2 (explicit task), participants were required to judge whether and which image, between the upper or lower, corresponded to their own body-effectors or objects. B) Examples of the experimental stimuli. For each category (body-effectors and inanimate objects), two stimuli (hands or feet and mobile phones or shoes) were presented.

For each experiment, at least one stimulus representing the participant's own body-effectors or inanimate-objects was presented in half of the trials (self trials), whereas in the other trials only stimuli representing body-effectors or inanimate-objects of other three people were presented (other trials). Stimulus presentation and randomization in a block were controlled using E-prime V1.1 software (Psychology Software Tools, Pittsburgh, PA) running on a PC. Each experiment consisted of 64 trials divided into two blocks, one with body-effectors (32 trials) and one with inanimate-objects (32 trials). In each block half trials represented self stimuli (i.e., participant's own body-effectors and inanimate-objects, respectively), whereas the other half represented other stimuli (i.e., pictures of other people's body-effectors or inanimate-objects, respectively). All participants performed the Experiments in one session, with 12 practice trials before each block. Since Experiment 1 investigated implicit and Experiment 2 explicit self-body recognition, Experiment 1 was conducted before Experiment 2. The order of the blocks in each Experiment was randomized between subjects.

### **4.3 Results**

In each experiment two ANOVAs were conducted with Type of stimuli (body-effectors and inanimate-objects) and Owner (one's own stimuli, "self", and other people's stimuli, "other") as within-subject variables and Group (healthy controls, HC, and first episode schizophrenia patients, FES) as between-group variable.

For each experiment, ANOVA was first conducted on the percentage of correct responses (accuracy). Then, to exclude a speed accuracy trade off, the same analysis was conducted on the Inverse Efficiency (IE) scores. To this aim, the median values for correct RTs were divided by their corresponding proportion correct score so that differences in reaction time performance decreased if differences in accuracy were large but remained the same if accuracy was identical. Thus, Inverse efficiency scores provided a measure of overall performance, simultaneously taking into account

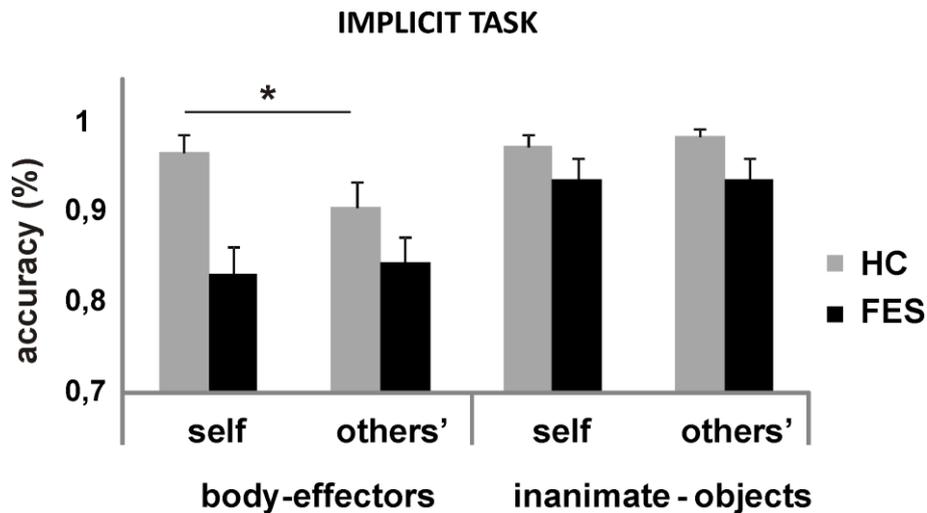
speed and accuracy (Towsend and Ashby 1983). Lower inverse efficiencies corresponded to better performance. These inverse efficiency scores were then entered an analysis of variance (ANOVA) for each task.

Previous studies showed misattribution bias in distinguishing one's own from other people's body-effectors in schizophrenic patients, mostly misattributions of agency (i.e., Daprati et al. 1997; Synofzik et al. 2010). Thus, only for Experiment 2, we compared the percentage of two types of errors between FES and HC by independent samples t-tests. Errors were classified as self-misattribution, when other people's body-effectors were erroneously attributed to oneself, and self-omissions, when one's own body-effectors were erroneously recognized other people's body-effectors.

#### *Experiment 1: implicit task*

##### Accuracy

The variable Group was significant [ $F_{(1,40)} = 13.3$ ;  $p < .001$ ], since HC were more accurate than FES patients (96% vs. 89%). The variable Type of stimulus was also significant [ $F_{(1,40)} = 20.2$ ;  $p < .001$ ], all participants being more accurate with inanimate-objects than with body-effectors (96% vs. 89%). More interestingly, the three-way interaction Group X Type of stimulus X Owner was significant [ $F_{(1,40)} = 5.5$ ;  $p < .05$ ]. Post-hoc analysis (Newman-Keuls) revealed that HC were more accurate with their own than with other people's body-effectors (97% vs. 90%,  $p < .05$ ), whereas FES patients did not show such difference (83% vs. 85%,  $p = .44$ ). No difference was found between one's own and other people's inanimate-objects in HC (97% vs. 99%,  $p = .54$ ) and in FES patients (94% vs. 94%,  $p = 1.0$ ) (figure 2).



**Figure2- Experiment 1.** Mean percentages of correct responses (accuracy) for one's own (self) and other people's (others') body-effectors and inanimate-objects in the implicit task. Error bars depict the standard error of the mean. \* indicates  $p < 0.05$ .

Inverse efficiency

When the same analysis was conducted on inverse efficiency scores, the variable Type of stimulus was significant [ $F_{(1,40)} = 71.5$ ;  $p < .001$ ], being participants' performance better with inanimate-objects than with body-effectors (1364 ms vs. 2069 ms). The other variables and their interactions were not significant, thus excluding that the effects found in the previous analysis conducted on the percentage of correct responses were due to a speed accuracy trade-off.

*Experiment 2: explicit task*

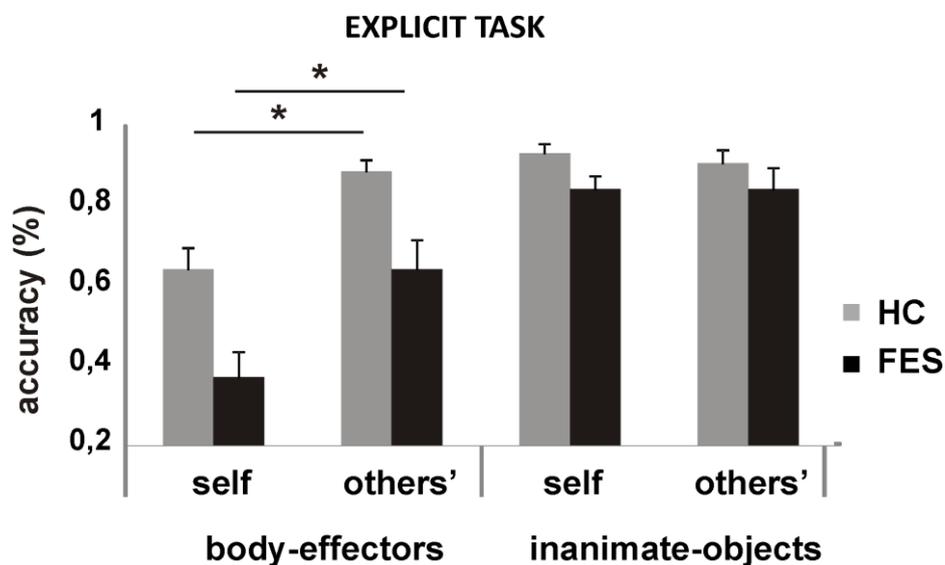
Accuracy

All the variables were significant: Group [ $F_{(1,40)} = 22.6$ ;  $p < .001$ ] (HC= 84% vs. FES=67%), Type of stimulus [ $F_{(1,40)} = 63.7$ ;  $p < .001$ ] (body-effectors=88% vs. inanimate-objects=64%) and Owner [ $F_{(1,40)} = 9.7$ ;  $p < .005$ ], (self=70% vs. other=82%). Also the interaction Group X Type of stimulus was significant [ $F_{(1,40)} = 8.6$ ;  $p < .01$ ], since HC were more accurate than FES patients with body-effectors (76% vs 51%,  $p < .001$ ) but not with inanimate objects (92% vs 84%,  $p = .08$ ). Finally, the interaction Type of stimulus X Owner was significant [ $F_{(1,40)} = 17.8$ ;  $p < .001$ ], participants being less accurate with their own than with other people's body-effectors (51% vs. 76%,  $p < .001$ ),

whereas they were equally accurate with their own and other people's inanimate-objects (89% vs. 88%,  $p=.82$ ). This effect was present in HC and in FES patients since the three-ways interaction Group X Type of stimulus X Owner was not significant ( $p=.98$ ) (figure 3).

