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Plasticity in body and peripersonal space representations

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Ai miei genitori

ABSTRACT

A successful interaction with objects in the environment requires integrating information concerning object-location with the shape, dimension and position of body parts in space. The former information is coded in a multisensory representation of the space around the body, i.e. peripersonal space (PPS), whereas the latter is enabled by an online, constantly updated, action-orientated multisensory representation of the body (BR) that is critical for action. One of the critical features of these representations is that both PPS and BR are not fixed, but they dynamically change depending on different types of experience. In a series of experiment, I studied plastic properties of PPS and BR in humans. I have developed a series of methods to measure the boundaries of PPS representation (Chapter 4), to study its neural correlates (Chapter 3) and to assess BRs. These tasks have been used to study changes in PPS and BR following tool-use (Chapter 5), multisensory stimulation (Chapter 6), amputation and prosthesis implantation (Chapter 7) or social interaction (Chapter 8). I found that changes in the function (tool-use) and the structure (amputation and prosthesis implantation) of the physical body elongate or shrink both PPS and BR. Social context and social interaction also shape PPS representation. Such high degree of plasticity suggests that our sense of body in space is not given at once, but it is constantly constructed and adapted through experience.

OVERVIEW OF THE THESIS

The aim of this dissertation is to investigate functional and plastic properties of body and space representation after different types of experience.

In order to successfully interact with objects in the external world, the brain needs to integrate information concerning the object location with the shape, dimension and position of body parts in space. Two different representations are thought to support this function. On one side, the notion of Peripersonal Space (PPS) captures the idea of a specific portion of space where body-objects interactions take place: tactile stimuli applied on a part of the body are integrated with visual and acoustic stimuli delivered on or near the same body part, taking into account proprioceptive information about the position of body parts in space. On the other side, information relative to dimension and position of the different body parts is processed by an online, constantly updated, action-orientated multisensory representation of the body (BR) and its parts. Properties and features of these two representations have been reviewed in Chapter 1 and 2. One of the critical features of these representations is that both PPS and BR are not fixed, but they can be dynamically modulated by different types of experience. In this dissertation, PPS and BR properties in humans, with a particular interest on plastic properties of these two representations, have been experimentally tested in a series of studies.

In the first part of this dissertation, properties of a multisensory representation of space in humans have been investigated using an audio-tactile interaction task. In particular, in Chapter 3 the neural basis of this representation have been studied, while in Chapter 4 I presented a new audio-tactile paradigm specifically developed to measure the extent of PPS representation. This task has been used across the thesis to measure PPS representation in different contexts and after several kinds of experience. In the second part of this work we focused on changes in PPS and BR as a function of different types of experiences. Particularly, in Chapter 5 we investigated plastic extension effects on PPS and BR after a change in body function, such as after a brief training with a tool. I then focused on a possible mechanism explaining plasticity in PPS representation after tool-use. As suggested by a neural network model, the extension of PPS could depend not on the physical presence of a tool, but it raises because of pairing of tactile stimuli at the hand with synchronized multisensory stimuli presented in the far space where the tool is used. In Chapter 6 I presented an experiment run to test this hypothesis.

In Chapter 7 we investigated whether PPS and BR change after a sudden change in the structure of the physical body, such as after amputation and prosthesis implantation. Finally, in Chapter 8, we investigated how our perception of space is shaped by social experience. Particularly, we studied whether PPS is shaped both by the presence of an unknown individual and by social interactions with other people.

"The body is our general medium for having a world."

Maurice Merleau-Ponty, Phenomenology of Perception, p169

"Visible and mobile, my body is a thing among things; it's caught in the fabric of the world, and its cohesion is that of a thing. But, because it moves itself and sees, it holds things in a circle around itself."

Maurice Merleau-Ponty, The Visible and the Invisible, 1964, p163

CHAPTER ONE: A MULTISENSORY BODY

Perception has been traditionally described as a modular function, with the different sensory modalities operating as independent and separated processes. Accordingly, distinct cognitive, sensory and motor functions can be localized in distinct areas of the brain. Although different sensory modalities have often been studied in isolation, in order to perceive the external and internal environment, our brain uses multiple sources of sensory information obtained from several sensory modalities. The coexistence of different sensory channels can potentially enhance the detection and identification of external stimuli. This property has obviously a high adaptive value, since external stimuli could be either potentially dangerous or particularly interesting, so they would need to be detected rapidly (Ernst & Bulthoff, 2004; Stein & Meredith, 1993; Stein, 1998). Since interactions with external stimuli have such an important value, it is not difficult to think that stimuli presented in the *space close to the body* – where preferentially any physical interaction with the environment takes place - should be specially treated by the brain in comparison to stimuli far from the body.

Despite the apparent unitary character of space representation, indeed, evidence from neurophysiology, neuropsychology and experimental psychology demonstrated the existence of different neuronal representations of space, each built in relation to the behavior we can perform. The notion of Peripersonal Space captures the idea of a multisensory representation of the space immediately surrounding the body, coding for position of external stimuli with respect to the body itself.

In every successful interaction however the human brain needs to concurrently represent not only the position and movements of external stimuli in the near space, but also the position and shape of body parts used to perform a successful interaction. The latter function is supported by a high-level multisensory representation of the body (Body Representation, BR) in the brain. In this chapter I will review evidence about the existence of both Peripersonal Space (Paragraph 1.1) and Body Representations (Paragraph 1.2).

1.1 The body in its space

The conscious perception we have of the space as a unitary medium surrounding the body is quite strong, but simplistic. Indeed, this unified percept of space is the result of distinct and modular representations of space. These representations include *personal, peripersonal* and *extrapersonal space*. The *personal* space represents the space occupied by the body (Vaishnavi, Calhoun, & Chatterjee, 1999; Coslett, 1998; Bisiach, Perani, Vallar, & Berti, 1986). The concept of *extrapersonal* space instead refers to the space beyond reaching of our limbs (Previc, 1998; Brain, 1941). Finally, the notion of *Peripersonal* Space captures the idea of a specific portion of space where every action take place: tactile stimuli applied on a part of the body are integrated with visual and acoustic stimuli delivered on or near the same body part, taking into account proprioceptive information about the position of body parts in space (Graziano & Cooke, 2006; Làdavas & Serino, 2008; Rizzolatti, Fadiga, Fogassi, & Gallese, 1997). In such space taxonomy, Peripersonal Space representation is particularly important, because the body can directly interact with the external world within its limits.

In the next paragraph I will review neurophysiological, neuropsychological and behavioral evidence for multiple multisensory space representations.

1.1.1 Neurophysiological evidence

The first support for a distinction between peripersonal and extrapersonal space came from neurophysiological studies in monkeys, revealing the existence of a pool of multisensory neurons coding specifically for the space immediately surrounding the body. The terms "peripersonal" was first introduced by Rizzolatti and colleagues (Rizzolatti, Scandolara, Matelli, & Gentilucci, 1981a; 1981b), referring to a "*limited sector of space around an animal whose spatial boundaries were defined by variations in the neuronal firing rate as a function of the proximity between an object and a given body part*" (see also Haggard, Rossetti, & Kawato, 2008). These cells have been described in different brain areas of the macaque, and they will be reviewed in the next paragraphs.

Figure 1.1 Peripersonal Space. Schematic diagram of visual receptive fields in the polysensory zone (PZ). Space near the body is represented by relatively more receptive fields, and space at increasing distances from the body is represented by fewer receptive fields. **Adapted from Graziano & Cooke, 2006.**

Premotor neurons

The precentral gyrus of monkeys contains a restricted zone in which neurons have multisensory properties responding to tactile stimuli administered on a given body part. These multisensory neurons were first reported at the level of the ventral promotor cortex (PMv) in the posterior part, named F4 (Matelli, Luppino, & Rizzolatti, 1985). Some authors refer to this multisensory zone as the polysensory zone (PZ; Graziano & Cooke, 2006). Many of the neurons studied in this area are bimodal neurons, having a tactile receptive field located on the hands, arms, face, trunk and shoulders. These neurons have a visual (Duhamel, Colby, & Goldberg, 1998; Graziano, Hu, & Gross, 1997a; Graziano, Yap, & Gross, 1994; Rizzolatti et al., 1981b) receptive field overlapping the tactile RF and extending in depth for about 30 cm. This means that these bimodal neurons respond to visual stimuli presented close to the tactilely stimulated body part. In most of brain visual areas the visual receptive fields are organized in retinotopic reference frame, which means that objects are represented in relation to their position on the retina. Instead, visual RFs of the bimodal neurons in PMv are coded in body-part reference frames that are in spatial register with the tactile receptive field: if the body part where the tactile RF is anchored moves, the visual RF shifts congruently (see Avillac, Deneve, Olivier, Pouget, & Duhamel, 2005, for a model of visual and tactile reference frames transformation). For example, some bimodal cells with tactile receptive fields on the right arm respond to visual stimuli presented on the right side of space when the arm is placed on the right hemi space. When the arm is moved into the centre of the visual field, the same neurons responded to visual stimuli presented in the centre, thus from the same spatial position of the tactile receptive field. These responses are also present in anesthetized monkeys (Graziano & Gandhi, 2000), which suggest that premotor neurons perform multisensory integration even when the monkey is not planning or performing an action.

Another characteristic of these bimodal neurons is that they continue to respond to visual stimuli also when these stimuli are no longer present, for instance in complete darkness (Graziano, Hu & Gross, 1997b). Graziano (1999) specifically tested the relative role of vision and proprioception in encoding limb position in the monkey brain. He tested the response of PMv multisensory neurons with a tactile receptive field on the arm and a visual receptive field anchored to the tactile one. The neurons were tested under different configurations, in which both the position on the arm and the visual information regarding the arm were manipulated (see Figure 1.2). Results demonstrated that both visual and proprioceptive information play an important role in building a coherent representation of the space around us. Moreover, results from this study demonstrated that these neurons responded not only to a visual stimulus presented close to monkeys’ arm, but also close to a fake but realistic arm placed in a realistic posture in front of the monkeys during the testing (Graziano, 1999). Interestingly, if the real arm was hidden from view, and the fake arm was moved, the movement of that fake arm caused a shift in the visual RF of the bimodal neurons.