Inverse efficiency

The variables Type of stimulus [ $F_{(1,40)} = 75.9$ ;  $p < .001$ ] (body-effectors= 4530 ms vs inanimate-objects= 1698 ms) and Owner [ $F_{(1,40)} = 17.7$ ;  $p < .001$ ] (self= 3937 ms vs other= 2291 ms) were significant. Also the interaction Type of stimulus X Owner was significant [ $F_{(1,40)} = 19.4$ ;  $p < .001$ ], participants' performance being worse with their own than with other people's body-effectors (6177 ms vs 2882 ms,  $p < .001$ ), whereas they performed equally with their own and other people's inanimate-objects (1696 ms vs 1701 ms,  $p=.99$ ). The interaction Group X Type of stimulus was not significant, excluding that between-group differences found in the previous analysis conducted on the percentage of correct responses were due to a speed accuracy trade-off.



**Figure 3- Experiment 2.** Mean percentages of correct responses (accuracy) for one's own (self) and other people's (others') body-effectors and inanimate-objects in the explicit task. Error bars depict the standard error of the mean. \* indicates  $p < 0.05$ .

### Errors

Independent samples t-test on percentages of self-misattribution errors showed a significant difference ( $t_{40} = -2,96$ ;  $p=.005$ ) between FES patients (17%) and HC (6%). Conversely, the same test on percentages of self-omission errors showed that they did not differ [ $t_{40} = -1.814$ ;  $p=.08$ ] between the two groups (FES= 24% vs HC= 16%).

### **4.4 Discussion**

The main result of the present study is that FES patients, coherently with our working hypothesis, did not show the self-advantage effect in the implicit task (Experiment 1), while they did not differ from HC in Experiment 2, where both groups of participants did not show a self-advantage when explicitly required to recognize their own body-effectors. Furthermore, FES patients, when failing to explicitly recognize their own body-effectors, showed a higher percentage of self-misattribution errors with respect to control participants.

Our results show that FES patients suffer of a disturbed implicit sense of their bodily self. Philosophers, psychologists, psychopatologists and cognitive neuroscientists have attempted to distinguish among several senses and kinds of self awareness. A variety of first- and third-person approaches have been used in order to define a “core” or “minimal” sense of self, by following the intuition that “even if all the unessential features of self are stripped away”, “there is a basic, immediate or primitive ‘something’ that we are willing to call a self” (Gallagher 2000, p. 15). This minimal sense of self has been referred to as consciousness of oneself as bodily subject of action, speaking of sense of agency (the sense of being the one who generates an action) and/or sense of ownership (the sense of being the one who undergoes any experience, no matter if internally or externally generated).

It has been recently proposed that there is a sense of body that is enactive in nature and that enables to capture the most primitive sense of self as bodily self (Gallese and Sinigaglia 2010;

2011). According to this perspective, the body is primarily given to us as “source” or “power” for action, that is, as the variety of motor potentialities that define the horizon of how we can interact with the world we live in. Such primitive sense of self as bodily self is conceived of as being antecedent the distinction between sense of agency and sense of ownership.

Schizophrenia spectrum has been described as a psychiatric condition associated with disorders that affect the functioning of “minimal” or “core self” (Zahavi 2005), which is also referred to as “ipseity” (Parnas 2000; Sass and Parnas 2003; Sass and Parnas 2007). The notion of “self-disorder” in schizophrenia indicates that minimal self is fragile and unstable, being affected in its basic phenomenological aspects: phenomenality (appearing), first-person perspective and self-presence (Cermolacce et al. 2007). In line with this account, “self-disorder” in schizophrenia has been elsewhere described as a disembodiment of the self (Fuchs 2005; Stanghellini 2009). In other words, “schizophrenic patient does not inhabit her body any more, in the sense of using as taken-for-granted its implicit structure [...] as a medium for relating to the world” (Fuchs 2005). More generally, the phenomenological approach to schizophrenia proposes the notion of embodiment as central to understand different symptoms, such as loss of self, loss of common sense, and intentionality disorders. According to this approach, the coherence between such heterogeneous symptoms can be caught only if their common bodily roots are deemed (de Haan and Fuchs 2010). Furthermore, the loss of the implicit functioning of the body in everyday life would lead also to the inability to interrelate with others (Fuchs 2005; Stanghellini and Ballerini 2011). In this sense, social dysfunctions in schizophrenic patients would primarily have their roots in disturbances of bodily self-experience (Parnas et al. 2002; Gallese 2003; Sass and Parnas 2003), rather than primarily concerning the intersubjective domain.

All these suggestions from the phenomenological account are supported by our results showing that FES patients suffer from a disturbed implicit bodily self-knowledge, as revealed by the absence of the self-advantage effect in the implicit task (Experiment 1). In previous studies we

tested the hypothesis that implicit and explicit bodily self knowledge tap into different sources of information (Ferri et al. 2011; Frassinetti et al. 2011). We showed that the implicit distinction between one's own body parts from other people's body parts takes advantage from the recruitment of sensorimotor information, whereas explicit self-other discrimination of the same body stimuli likely recruit different cognitive and/or perceptually-based mechanisms (Ferri et al. 2011; Frassinetti et al. 2011). Results from the present study suggest that self-other discrimination impairments in schizophrenia are already present at the very basic level of an implicit, rather than an explicit, processing of body stimuli. Indeed, in the explicit task (Experiment 2) the main difference we found between FES patients and control participants was a higher percentage of self-misattribution errors in the former than in the latter group. This means that, when required to explicitly discriminate whether body parts presented on the screen were their own or not, schizophrenic patients beside failing in recognizing their own body parts from those of other people, as healthy controls, also tended to misattribute other people's body parts to themselves.

A similar self-misattribution was observed by a previous study aimed at testing the abilities of schizophrenic patients to attribute an action to its proper agent (Daprati et al. 1997). Healthy participants and schizophrenic patients with and without hallucinations and/or delusional experiences were required to execute simple finger and wrist movements, without direct visual control of their hand. One of three possible images of a hand could be presented to the participant on a TV-screen in real time: their own hand, the experimenter's hand performing the same movement as participant's hand, the experimenter's hand performing a different movement. The task for participants was to explicitly discriminate whether the hand presented on the screen was their own or not. Only when presented with images of the experimenter's hand performing the same movement, hallucinating and deluded schizophrenic patients were more impaired in discriminating their own hand from the alien one than the non-hallucinating ones, and tended to misattribute the alien hand to themselves. Besides the differences between Daprati and colleagues' (1997) and our

study, mainly concerning the symptom severity in patients and the object of the required attribution judgment (body parts vs. action), in both cases it is observed that, when required to explicitly discriminate their own body parts from those of another, schizophrenic patients show a clear tendency to misattribute the alien body parts to themselves. We add to previous knowledge, firstly, that such tendency is already present in first episode schizophrenia patients; secondly, that a more basic self-impairment (revealed by the lack of the self-advantage effect) is present at an implicit level, likely before and below the misattribution tendency at the explicit level.

Empirical evidence supporting the idea of a weaker or more flexible sense of bodily self in schizophrenia comes also from the literature on the rubber hand illusion (RHI; Peled et al. 2000). The Rubber Hand Illusion (RHI, Botvinick and Cohen 1998) consists in watching a rubber hand being stroked together with one's own unseen hand. If the stroking of the rubber and real hands occurs synchronously, the position sense of the real hand shifts towards the location of the dummy hand. Participants report that they feel the dummy hand to be part of their body. A recent study (Thakkar et al. 2011) demonstrated that patients with schizophrenia experience a stronger RHI than healthy controls, indexed by self-report and mislocalization of their own hand. These data clearly suggest that body ownership is disturbed in schizophrenia. However, it is worth reminding here that, as recently argued (Gallese and Sinigaglia 2010, 2011), different studies on RHI have shown that the multisensory integration leading to the experience of our body as our own, far from being the outcome of a mere visual–proprioceptive perceptual association is conditioned by the possibility- or not- to perform actions with a given body part (Tsakiris and Haggard 2005; Tsakiris et al. 2006; Tsakiris et al. 2007). Thus, converging evidence suggests that the weaker sense of bodily self in schizophrenia can be related to an impaired possibility to live one's own body in terms of its motor potentialities.

The last point to be addressed is that no difference was found between patients and controls concerning inanimate objects, neither in the implicit nor in the explicit task. A simple explanation

could be that in both tasks the object discrimination is easier than the body-effector discrimination, as indicated by analyses of accuracy. However, the fact that schizophrenic patients are more impaired in processing body-effectors than objects is not entirely new. For example, de Vignemont and colleagues (2006) showed that schizophrenic patients performing a laterality judgment task are less accurate than controls when mentally rotating body parts, but are as accurate as controls when mentally rotating inanimate objects, like letters.

Previous work has demonstrated that the rotation of body parts requires participants to simulate a motor rotation of their own body parts (Parsons 1994; Kosslyn et al. 1998; Wraga et al. 2005; Zacks 2008), whereas the rotation of objects involves the manipulation of an object-relative frame of reference (Kosslyn et al. 1998; Wraga et al. 2005; Zacks 2008). Thus, mental rotations of body parts emphasize the motor representation of the bodily self to a greater extent than mental rotations of objects. The lesser accuracy of schizophrenic patients than controls when judging the laterality of body parts, but not when judging the laterality of objects, may be related to deficits in the motor representation of their bodily self. Evidence that schizophrenic patients are unable to generate accurate internal images of their own movements and have difficulty with maintaining an internal representation of intentional behavior (e.g., Danckert et al. 2002; Maruff et al. 2003) would further support the above mentioned hypothesis of an impaired motor representation of their bodily self. In other words, schizophrenic patients would not experience themselves as a bodily structure that affords a given range of actions. According to this hypothesis, we could speculate that the lack of the self-advantage effect we observed in first episode schizophrenic patients is mainly due to a disruption of their awareness of the bodily self as power for action.

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## Chapter 5

## **5. Out of touch with reality? Social perception in first-episode psychosis.**

### **5.1 Introduction**

The constitution of an empathic interrelationship with other individuals is a crucial component of social cognition. From a neurobiological perspective, it has been suggested that multimodal brain regions underlying bodily self-experiences are also involved with the pre-reflective understanding of the feelings and behaviours of other individuals, establishing an intersubjective link between self and other during social perception (Gallese 2003a/b; Gallese et al. 2004; Keysers and Gazzola 2009).

However, it was also argued that distinguishing to whom these behaviors and feelings belong is crucial in order to maintain a coherent sense of self during social perception (Batson et al. 1987; Eisenberg et al. 1989; Banissy et al. 2009). Several authors proposed that social perception does not engage a completely overlapping neural network between self and others' bodily experiences (Gallese 2003a; Singer et al. 2004; Keysers et al. 2010; Lamm et al. 2011). Furthermore, specific brain regions involved with self-experiences and awareness (Craig 2002; Farrer et al. 2003; Karnath et al. 2005; Tsakiris et al. 2007) rather appear to differentiate between self and other. For example, posterior insular cortex (pIC) showed opposite activation patterns for first-person tactile experiences (positive modulation) and the observation of affective tactile stimulations in other individuals (negative modulation) (Ebisch et al. 2011). In addition, overlapping activation for experienced and observed tactile stimulations is reported in brain regions that contain multisensory representations, like premotor cortex (PMC) or intraparietal sulcus, integrating motor representations with information from vision, touch, audition and proprioception (Bremmer et al. 2001; Makin et al. 2007; Ebisch et al. 2008).

Social perception may thus emerge as a multifaceted function relying on the dynamic interaction between vicarious processes grounding an experiential understanding of others' feelings,

and self-regulation processes (multisensory integration, self-other differentiation), allowing a coherent and unique sense of self (Batson et al. 1987; Cheng et al. 2007; de Waal 2008).

Schizophrenia is a pervasive and complex neuropsychiatric disorder with prominent deficits in social cognition (Pinkham et al. 2003; Burns 2006; Derntl et al. 2009). Social impairments may exist independently of neurocognitive impairments, they are related to functional outcome and community functioning, they are present during the prodromal phase of schizophrenia as well as in unaffected family members, and persist when patients are in remission (Couture et al. 2006; Bellack et al. 2007; Addington et al. 2008a; Phillips and Seidman 2008; Horan et al. 2009; Eack et al. 2010; Fett et al. 2011). However, the exact nature of impaired social abilities in schizophrenia remains a topic of speculation and their underlying causes unknown.

In particular, although a crucial role has been attributed to the self and its pre-reflective relationship with the external world in schizophrenic pathology since the early 19th century (Bleuler 1911; Minkowski 1927), it still remains an open issue whether functional abnormalities underlying the inability to interrelate with others in schizophrenia specifically concern the intersubjective domain or primarily have their roots in disturbances of self-experience and awareness (Parnas et al. 2002; Gallese 2003b; Fisher et al. 2008). For example, along with the loss of a coherent sense of self, the relationship and the distinction between self and other may blur (Sass and Parnas 2003). From a neurobiological perspective, this postulates the concrete question whether patients with schizophrenia may show altered vicarious neural activations or rather aberrant neural processes underlying multisensory integration and differentiation between self and others' bodily experiences during social perception.

Moreover, many studies have described specific impairments in the social perception of affective material in schizophrenia, including first-episode samples (Addington et al. 2008b; Huang et al. 2009; Dickey et al. 2010; Amminger et al. 2011). Often, affective perception was explicitly

assessed. It remains unclear whether and how implicit social affective processing is affected in schizophrenia (Roux et al. 2010; Linden et al. 2010).

The present study aimed at investigating these issues by means of functional magnetic resonance imaging (fMRI), focusing in particular on the role of brain regions involved in processing first-person somatosensory stimulation during social perception.

Touch may play a peculiar role in this context, constituting an elementary aspect of self-awareness (Husserl 1989; Tsakiris et al. 2007). Moreover, somatosensation is considered a crucial component of social perception and empathy (Keysers et al. 2004; Avenanti et al. 2005; Blakemore et al. 2005; Bufalari et al. 2007; Ebisch et al. 2008; Pitcher et al. 2008; Schaefer et al. 2009; Wood et al. 2010; Pihko et al. 2010; Bolognini et al. 2011; Cardini et al. 2011; Meyer et al. 2011; for a comprehensive review see Keysers et al. 2010).

For this purpose, 24 patients with first-episode schizophrenia (FES), a first manifestation of schizophrenia and an important condition to study primary aspects of the pathology without chronicity-related confounds, and 22 matched healthy control (HC) participants underwent fMRI scanning during a social perception task. This task required them to watch video clips depicting actors experiencing neutral inanimate touch, or neutral or affective social touch, but without explicitly processing the sensory and affective characteristics of the depicted touch. A tactile stimulation task was added to map brain activation patterns related to first-person bodily experiences.

It could be hypothesized that FES patients during the visual perception of others' tactile experiences show aberrant activation in brain regions involved with first-person tactile experiences, for example, the somatosensory cortices. Alternatively, FES patients may show altered activation patterns in brain regions differentiating between self and other conditions, or in multisensory regions grounding a coherent self-experience, possibly correlating with self-experience disturbances. Moreover, given the abnormalities in the processing of affective material in

schizophrenia, altered activation patterns could be expected in particular when affective experiences are implicated.

## **5.2 Materials and Methods**

### *Participants*

Twenty-four out-patients with FES and 22 matched HC participants were included in the present study. All participating FES patients had a history of a single psychotic episode and all received a diagnosis of schizophrenia according to DSM-IV criteria six months after the episode. Nineteen of the HC participants were the same as those reported in our previous study (Ebisch et al. 2011).

FES patients were evaluated by the Structured Clinical Interview for DSM-IV Axis I Disorders (First et al. 1996), rated for symptom severity with the Positive And Negative Symptom Scale (PANSS) (Kay et al. 1987), and evaluated for the presence of Basic symptoms (BS) (Klosterkötter et al. 2001) by means of the Schizophrenia Proneness Instrument (SPI-A)(Schultze-Lutter et al. 2011) by trained psychiatrists. HC participants were evaluated by means of the Structured Clinical Interview for DSM-IV Axis II personality Disorders (First et al. 1996). Social abilities of the participants were assessed by means of the Empathy Quotient (EQ) questionnaire (Baron-Cohen and Wheelwright 2004; Lawrence et al. 2004).

The study was approved by the local Ethics Committee. Written informed consent was obtained from all participants after full explanation of the procedure of the study, in line with the Declaration of Helsinki.

Demographic information and participant characteristics are provided in Table 1.