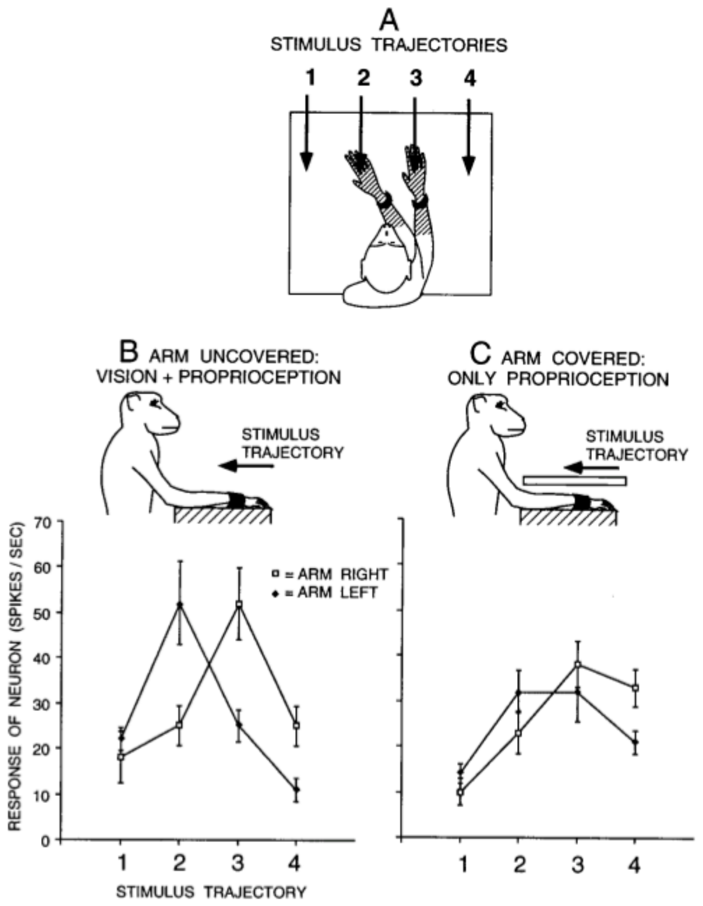

Figure 1.2 Visual responses of a typical premotor neuron with a tactile RF (hatched) on the forearm and hand, and a visual RF within 10 cm of the tactile RF. (A) On each trial, the arm contralateral to the neuron was fixed in one of two positions and the visual stimulus was advanced along one of four trajectories (1–4). For this neuron, the two arm positions were chosen to align the visual RF near the hand and forearm with trajectories 2 and 3. For other neurons, the arm was moved to different extents depending on the location of the visual RF, to better capture the movement of the visual RF with the arm. (B) Responses of the neuron to the four stimulus trajectories when the arm was visible to the monkey. When the arm was fixed on the right, the response was maximum at position 3. When the arm was fixed on the left, the maximum response moved to the left, to position 2. (C) Responses of the neuron when the arm was covered. The movement of the visual RF with the arm was reduced but not eliminated, indicating that the neuron combined both proprioceptive and visual information about the position of the arm. Each point is a mean of 10 trials. Error bars are standard error. **Adapted from Graziano, 1999.**

These multisensory neurons are particularly sensitive to moving stimuli. Some neurons are directionally selective, that is they code preferentially for neurons moving along a specific trajectory. They also code for stimulus velocity (Fogassi, Gallese, Fadiga, Luppino, Matelli, & Rizzolatti, 1996).

Not only bimodal, but also trimodal neurons are located in PMv. These neurons respond to a tactile stimulus located on the back and the side of the head and to a visual and/or auditory stimulus presented close to the body part where the tactile stimulus is administered (Graziano, Reiss & Gross, 1999). In Figure 1.3, a typical response of a trimodal neuron is shown: this neuron respond to sounds produced near the contralateral side of the head. Specific testing of trimodal neurons properties of an awake monkey revealed that the auditory responses in PMv clearly span the entire contralateral space, and seem to represent the space behind of the head more densely than the space in front of the head (Graziano et al., 1999).