**Table 1.** Demographic information about the First-Episode Psychosis (FEP) group and Healthy Control (HC) group

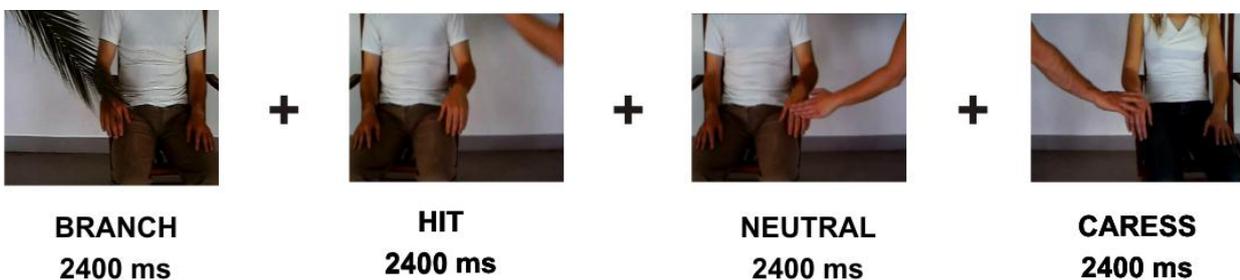
	FEP group (N = 24)	HC group (N = 22)
Age <sup>a</sup> (Mean ± SD)	27.3 ± 4.8	27.5 ± 3.3
Mean time from psychotic episode (months, mean ± SD)	8 ± 5	n.a.
Handedness score <sup>b</sup> (mean ± SD)	65.3 ± 18.1	69.3 ± 15.8
Male/female <sup>c</sup>	16 / 8	12 / 10
Diagnosis	First Episode Psychosis	n.a.
Intelligence Quotient (mean ± SD)	100 ± 8.5	n.a.
Empathy quotient <sup>d</sup> mean ± SD (cognitive empathy <sup>e</sup> /emotional reactivity <sup>f</sup> /social skills <sup>g</sup> )	38 ± 11.4 (12.4 ± 5.4 /12.2 ± 5.2 / 6.3 ± 2.8)	45.4 ± 9.7 (14.5 ± 4.6 /14.6 ± 4.4 /8.1 ± 2.3)
SCID-II Cluster A	n.a.	negative
SCID-II Cluster B	n.a.	negative
SCID-II Cluster C	n.a.	negative
PANSS Positive scale individual scores (mean ± SD)	16 10 9 14 17 16 21 14 12 16 18 12 10 12 13 11 19 13 8 13 9 10 11 15 (13.3 ± 3.4)	n.a.
PANSS Negative scale individual scores (mean ± SD)	8 10 10 9 10 11 12 16 12 24 12 8 10 9 11 9 11 22 9 14 9 8 12 22 (12 ± 4.5)	n.a.
PANSS General Psychopathology scale individual scores (mean ± SD)	22 20 20 30 18 24 32 25 22 37 22 22 20 20 23 21 25 25 19 25 20 19 22 35 (23.6 ± 5)	n.a.
SPI-A total individual scores (mean ± SD)	138 28 74 91 115 71 67 5 0 114 40 36 97 17 12 27 42 22 83 82 45 40 49 85 (61.1 ± 38.4)	n.a.
Medication <sup>h</sup>	6 Quetiapine, 7 Risperidone, 3 Paliperidone, 4 Aripiprazole, 3 Olanzapine 1 Drug Free	n.a.

Notes: <sup>a/b/c</sup> No significant differences between the HC and FEP group; <sup>d</sup> Significant difference between the HC and FEP group ( $p = 0.02$ ); <sup>e/f</sup> No significant differences between the HC and FEP group; <sup>g</sup> Significant difference between the HC and FEP group ( $p = 0.02$ ); <sup>h</sup> Clorpromazine equivalent mean dose = 422 mg/die SD = 395.5 (calculated on 21 patients because no equivalents are available for paliperidone).

### *fMRI data acquisition and paradigm*

For each subject, whole-brain blood oxygen level dependent (BOLD) contrast fMRI was performed (Philips Achieva 1.5T at the ITAB, Chieti). fMRI data acquisition parameters and procedures were the same as those described in Ebisch et al. (2011). Four rapid event-related fMRI touch observation runs (social perception task) and one block-design fMRI touch experience run (tactile stimulation task) were acquired for each subject.

The stimuli of the social perception task consisted of 208 randomized video clips of 2400 ms each, representing a touch event according to one of four experimental conditions. In the neutral inanimate condition (BRANCH), a wind-moving palm tree branch, moved by an invisible fan, touched either a male or female hand. In the animate or social conditions, either a male hand touched the back of a female hand or a female hand touched the back of a male hand by means of a neutral social touch (NEUTRAL) or an affective social touch that could have a negative (HIT) or positive (CARESS) valence. In addition to the touch video clips, 31 no touch video clips were randomly inserted in the visual runs, showing either a hand or palm tree branch moving near the hand of the other person, but without touching it. The video clips were separated by a fixation cross at the centre of the screen with a randomized duration (2400/4800/7200ms). Examples of the visual stimuli and the temporal course of the touch observation runs are visualized in Figure 1.



**Figure 1.** Visual representation of the temporal course of the touch observation runs.

Participants were instructed to watch the video clips attentively during scanning and to mentally count the number of no touch video clips in every run. They had to report the counted number verbally to the experimenter during the break between two runs (mean= 8/run). The no touch trials were not included in the statistical analyses; this task was added to direct participants' attention to the touch during the experiment, without requiring an explicit processing of the sensory and affective characteristics of the depicted touch. fMRI runs with more than two omissions were excluded from data analysis (HC: 2/FES: 0). There was no significant difference between the HC and the FES group with respect to task performance ( $p > 0.05$ ).

During the tactile stimulation task, always run after the touch observation runs, the experimenter stimulated the back of either the right or the left hand by means of 1 Hz soft back and forth stroking with a washing glove covering the surface between the wrist and the knuckles.

#### *fMRI data analysis*

The fMRI preprocessing procedure was the same as described in Ebisch et al. (2011). After a percent signal change normalization of the time series from the different runs, the fMRI parameters (beta values) estimated in individual-subject analysis were entered in a second level voxel-wise random effects group analysis in order to search for activated voxels in relationship with the experimental paradigms (social perception task, tactile stimulation task). The fixation cross was used as baseline in the analysis of task-related BOLD response modulations. Statistical significance was assessed by means of paired t-tests.

The p-value of the statistical maps ( $p < 0.001$  for touch observation, touch experience and conjunction analyses;  $p < 0.005$  for between-group contrasts) and an estimate of the spatial correlation of voxels were used as input in a Monte Carlo simulation (1000 simulations) to assess the overall significance level and to determine a cluster size threshold ( $k$ ) in order to obtain a significance level of  $p < 0.05$  cluster level corrected for multiple comparisons (Forman et al. 1995).

### *Conjunction analysis*

In order to determine overlapping or differential activation between the social perception task (touch observation) and the tactile stimulation task (touch experience), conjunction analysis was performed [(contrast: any touch observation condition vs. baseline)  $\cap$  (tactile stimulation vs. baseline)] (Nichols et al. 2005), separately for the HC and the FES group. Overlapping activation was defined as a positive modulation of BOLD response, compared with baseline, by both the social perception and tactile stimulation task, whereas differential activation was defined as a positive modulation of BOLD response by one task, compared with baseline, and a negative modulation by the other task ( $p < 0.05$  corrected,  $k > 5$ ).

### *Between-group comparisons: voxel-wise analysis*

Group statistical maps of the HC and FES group were compared for the social perception task (any touch observation condition vs. baseline) by means of a voxel-wise random-effects analysis. In order to focus specifically on voxels activated by the tactile stimulation task as well as the social perception task, an inclusive mask was created including the voxels that were significantly active during the tactile stimulation task ( $p < 0.05$  corrected,  $k > 5$ ) in either the HC or FES group. Voxelwise between-group contrasts were also performed without a mask ( $p < 0.05$  corrected,  $k > 8$ ).

### *Between-group comparisons: pIC ROI analysis*

Ebisch et al. (2011) showed that pIC differentiates between self and other conditions when affective experiences are implicated, whereas schizophrenia has been associated with a dysfunctional social perception of affective information as well as an altered self-other distinction, the latter also related to impaired pIC functioning (see Introduction/Discussion). Given that differential activation for touch experience and observation in pIC was clearly present in the HC

group, but absent in the FES group (see Conjunction analysis results and Figure 2a), it was investigated more specifically whether FES patients showed significant alterations concerning the differentiation between self and other during social perception in pIC.

Independent regions of interest (ROIs) were created with a 6 mm radius (Bastiaansen et al. 2011; Poldrack 2007). These ROIs were centred on Talairach coordinates based on structural definitions of pIC (LH pIC: -38, -12, 7; RH pIC: -38, -10, 7; Taylor et al. 2009; Figure 2b). Analysis of variance was performed with diagnosis (HC/FES) as between-subject factor, observation condition (BRANCH/NEUTRAL/CARESS/HIT) as within-subject factor, and the average beta values extracted from the pIC ROIs as dependent variable.

#### *Covariance analysis*

Beta values of the individual patients extracted from the brain regions showing differential activation patterns between the HC and FES group were correlated with chlorpromazine equivalence values.

The relationship between BOLD responses during the social perception task in the FES group and symptom severity was investigated by means of voxel-wise covariance analyses between activation patterns for the different touch observation conditions, and PANSS and total SPI-A scores. In order to focus on brain regions also involved in first-person tactile experiences, group statistical maps ( $p < 0.05$  corrected) of the tactile experience task in the HC and FES group were used as an inclusive mask. Covariance group statistical maps were thresholded at  $p < 0.05$  corrected ( $k > 8$ ), corresponding to a correlation coefficient of  $r > 0.50$ .

### **5.3 Results**

#### *Conjunction analysis in the HC and FES group*

Group statistical maps showed overlapping activation in the HC group between the touch experience and touch observation conditions in left hemisphere (LH) anterior and posterior secondary somatosensory cortex (a/pSII), ventral postcentral gyrus (vPostCG) and anterior superior parietal cortex (aSPC), right hemisphere (RH) ventral PMC (vPMC) and posterior superior temporal cortex (pST), and bilateral OT (Table 2). At an uncorrected statistical threshold ( $p < 0.001$ ), overlapping activation was detected also in RH pSII and aSPC, and LH mid cingulate cortex (MCC).

Significant differential activation between the experience and observation of touch in the HC group was found in bilateral pIC (Table 2; Figure 2a/b). Whereas BOLD response in bilateral pIC was increased, compared with baseline, during the experience of touch, BOLD response was decreased, compared with baseline, during the observation of touch. In the FES group, overlapping activation between the experience and observation of touch was partly similar to the HC group; no overlapping activation was found in LH TO and MCC, and RH vPMC and RH pSII (Table 2).

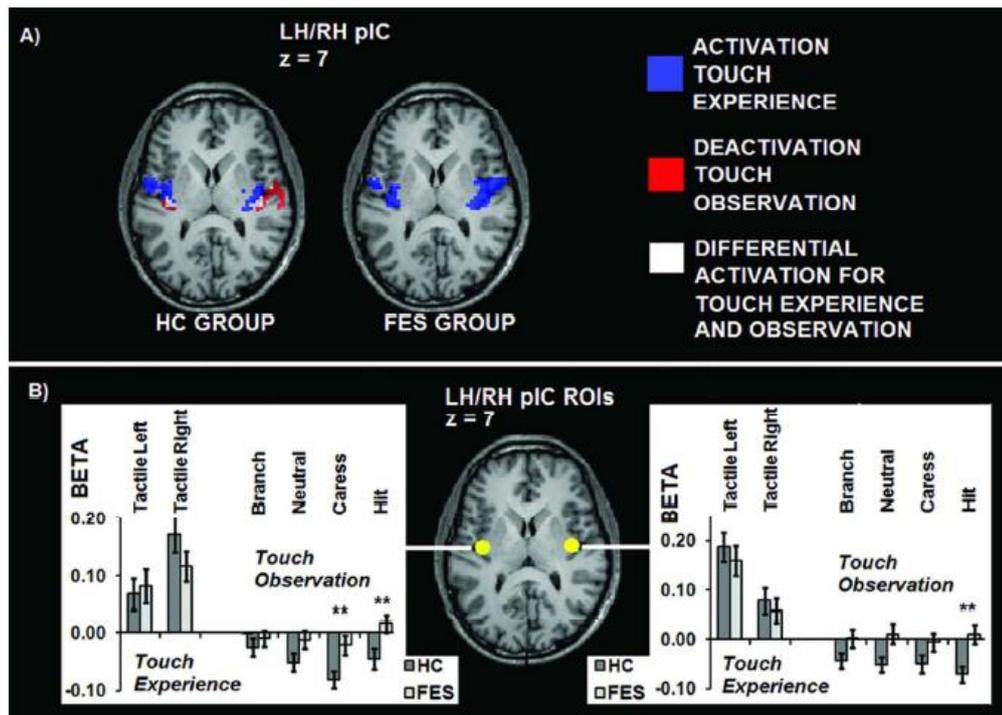
The absence of overlapping activation in LH MCC and RH vPMC could be explained by a lack of activation during both the touch experience condition and the touch observation conditions. The absence of overlapping activation in LH TO could be due to a lack of activation for the touch experience condition and in RH pSII due to a lack of activation for the touch observation conditions.

Moreover, no differential activation between the experience and observation of touch was found in bilateral pIC in the FES group, even at  $p < 0.01$  uncorrected. Whereas pIC was positively modulated by the touch experience condition, modulation of activation in pIC during the touch observation conditions was absent in the FES group (Figure 2a/b).

**Table 2.** Brain regions showing overlapping or differential activation for experienced and observed tactile stimulation in the healthy control and first-episode psychosis group as detected by conjunction analysis. Positive t-values indicate overlapping activation, whereas negative t-values indicate differential activation patterns for the touch experience and observation conditions.

Brain region	Healthy controls			First-episode psychosis		
	Talairach coordinates Peak-coord.	Cluster size	Peak t-value conjunction	Talairach coordinates Peak-coord.	Cluster size	Peak t-value conjunction
LH aSII	-57,-19,19	1304	6.308	-47,-27,19	1608	5.638
LH pSII	-45,-28,22	272	5.199			
LH vPostCG	-57,-22,34	1392	5.063	-54,-22,31	503	4.880
LH aSPC	-33,-43,-46	1582	5.667	-33,-46,47	81	4.264
LH TO	-51,-59,-2	1656	6.544	-	-	-
RH vPMC	51,8,28	214	4.540	-	-	-
RH pST	54,-37,16	839	5.315	59,-30,19	242	4.481
RH TO	51,-54,4	487	4.373	40,-58,4	456	5.117
RH aSPC	33,-42,46	97	4.514	30,-42,48	391	4.652
RH pSII	49,-27,22	54	4.185	-	-	-
LH MCC	-9,-27,43	108	4.064	-	-	-
LH pIC	-37,-17,11	613	-6.972	-	-	-
RH pIC	44,-13,11	1266	-5.299	-	-	-

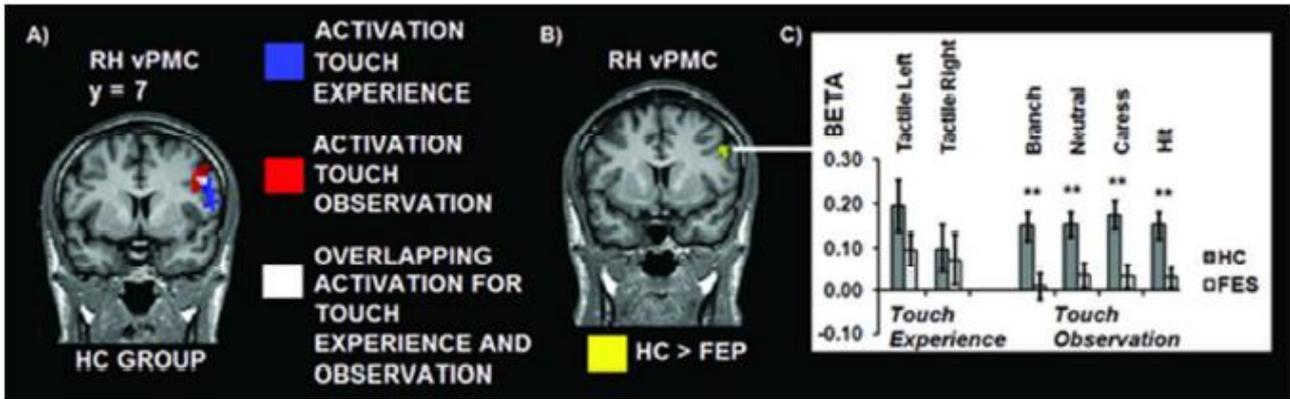
LH: left hemisphere, RH: right hemisphere, a/pSII: anterior/posterior secondary somatosensory cortex, vPostCG: ventral postcentral gyrus, aSPC: anterior superior parietal cortex, TO: temporal-occipital junction, vPMC: ventral premotor cortex, pST: posterior superior temporal cortex, MCC: mid cingulate cortex, pIC: posterior insular cortex.



**Figure 2.** A) Conjunction analysis. Group statistical maps ( $p < 0.05$  corrected) of the healthy control (HC) and first-episode schizophrenia (FES) group depicting positive BOLD modulation clusters for the tactile stimulation task (blue), negative BOLD modulation for the social perception task (red; absent in FES), and significant differential activation patterns for touch experience and observation (white; absent in FES) in posterior insular cortex (pIC); B) ROI-based analysis. Graphs showing activation patterns (beta values) for the different touch experience and observation conditions in the regions of interest (ROIs) in posterior insular cortex (pIC), and between-group differences (\*  $p < 0.05$ ; \*\*  $p < 0.01$ ).