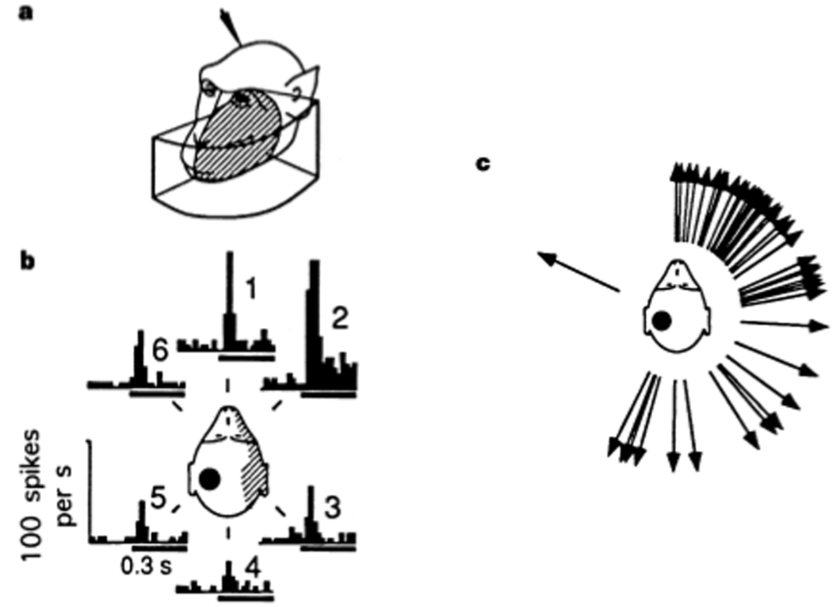

Figure 1.3 Responses of bimodal and trimodal neurons in PMv.
a) Receptive fields of a typical bimodal, visual-tactile neuron. The tactile receptive field (shaded) is on the front of the face contralateral to the recording electrode (indicated by the arrowhead). The visual receptive field (boxed) is confronted to a region of space within about 10 cm of the tactile receptive field. b) Responses of a typical trimodal, visual-tactile-auditory neuron. The tactile receptive field is

contralateral to the recording electrode (indicated by the black spot) and includes the ear and back of the head. The visual receptive field (not shown) extends about 20 cm into the space near the contralateral side of the face. The histograms show the response, summed over ten trials, to a burst of white noise presented 10 cm away at the indicated azimuth angles. c) The calculated preferred direction of the auditory response for 43 trimodal neurons. Each arrow shows the result for one neuron. **Adapted from Graziano, Reiss, & Gross, 1999.**

Parietal neurons

Multisensory bimodal and trimodal neurons with similar properties as compared to the ones in the PMv were found also in the posterior parietal cortex of monkeys' brain, specifically at the level of the ventral intraparietal sulcus (VIP), and in area 7b. VIP area is located in the fundus of the intraparietal sulcus and it receives projections from the middle temporal visual areas, as well somatosensory, auditory, and vestibular regions (Graziano & Cooke, 2006). Most neurons in area VIP exhibit bimodal visuo-tactile properties, in the sense that they respond to stimuli applied in either sensory modality (Duhamel et al., 1998). The tactile RFs are equally distributed on the top, side, or back of the head, and on the neck, meaning that this area primarily describes spatial area around the face, but they can sometimes be on the chest, shoulder, or arm (Graziano & Cooke, 2006). Some of these neurons are also selective for the distance at which the visual stimulus is presented and they show a strong sensitivity to speed and direction of motion of both visual and tactile stimuli (Duhamel et al., 1998). Some VIP neurons are sensitive to the three-dimensional trajectory of objects. Moreover, some VIP neurons are trimodal, responding to visual, tactile and auditory stimuli, with the three receptive fields usually aligned (Schlack, Hoffman & Bremmer, 2003). Differentially from multisensory neurons described in the PMv, whose RFs are mainly arm centred, bimodal neurons in VIP area have tactile receptive fields encoding a head-centered reference frame, whereas visual receptive fields are widely distributed between eye-to head-centered coordinates.

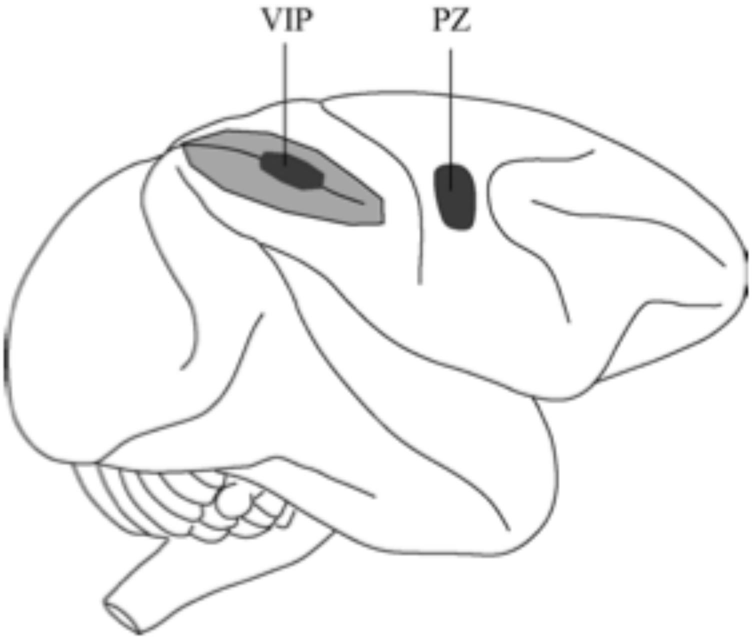

Figure 1.4 Schematic side view of macaque monkey brain showing approximate location of the ventral intraparietal area (VIP) and the polysensory zone (PZ). Intraparietal sulcus is shown opened up, with light shaded area indicating buried cortex. **Adapted from Graziano & Cooke, 2006.**

Area 7b is prevalently a somatic area, with most of its neurons being somatosensory or somato-motor (Gross & Graziano, 1995; Hyvarinen, 1981), even if a part of the neurons studied in this area is bimodal, responding to both visual and tactile stimulation. Here the majority of the neurons have bilateral RFs located on the limbs often covering the whole body (Leinonen, Hyvarinen, Nyman, & Linnankoski, 1979). Finally at a subcortical level, the putamen has a complete somatotopic map of the body, including a large proportion of bimodal neurons with tactile RFs centred on the head (Graziano & Gross, 1993).