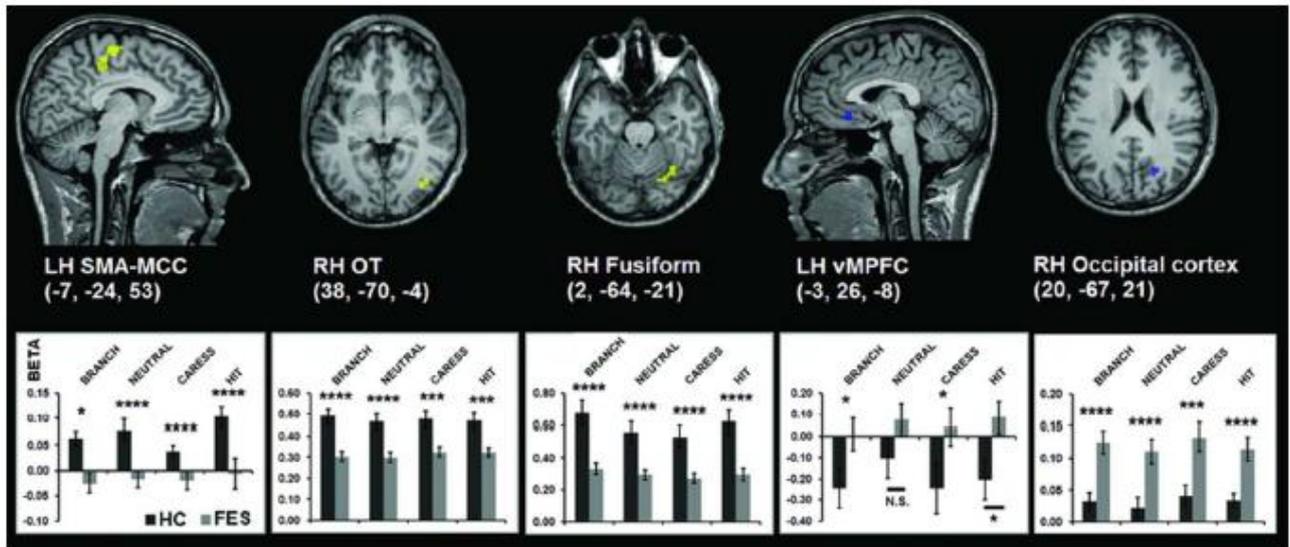
#### *Between-group comparisons: voxel-wise analysis*

Voxel-wise contrasts including voxels that were also active during the tactile stimulation task yielded significantly increased activation in RH vPMC for the HC group, compared with the FES group, for the social perception task (Talairach coordinates: 50, 7, 32; cluster size= 13). Group statistical maps and graphs of the between-group contrasts within the touch experience mask are shown in Figure 3a-c.



**Figure 3.** A) Conjunction analysis. Group statistical map ( $p < 0.05$  corrected) of the healthy control (HC) group depicting activation clusters for the tactile stimulation task (blue), social perception task (red) and overlapping activation patterns for touch experience and observation (white; all absent in FES) in right hemisphere ventral premotor cortex (RH vPMC); B) Masked voxel-wise analysis. Voxels showing significantly reduced activation in the FES group (yellow) in RH vPMC during the social perception task; C) Graphs showing activation patterns (beta values) for the different touch experience and observation conditions in RH vPMC, and between-group differences (\*  $p < 0.05$ ; \*\*  $p < 0.01$ ).

Whole-brain voxel-wise contrasts showed additionally increased activation for the HC group in RH OT, RH fusiform gyrus and LH MCC/supplementary motor area (SMA), whereas increased activation for the FES group, compared with the HC group, was found in LH ventromedial prefrontal cortex (vMPFC) and RH occipital cortex (Figure 4).



**Figure 4.** Whole-brain voxel-wise contrasts. Group statistical maps ( $p < 0.05$  corrected) depicting different neural activation patterns during the social perception task between the healthy control (HC) and firstepisode schizophrenia (FES) group in brain regions not activated by the tactile stimulation task, and corresponding graphs representing neural activation (beta values) for the

different touch observation conditions and groups (\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.005$ ; \*\*\*\*  $p < 0.001$ ; LH: left hemisphere; RH: right hemisphere; SMA: supplementary motor area; MCC: mid cingulate cortex; OT: occipital-temporal cortex; vMPFC: ventromedial prefrontal cortex).

#### *Between-group comparisons: pIC ROI analysis*

Between-group comparisons concerning the pIC ROIs demonstrated significant differences between the HC and FES group: a significantly stronger BOLD response decrease was found during the social perception task for the HC group, compared with the FES group (main effect LH pIC:  $F_{1,44} = 5.990$ ,  $p < 0.01$ ; main effect RH pIC:  $F_{1,44} = 4.975$ ,  $p < 0.05$ ).

With respect to the individual touch observation conditions, a significantly stronger BOLD signal decrease was found in LH pIC in the HC group, compared with the FES group, specifically for the observation of affective touch, that is, CARESS ( $F_{1,44} = 8.624$ ,  $p < 0.005$ ) and HIT ( $F_{1,44} = 6.680$ ,  $p < 0.01$ ). Concerning RH pIC, between-group comparisons showed a significantly stronger BOLD signal decrease in the HC group, compared with the FES group, for the observation of a HIT ( $F_{1,44} = 6.992$ ,  $p < 0.01$ ).

Graphs demonstrating the beta-values of the individual conditions in both groups in the pIC ROIs are demonstrated in Figure 2b.

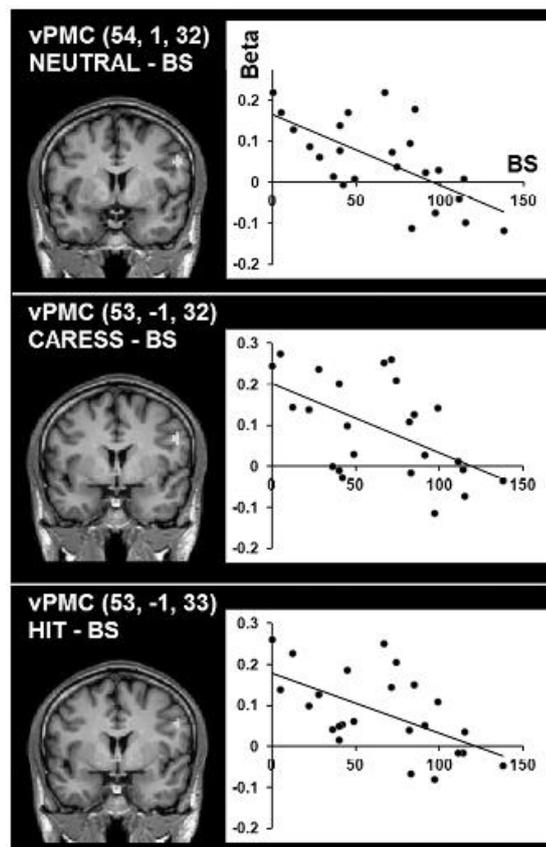
#### *Covariance analyses*

No significant covariance effect was found for chlorpromazine equivalences in the FES group, suggesting that there was no linear relationship between medication dose and differential activation between the HC and FES group.

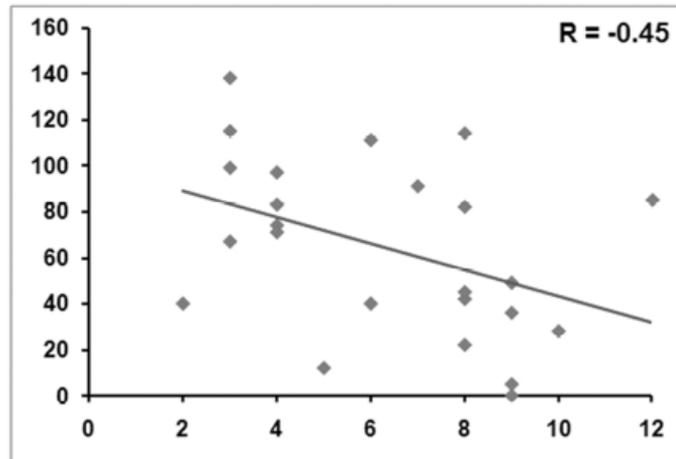
Voxel-wise covariance analyses showed a significant negative relationship between BS and brain activation in the FES group during the observation of a social touch (NEUTRAL/CARESS/HIT;  $p < 0.05$  corrected) in RH vPMC: the higher the total score on the

SPIA, the weaker BOLD response in RH vPMC (Figure 5). No significant correlations were observed for the observation of an inanimate touch (BRANCH) or PANSS scores.

Concerning the EQ questionnaire, significantly lower total EQ scores ( $p < 0.05$ ) and Social Skill subscale scores ( $p < 0.05$ ) were found for the FES group, compared with the HC group (table 1). A significant correlation was found in the FES group between total SPI-A score and the Social Skill subscale score ( $r = -0.45$ ,  $p < 0.05$ ; Figure 6).



**Figure 5.** Group statistical maps and corresponding scatter plots showing significant correlations ( $p < 0.05$  corrected,  $r > 0.51$ ) between basic symptoms (BS) of the FES patients and neural activation (beta values) in right hemisphere ventral premotor cortex (vPMC) during the different social touch observation conditions.



**Figure 6.** Correlation between social skill score (x-axis) and basic symptom severity (y-axis).

#### 5.4 Discussion

The current study aimed at investigating the neural mechanism underlying pre-reflective social perception in FES. In a previous neuroimaging study, it was shown that a neural network involved in first-person tactile experiences may underpin the sharing of others' bodily feelings on the one hand, and, on the other hand, self-related processes concerning multisensory integration and self-other distinction during social perception (Ebisch et al. 2011). Here, the same experimental paradigm was used to answer the question whether in FES, compared with HC participants, functional abnormalities during social perception of other individuals' affective tactile stimulation specifically concern the intersubjective domain or primarily have their roots in disturbances of self-experience.

##### *vPMC and a coherent sense of self*

In the HC group, increased BOLD response was found for all the touch observation conditions in RH vPMC, whereas it was significantly weaker in the FES group in all cases. In contrast with the HC group, BOLD response modulation in RH vPMC was also absent during the

tactile stimulation task in the FES group, suggesting that the absence of overlapping activation in RH vPMC was not exclusively due to aberrant neural processes for the social perception task.

The coordinates of the vPMC cluster in the present study (50, 7, 32) are strikingly similar to the coordinates reported by other studies: 52, 10, 30 (Bremmer et al. 2001); 53, 11, 12 (Makin et al. 2007). This suggests that this region reflects the putative human homologue of monkey premotor area F4 (Bremmer et al. 2001; Buccino et al. 2001; Galati et al. 2001; Makin et al. 2007; Serino et al. 2011). Indeed, consistent with the multisensory properties of F4, in the present study this region responded to visual as well as somatosensory events in the HC group (Rizzolatti et al. 1981a/b; Bremmer et al. 2001). It has been proposed that this region could be involved in the integration of multisensory information from vision, touch and proprioception onto the motor representations of different body-parts (Fogassi et al. 1996a/b; Graziano 2001; Rizzolatti et al. 2002).

In the present study, activation in vPMC for the experience and observation of touch likely reflects a monitoring/integration of multisensory information, including proprioceptive, visual and tactile self-experiences, related to one's body in different situations. Adequate self-monitoring of multisensory information is crucial for the experience of a coherent sense of self and other (Parnas et al. 2002). The lack of activation in RH vPMC in the FES group would suggest a disruption of an integrated multisensory representation of the bodily self. Interestingly, activation in this region in the FES group correlated negatively with BS severity: activation in vPMC decreased with augmented symptom severity. This relationship was consistently found between the social touch observation conditions and BS severity, but not with the degree of positive or negative symptoms. BS represent subjective experiential disturbances in the domains of cognition, perception, bodily experience, action, and emotion (Huber 1983; Klosterkötter 1992). Therefore, the present results support a close link between impaired multisensory representations and a disrupted sense of a coherent self in everyday life (Parnas et al. 2002). A

breakdown of self-monitoring has been suggested before in schizophrenia (Frith 1987; Blakemore et al. 2000; Vinogradov et al. 2008) and vPMC could be a key structure underlying this link.

Such alteration could reasonably lead to the blurring of self boundaries and confusion in the interrelationship with others (Sass and Parnas 2003). Indeed, it was reported that schizophrenic patients with high self-monitoring skills had better social skills (Ihnen et al. 1998). This interpretation offers an intriguing hypothesis for further investigations regarding the multisensory properties of vPMC in relationship with self-experience disturbances. Moreover, given that BS remain stable during the entire disease progression, including the prodromal phase of schizophrenia, the study of their relationship with cortical processes and social deficits would be useful also from a clinical point of view, especially in the light of preventive approaches and an early diagnosis of schizophrenia (Addington et al. 2008a; Schultze-Lutter 2009).

#### *pIC and self-other distinction*

A second brain region of interest where differences were identified between the HC and FES group was pIC. In the HC group, BOLD response in pIC was positively modulated, compared with baseline, during first-person experience of touch, but negatively modulated (deactivated), compared with baseline, during the observation of touch in another individual. By contrast, differential activation for first-person touch experiences and the observation of touch in another individual was absent in the FES group; no deactivation was found in pIC during the observation of touch, though normal activation patterns were found in pIC for first-person touch experiences. Deactivation in pIC in the HC group was specific for the observation of social affective touch (Ebisch et al. 2011). Accordingly, significant differences in LH pIC between the HC and FES group were found specifically for the observation of affective social touch, either with a positive (caress) or with a

negative (hit) valence in LH pIC. Significant differences in RH pIC between the HC and FES group were found specifically for the observation of a hit.

pIC is considered a central brain region for interoception (Craig 2002). Thalamo-cortical pathways may provide a direct representation of homeostatic afferent information to pIC, that interacts with limbic, somatosensory and motor regions, subserving the awareness of bodily feelings (Augustine 1996; Saper 2002; Critchley 2005; Craig 2009). Regarding the cutaneous senses, pIC could constitute the primary cortical locus of an interoceptive system regulating threatening (Craig 2002) or comforting (Olausson et al. 2002; Loken et al. 2009) information from the skin.

In accordance with the idea of pIC as a central cortical node in a system constituting a neural representation of “the material me” (Craig 2002), empirical evidence also suggests that pIC is involved in self-awareness. A PET study in healthy adults showed a positive relationship between the subjective experience of the Rubber Hand Illusion (RHI: a condition in which an observed rubber hand is subjectively experienced as if it actually were one’s own hand; Botvinick and Cohen 1998) and neural activation in pIC (Tsakiris et al. 2007). pIC has also been related to body part awareness in anosognosia patients with hemiplegia/hemiparesis (Karnath et al. 2005), and to the sense of agency (Farrer et al. 2003).

Finally, fMRI evidence suggests that pIC is involved in social perception. Opposite activation patterns for the experience and observation of touch suggest that pIC differentiates between self and other conditions during social perception when affective experiences are implicated (Ebisch et al. 2011). An inhibitory mechanism at the level of pIC during social perception may facilitate the observer to distinguish at the phenomenal level to whom the observed tactile experience belongs.

Hence, the reduced BOLD suppression in pIC reported here in FES could indicate an impaired differentiation between self and other conditions during social perception. We propose

that the absence of deactivation in pIC during the observation of touch in another individual in FES reflects a deficit in the pre-reflective suppression of self-oriented affective arousal, which likely normally contributes to the differentiation between self and other conditions.

Indeed, previous studies in schizophrenia revealed confusion in the attribution of events in the external world to their origin (Bentall et al. 1991; Blakemore et al. 2000; Franck et al. 2001; Vinogradov et al. 2008; Voss et al. 2010). A relationship has been demonstrated between aberrant pIC activation and an impaired sense of agency in schizophrenia (Farrer et al. 2004). Furthermore, the RHI, associated with pIC functioning (Tsakiris et al. 2007), has been found enhanced in schizophrenic pathology (Peled et al. 2000; Morgan et al. 2011).

It remains unclear what may be the dysfunctional neural mechanism underlying the observed reduced suppression of BOLD response in pIC during affective touch observation in FES. Possibly, it could be based on altered connections involved in top-down control processes. Future (functional) connectivity studies are urged to elucidate this issue.

#### *Between group differences in other brain regions*

Some differences could be observed between HC and FES in brain regions not involved in first-person tactile experiences, too. Stronger activation in the HC group during the observation of others' tactile experiences, compared with the FES group, was found in higher order visual areas (ventral fusiform and OT cortex; Downing et al. 2006; Peelen and Downing 2007) and regions underlying action-perception coupling (MCC/SMA; Vogt 2005; Dayan et al. 2007). These results may suggest a reduced involvement of brain regions related to the visual and multimodal processing of bodies, animate objects and motion in FES. By contrast, increased activation in the FES group, compared with the HC group, in occipital cortex during the observation of the touch videos, may indicate a stronger involvement of low-level visual cortices in FES patients.

Finally, weaker deactivation was observed in vMPFC in the FES group, compared with the HC group, during touch observation. vMPFC has been associated with the coding of the self-relatedness of stimuli (Northoff 2007), self-regulation (Heatherton 2011) and dysfunctional self-processing in schizophrenia (van der Meer et al. 2010). However, since vMPFC often is characterized by task-negative activation patterns (Gusnard and Raichle 2001), possibly indicating increased self-related processing during periods of rest, it remains to be established whether the observed decreased deactivation in vMPFC in FES may be caused by a reduced activity during periods of rest (fixation cross) or by a failure to suppress vMPFC activity during touch observation (Northoff 2007). Whereas the former can be interpreted as dysfunctional self-related processes, the latter may suggest that FES patients fail to disengage self-related processes during social perception or to distinguish between self and other conditions.

#### *General discussion and conclusions*

In conclusion, the present study supports the hypothesis that social perception at a pre-reflective level in FES is primarily characterized by altered neural activation patterns underlying disturbances of self-experience and self-related processing, concerning both self-other distinction and a multimodal representation of the bodily self. No abnormalities were found in FES with respect to shared activation between experienced and observed touch in somatosensory cortices. Nevertheless, self-reported social skills scores regarding an intuitive understanding of social situations were significantly reduced in the FES group and negatively correlated with BS, reflecting disturbed subjective self-experiences. BS also negatively correlated with neural activation in RH vPMC in the FES group. Therefore, self-experience disturbances in schizophrenia may extend to the social domain as well (Parnas et al. 2002; Sass and Parnas 2003; Gallese 2003b). For example, an incoherent sense of one's self-experiences accompanied by the

loss of grip on the world may lead to a fading of the very distinction between self and other, and an incapacity to intuitively grasp the meaning of social situations.