1.1.2 Sensory-to-motor function

These neurons described in the previous paragraph also have a motor function. Most of both premotor (Fogassi et al., 1996) and parietal neurons (Leinonen et al., 1979) are active during movements of the body part where their visuo-tactile receptive fields are anchored. In addition, electrical stimulation of neurons in the ventral premotor cortex (Graziano, Taylor & Moore, 2002) evokes movements of the body part anchoring the aforementioned tactile, visual or acoustic RFs. Similarly, stimulating areas in the fundus of the intraparietal sulcus, corresponding to VIP, evoked different types of movement including included eye movements, reaching, bringing the hand to the mouth, aggressive displays, and defensive movements (Stepniewska, Fang, & Kaas, 2005). Finally, as described before, these neurons encode the location and trajectory of objects, with an emphasis on objects that are near or approaching the body. This specificity for moving stimuli as compared to static one can be considered a hallmark of the clear sensory-to-motor function of peripersonal space representation. Indeed looming stimuli are an essential component of threat (Gibson, 1972; Graziano & Cooke, 2006). For obvious adaptive reason, a stimulus approaching the body need to be detected as fast as possible, in order to plan a proper motor reaction. The neurons in VIP and PMv could be described as looming detectors in general sense (Graziano & Cooke, 2006).

Taken together, all these properties demonstrate the sensory-motor function of PPS representation: coding the spatial position and dynamics of an external stimulus with respect to a part of the body potentially interacting with it, in order to plan an approach toward an interesting object (Rizzolatti et al., 1997) or evade a potential threat (Graziano & Cooke, 2006).

1.1.3 Neuropsychological evidence

Neglect

The first evidence for dissociated spatial representations in humans came from patients affected by hemi spatial neglect. Neglect has long been recognized as a multi-component syndrome, usually observed following brain lesions affecting the right hemisphere, in particular at the level of the right inferior parietal cortex (inferior parietal lobule, angular and supramarginal gyrus) and right temporo-parietal junction (Vallar & Perani, 1986). Neglect patients are characterized by a failure to respond, to attend or to orient voluntarily to objects placed in the contralesional space. This contralesional unawareness may occur selectively for different sectors of space. Specifically, a form of neglect, known as personal neglect, has been described, characterized by the presence of deficits relative to the side of the body contralateral to the lesion. Bisiach and colleagues (1986) investigated the dissociation between different forms of neglect for different sectors of space. They first reported evidence of a double dissociation between patients selectively affected by neglect for personal and extrapersonal space. In addition, Halligan and Marshall (1991) presented a case of a patient selectively affected by neglect limited to the peripersonal space. This patient showed a typical neglect bias in a bisection line task; when he was asked to bisect a horizontal line placed closed to him, in the near space, the patient committed rightward errors. Instead, when the line was positioned in the far space (i.e. at two meters distance), these rightward errors disappeared (see also Berti & Frassinetti, 2000 for a similar case).

Extinction

The study of crossmodal extinction has brought a considerable contribution in investigating how multisensory stimuli are perceived and integrated in order to build the representation of the space around us.

Extinction is a neuropsychological syndrome generally following a right brain lesion, most typically in the posterior parietal region. In these patients, the perception of a contralesional tactile stimulus is affected by the presentation of a concurrent ipsilesional visual stimulus (Bender, 1952), with the almost normal detection of contralesional stimuli presented in isolation. Extinction (and neglect as well) could affect all sensory modalities, either within a single modality i.e. (unimodal extinction) or between different sensory modalities (i.e. crossmodal extinction; Mattingley, Driver, Beschin & Robertson, 1997). Crossmodal extinction has been extensively studied as a model to study the multisensory neural representation of space. Authors initially investigated cases of visuo-tactile extinction. Patients suffering from this syndrome were unable to correctly perceive a tactile stimulus administered at the controlesional hand, when a concurrent visual stimulus was presented in the ipsilesional side of space. Làdavas and colleagues (di Pellegrino, Làdavas, & Farnè, 1997; Farnè & Làdavas, 2000), in a series of studies, demonstrated that crossmodal extinction was also spatially dependent. By using a visuo-tactile stimulation paradigm in right brain damaged patients affected by left tactile extinction, they demonstrated that tactile detection at that hand was inhibited by a visual stimulus presented in the right hemi space. Interestingly, the presence of the visual stimulus produced crossmodal extinction at the same extent as an ipsilesional tactile stimulus in case of unimodal tactile extinction. Critically, this degree of cross modal extinction occurred only when the visual stimulus was presented close to the patient’s hand (i.e. within the peripersonal space), but was much weaker or absent when the visual stimulus was placed at a distance (in ‘far’ or ‘extrapersonal’ space). Two stimuli are more likely to interact when presented in the same spatial representation: when a visual stimulus is presented far from the body, that is in the extrapersonal space, it does not interact with tactile stimuli presented close to the hand, because they are presented in two different representations. So, crossmodal extinction has been taken as an evidence of the existence of separate representations of space.

A model addresses the competitive dimension of extinction (and neglect as well) by proposing that these phenomena result from a breakdown in the dynamic balance that normally exists in the reciprocal inhibition between homologous areas of the two hemispheres that orient spatial attention in opposing, contralateral directions (Kinsbourne, 1977; Kinsbourne & Bruce, 1987; see Jacobs, Brozzoli, Hadi-Bouziane, Meunier, & Farnè, 2011, for a review).

The same extinction effect previously described for the hand has been demonstrated with tactile stimuli presented at the face (Farnè & Làdavas, 2002; Làdavas, Zeloni, & Farnè, 1998a), suggesting the existence in humans, as in monkeys, of a modular representation of space surrounding different body parts. Farnè and colleagues (Farnè, Demattè & Làdavas, 2005) tested whether these representations effectively operate in a modular way in a group of right brain damaged patients by using cross modal extinction paradigm. They measured the level of cross modal extinction when visual and tactile stimuli were presented on homologous body part (for instance, tactile stimulus at the contralateral hand and visual stimulus near the ipsilesional hand) and non-homologous body parts (i.e. tactile stimulus at the hand and visual stimulus near the face). Results showed a dissociation between the representation of the peripersonal space around the hand and the peripersonal space around the face, revealing that a visual stimulus presented near the face did not interact with tactile stimulation at the hand and vice-versa. These results confirmed the hypothesis of an organization of space in separated moduli around different body parts.

Interestingly, in order to examine the spatial coordinates used by this multisensory system to code peripersonal space, di Pellegrino and colleagues (di Pellegrino et al., 1997) tested a patient with tactile extinction by manipulating hands' position in space. They asked the patient to perform the task with the hands crossed; this way, the left hand was placed in the right hemi space and the right hand in the left hemi space. Results showed that a visual stimulus presented near the right hand (that is in the left hemi space) extinguished tactile stimuli at the left hand (that is in the right hemi space). Results of the present studies offered interesting insights on the idea the representation of peripersonal space (peri-hand space, in this case) was anchored to a specific body part, in line with neurophysiological results on monkeys.

Modulation of tactile extinction not only by visual but also auditory stimuli has been investigated in neuropsychological patients (Làdavas, Pavani, & Farnè, 2001; Farnè & Làdavas, 2002). Indeed, in a group of right brain damaged patients Làdavas and colleagues demonstrated that tactile detection at the neck was influenced by the presentation of auditory stimuli presented near, but not far, the patients' face. Interestingly, spatially dependent interactions between audition and touch were strongest when the auditory stimuli came from the back, rather than from the front, of the patients' head. This spatial specificity from a particular sector of space, that is the back of the head, is particularly relevant in the case of audio-tactile interaction. Indeed it makes perfectly sense that the backspace, where vision is not available, is more deeply represented through audio-tactile interaction. Moreover, in this study the authors investigated whether this spatial modulation of touch by audition was dependent on the complexity of the stimuli used. They found that white noise sound, that is a more complex sound, has a stronger effect on tactile perception than pure tones. These results are in line with neurophysiological results in monkeys, showing that multisensory neurons coding for peripersonal space around the head (Graziano et al., 1999) did not respond to pure tones. This specificity could be due to the fact that white noise sounds are more similar to ecologic sounds. Thus, the reduced effect operated by a pure tone might reflect a sort of impenetrability of the integrated auditory – tactile system to a sound that has a little chance to occur in nature (Farnè & Làdavas, 2002).

The near-far modulations of crossmodal extinction here described have been considered as the first behavioural demonstrations of the existence of peripersonal representation in humans (di Pellegrino et al., 1997; Làdavas et al., 1998a; Làdavas, di Pellegrino, Farnè & Zeloni, 1998b).