Differently from previous studies (Kohler et al. 2000; Shean et al. 2005; Marjoram et al. 2005; Phillips et al. 2003), no relationship was detected between brain activation during social perception, social abilities, and positive and negative symptoms. A possible explanation for this is that the included patients had a very recent illness onset and relatively low PANSS scores. Further studies will be needed to investigate patients with more pronounced positive and negative symptoms as well as chronic samples for a better understanding of the relationship between psychotic symptoms, altered social perception, and its progress over time.

There is growing evidence that social cognition deficits are related to social dysfunction in schizophrenia. The present results shed new light on the cortical basis of how self-experience disturbances in schizophrenia pervade the social domain at a relatively early stage. However, the present findings also depict dysfunctional social perception in schizophrenia as a complex impairment at multiple neural processing levels, rather than being confined to brain regions involved with first-person bodily (tactile) experiences.

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## Chapter 6

## 6. General Discussion and Conclusions

The first aim of my thesis was to shed new light on the contribution of the motor experience of one's own body, as the minimalist level of bodily self experience, to our ability to implicitly differentiate between self and other. We started from the idea that the awareness of oneself, as bodily self, emerges from the experience of oneself as agentive. However, such knowledge is not limited to the "online" sense of being the one who generates action, which relies on the congruence between self-generated movements and their expected consequences (Central Monitoring Theory of action recognition), but rather it emerges also when actions remain covert (Jeannerod 2007), before and below the sense of agency. Indeed, as demonstrated by the studies described in chapters 2 and 3, self-body knowledge hinges on the implicit recruitment of motor simulation. In those studies right-handed participants were submitted to a hand laterality judgment task. In order to judge the laterality of the visually presented hand, participants simulated a motor rotation of their own hand. Behavioral results (chapter 2 and 3) showed that participants were faster in judging the laterality of one's own right hand than all the other hand stimuli. Neuroimaging data (chapter 3), besides revealing a neural network for the general representation of the bodily self encompassing the supplementary and pre-supplementary motor areas, the anterior insula and the occipital cortices, crucially, highlighted that the representation of one's own dominant hand turned out to be primarily confined to the left premotor cortex. These data support the existence of a sense of bodily self encased within the sensorimotor system. How much the representation of the body within this system, in terms of neural efficiency, articulates as "self", seems to depend upon participants' motor experience and motor skills, as demonstrated by the evidence that right-handed participants showed a self-advantage (see 1.2) only for their right hand. Moreover, in both studies described in chapters 2 and 3 participants did not show the self-advantage when self-recognition was explicitly required

(see also chapter 4). Finally, we conclude that only an implicit recognition of the bodily self, mapped in motor terms, leads to self-advantage. However, despite engaging sensorimotor cortices, the condition for the self-advantage to emerge is not the motor nature of the task. Indeed, this effect was revealed for the first time by using a visual matching task of still pictures of body-parts (Frassinetti et al., 2008). In addition, that the sensorimotor system is involved during implicit self-processing, regardless of the motor nature of the task, is confirmed also by a recent study using a tactile detection task (Cardini et al. 2010).

It appears therefore that the necessary condition for the bodily self-advantage to come out is that the sensorimotor representation of oneself, as bodily self, is implicitly, rather than explicitly accessed (Chapter 2, 3, 4). This evidence evokes a well-known effect described by Schooler and Engstler-Schooler (1990) as the “verbal overshadowing” effect, which refers to the fact that verbalizing ineffable perceptual experiences impairs later retention. In other words, explicit verbalization creates a language-based representation that overshadows difficult-to-verbalize aspects of the perceptual memory. Verbal overshadowing has been observed in domains as diverse as taste (Melcher & Schooler, 1996), audition (Houser, Fiore, & Schooler, 2003), map memory (Fiore & Schooler, 2002), and insight problem solving (Schooler et al., 1993), thus establishing that the effect is not limited to visual memories per se. More relevant for our purposes, the processes underlying this phenomenon contribute also to the tendency for conscious reflection to interfere with skilled action (Flegal and Anderson, 2008).

In conclusion, our proposal is that the awareness of oneself, as bodily self, articulates from one’s own motor experience. Such experience provides us with a pre-reflexive and pre-verbal knowledge of our potentialities for action, which is the basis of the sensorimotor representation of ourselves as bodily selves. Thus, when we look at the picture of a body-effector, the more we can implicitly associate our motor potentialities to it, the more we immediately recognize it as ours. Conversely, the more such implicit and pre-verbal knowledge is overshadowed by the recruitment

of different cognitive and/or perceptually-based abilities, as required by the task, the less the self-advantage can emerge. The interesting point is that this happens also when one is required to make a self/other discrimination. This confirms that we cannot rely on a pre-defined, explicit and reflective self-knowledge. Conversely, an implicit bodily self-knowledge, which is fed by motor experience, facilitates the self-advantage effect. This evidence is in line with what reported in the introduction (pag. 6-7) by Cermolacce and colleagues (2007): “the field of experience is not yet considered to be *subjective* because this predicate already implies that there is a subject. For phenomenology, the very idea of the *subject* articulates itself in experience. In this sense, the manifestation and appearing of experience are the *conditions for* the experience of the subject in question”.

The second aim of my thesis was to test whether the disturbance of the basic sense of self in schizophrenia, described as mainly consisting of a loss of the “implicit structure of the body” (Fuchs 2005), is reflected by the loss of the self-advantage effect above described in healthy people. Twenty-one out-patients with a diagnosis of first-episode schizophrenia (FES) and twenty-one matched healthy control (HC) participants were submitted to a visual matching task, as the implicit self-recognition task, and to an explicit self/other discrimination task (Frassinetti et al. 2011). Both tasks employed as stimuli either participant’s own and other people’s body-effectors or participant’s own and other people’s inanimate objects. We found that that FES patients did not show the self-advantage effect in the implicit task. Furthermore, both groups of participants did not show a self-advantage in the explicit task, where FES patients showed a higher percentage of self-misattribution errors with respect to control participants. Previous studies had already shown that bodily self-knowledge is impaired in schizophrenic patients, as revealed by deficits of sense of agency (Daprati et al. 1997) and sense of body ownership (Thakkar et al. 2011). However, these studies could not definitely account for the loss of the “implicit structure of the body”, because in both cases

participants' bodily self awareness was explicitly tested. Moreover, as discussed above, we believe that the bodily self-advantage relies upon a sensorimotor representation of one's own body, which is conceived of as being antecedent the distinction between sense of agency and sense of ownership (Gallese and Sinigaglia 2010).

Finally, our results add to previous knowledge that a more basic impairment of bodily self-knowledge, namely a lack of the self-advantage effect, i) is already present at an implicit level, that is, in absence of an explicit requirement to make a self/other distinction or attribution, ii) is revealed by a task not requiring to overtly execute or observe actions, iii) is already present in first episode schizophrenia patients.

The third aim of my thesis was to investigate whether and to what extent social deficits in schizophrenia are primarily due to disturbances of bodily self-experience or rather are mostly determined by a primary deficit of the intersubjective domain. The hypothesis was that patients with schizophrenia may either show aberrant neural processes underlying multisensory integration and differentiation between self and others' bodily experiences, or altered vicarious neural activations (mirror mechanism) during social perception. Twenty-four FES patients and twenty-two healthy control participants underwent functional magnetic resonance imaging during a social perception task requiring them to watch videos depicting other individuals' inanimate and animate/social tactile stimulations, and a tactile localizer condition. Activation in ventral premotor cortex (vPMC) for observed bodily tactile stimulations was reduced in the FES group and negatively correlated with self-experience disturbances. We propose that vPMC could be a key structure underlying the breakdown of self-monitoring previously suggested in schizophrenia (Frith 1987; Blakemore et al. 2000; Vinogradov et al. 2008) and that such alteration could reasonably lead to the blurring of self boundaries and confusion in the interrelationship with others. Accordingly, the reduced BOLD suppression in pIC during the observation of touch in

another individual could indicate an impaired differentiation between self and other conditions during social perception. We propose this reflects a deficit in FES in the pre-reflective suppression of self-oriented affective arousal, which likely contributes to the differentiation between self and other conditions. Strikingly, no abnormalities were found in FES with respect to shared activation between experienced and observed touch in somatosensory cortices.

In conclusion, it has been argued that (Stanghellini 2001) analyzing disorders of self-experience in schizophrenia, as “lack of ipseity” and “hyper-reflexivity”, may ignore the fact that the self, far from being merely individual, is essentially shaped by intersubjectivity, which is antecedent to the self-other distinction. While agreeing upon the impossibility of conceiving of a properly developed sense of self outside of the social domain, however, our results suggest that disturbances of bodily self-experience may have a primary role in schizophrenia and that they may – at least partly– account for social deficits in schizophrenic patients.

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