1.1.4 Behavioural evidence

A series of studies conducted on healthy human subjects confirmed the existence of spatially dependent cross-modal interactions. Most of these studies investigated specifically visuo-tactile interactions. One of the best-known paradigms used to investigate this issue is the cross-modal congruency task. In this task, participants receive a vibrotactile stimulus either at the thumb or the index finger of the hands. At the same time a visual stimulus (a distractor) is presented at four possible positions, corresponding to the four possible locations of the vibrotactile stimuli. Thus, for each trial the visual distractor could be either close to the tactilely stimulated hand or to the other hand. Moreover, the visual distractor could be ”congruent” or ”incongruent in elevation with the tactile target stimuli. Participants are asked to make a speeded up/down discrimination judgement in response to the tactile stimuli, by pressing a foot pedal, ignoring the visual distractors. A series of studies (Spence, Pavani, & Driver, 2000; Pavani, Spence, & Driver, 2000; Spence, Pavani, Maravita, & Holmes, 2004; see also Brozzoli, Pavani, Urquizar, Cardinali, & Farnè, 2009) using this paradigm revealed that incongruent visual distractors (that is distractors presented at a different elevation as compared to the vibrotactile stimuli) slowed down the judgements about the tactile stimuli and produced more errors. This effect of visual stimuli on tactile one was spatially dependent, since it was stronger from stimuli coming from the same side of space (Spence et al., 2004). When the posture of participants was manipulated, this cross modal effect changed accordingly: for instance, in a crossed hand condition, if the right hand is placed in the left hemi space, a visual distractor in the left space affected tactile detection at the right hand. These results demonstrated that visuo-tactile interactions take changes of posture into account (e.g. Macaluso, Driver, van Velzen, & Eimer, 2005), in agreement with neurophysiological properties of neurons in the parietal and premotor cortex. Interestingly this spatial modulation appeared to be present also when patients were not actually able to see their hand, suggesting the importance of tactile and proprioceptive information in building a strong percept of limb position and, accordingly, of the representation of the space surrounding it.

The particular link between vision and touch for the construction of a congruent representation peripersonal of space is such that even the image of a fake, but spatially congruent, limb can affect tactile perception. Pavani and colleagues (2000) investigated the cross-modal effect of visual distractors on tactile judgments using the cross modal congruency task previously described. Participants were asked to discriminate the location of vibrotactile stimuli administered at the hand (upper, at the index finger, vs. lower, at the thumb), with the hand occluded under a table, while ignoring distractor lights that could independently be upper or lower with respect to the tactile stimulation. In line with previous results obtained with the same task, an incongruent (with respect to the elevation of the tactile stimuli) visual stimulus presented close to the hand interfered with tactile detection. Critically, the same results was obtained when the visual stimulus was presented close to a fake, realistic hand placed on the table in front of the participants, but only when the hand was placed in an anatomically plausible posture (see also Farnè, Pavani, Meneghello, & Làdavas, 2000, for a similar result on extinction patients). This indicates that, although strongly interrelated, tactile and visual spatial representations are also flexible, and can change to maintain spatial alignment of multisensory signals arising in the peripersonal space. Taken together all these studies support the claim that the human brain represents PPS through an integrated visuo-tactile system.

Cross modal spatially dependent interactions has been described also between audition and touch. Auditory peripersonal space has been first described around the head, both in monkeys (Graziano et al., 1999) and in humans in brain damaged patients (Farné & Làdavas, 2002; see Paragraph 1.1.3). Behavioral studies investigated the existence of auditory-somatosensory interaction around the head (Tajadura-Jimenez, Kitagawa, Väljamäe, Zampini, Murray, & Spence, 2009), particularly in the space *behind* the head (Kitigawa, Zampini, & Spence, 2005) and around the hand (Murray, Molholm, Michel, Heslenfeld, Ritter, et al., 2005; Zampini, Torresan, Spence, & Murray, 2007) in healthy subjects using different paradigms.

In Kitigawa and colleagues' study (2005) participants performed a temporal order judgment (TOJ) task about pairs of auditory and tactile stimuli presented at different interstimulus interval. Tactile stimuli were applied at participant's earlobes, while the auditory stimuli were presented through loudspeakers placed 20 cm behind participant's head, both in left and right hemispaces. Participants were asked to report the modality (auditory or somatosensory) of the first stimulus they perceived. Results indicated a better performance for stimuli presented from different sides of space. In a second experiment, participants performed a tactile left/right discrimination task while auditory distractors were presented simultaneously from the same or opposite side. Results showed slower (and less accurate) tactile RTs when the auditory distractors were presented on the opposite side from the target tactile stimuli. Interestingly, in this study, in line with previous results both in monkeys (Graziano et al., 1999) and in humans (Farnè & Làdavas, 2000), when bursts of white noise (a more ecologic sound) were used, authors found a greater effect of crossmodal interference when the auditory stimuli were presented close to participant's head rather then far apart. These results suggested that auditory and tactile stimuli interacted preferentially in the space immediately surrounding the head exhibiting different responses according to the complexity of the auditory stimuli used. These results seem to be in contrast with results obtained by Zampini and colleagues (Zampini, Brown, Shore, Maravita, & Roder, 2005) in a similar experiment in which audio-tactile interaction were investigated through a TOJ task in the front space. In this experiment results showed that participants' responses to tactile stimuli presented at the finger were not affected by the spatial position of auditory stimuli. However this experiment was conducted in the front space, while a series of evidence in the literature suggested that auditory-tactile interaction are more likely to take place in the back space, where vision is not available and where information coming from audition are more relevant (see also Occelli, Spence, & Zampini, 2011, for a review). Interestingly in a series of experiments, Tajadura-Jimenez and colleagues (2009) further demonstrated a spatial modulation of auditory–somatosensory interactions when auditory stimuli were presented in the space close to the head, at different distance to the left and the right of the center of participants' head.

Audio-tactile interactions have been studied also in the space around the hand. Murray and colleagues (2005) investigated the possible interaction between spatially aligned and misaligned (across left and right directions) auditory and somatosensory pairs of stimuli - using a simple reaction time task - and the electrophysiological correlates of this phenomenon - using ERPs. Participants were asked to respond to a tactile stimulation at the hands, while auditory stimuli were presented from loudspeakers placed either close to the left or to the right hand. Results showed that participants' RTs were facilitated for multisensory stimuli. Additionally, the extent of facilitation did not change as a function of the spatial alignment of the stimuli, showing that auditory stimuli facilitated tactile RTs independently of the alignment of auditory stimuli with respect to the tactile stimuli. Accordingly, ERPs results showed a greater response, at 50-90 ms post stimulus onset, for multisensory audio-tactile stimuli, as compared to the summation of the constituent unisensory ones, at lateral central scalp sites over the hemisphere contralateral to the stimulated hand, for both the aligned and misaligned configurations. The source of these interactions were localized to unimodal rather then multimodal area, at the level of the auditory association cortices in the hemisphere contralateral to the hand being stimulated, independently of the location of the auditory stimulus. Taken together, both behavioral and electrophysiological results from the present study provided evidence for the existence of multisensory auditory-somatosensory interaction across spatial separations. One proposition from these results is that the brain regions involved in processing auditory–somatosensory stimuli contain large spatial RFs, which allow for the integration of stimuli that happen to be separated by a relatively large distance in external space (Murray et al., 2005; see also Zampini et al., 2007). Zampini and colleagues (2007) further investigated audio-tactile interaction at the hand both in front and rear space. Results confirmed a facilitation for multisensory stimuli as compared to unisensory ones, regardless of the spatial location from which the auditory stimuli were presented or the specific body posture adopted by participants.

Taken together, these studies revealed the existence of audio-tactile interaction mechanisms in humans. However, these studies did not clearly establish whether these audio–tactile integrative mechanisms are modulated by the spatial location of auditory stimuli. A study of Serino and colleagues (Serino, Bassolino, Farnè, & Làdavas, 2007), by using an audio-tactile interaction task, demonstrated a space dependent audio-tactile interaction mechanism. In this paradigm participants received tactile stimuli at their index finger, while a concurrent sound was presented. The sound position in space was manipulated, so that in different trials it was presented either close to the participant's hand (near condition) or far from it, at a distance of around 125 cm (far condition). Participants were asked to verbally respond to the tactile stimulation as quickly as possible, by saying TAH in a microphone. They were also asked to completely ignore the auditory stimuli during the task. Results showed that tactile detection was speeded up when the sound was presented close to the body as compared to when it was presented far apart, revealing the existence of an integrative auditory peri-hand space in humans, in line with studies on visuo-tactile interaction.

1.1.5 Neural basis of PPS in humans

Human imaging studies suggest that a neural system dedicated to multisensory integration in the peripersonal space also exists in the human brain. An increasing number of studies in healthy humans using fMRI (Bremmer, Schlack, Shah, Zafiris, Kubischik, Hoffmann, et al., 2001; Makin, Holmes, Brozzoli, Rossetti, & Farnè, 2009; Brozzoli, Gentile, Petkova, & Ehrsson, 2011) and EEG (Sambo & Forster, 2009) suggested that the multisensory representation of PPS in the human brain is implemented in a fronto-parietal network, encompassing premotor and posterior parietal areas largely corresponding to PMv and VIP areas in the monkey's brain.

Bremmer and colleagues (2001) measured changes in neural activity in healthy volunteers using functional magnetic resonance imaging (fMRI) in order to identify a set of common areas involved in polymodal information processing. Indeed participants were tested in fMRI while presenting moving visual, tactile, or auditory stimuli. They demonstrated that portions of the posterior parietal cortex (PPc), around the intraparietal sulcus and the ventral premotor cortex (vPMc) were activated by tactile and by visual and auditory stimuli moving towards the head (see also Macaluso & Driver, 2001; 2005). The homologous of this set of areas in the monkey's brain is extensively activated by moving - rather than stationary - multisensory stimuli, preferentially approaching towards the body (Colby, Duhamel & Goldberg, 1993). Moreover, Sereno & Huang (2006) described aligned maps of tactile and peri-face visual stimuli in the ventral part of the intraparietal sulcus, coding the location of visual stimuli with respect to the face, and not with respect to the eye. A different fMRI study in healthy participants (Makin, Holmes, & Zohary, 2007) showed that activity in PPc and vPMc was selectively modulated by a visual stimulus approaching the hand, compared to seeing the same stimulus moving away from the hand. Neural activity in PPc and vPMc was sensitive to the position of the hand relative to the visual stimulus, as signalled both by visual and proprioceptive information.

These results are in line with a recent fMRI study by Brozzoli and colleagues (Brozzoli et al., 2011) using an adaptation mechanism. They found a consistent adaptation in premotor and parietal areas exclusively for objects near the hand. Finally, Gentile and colleagues (Gentile, Petkova, & Ehrsson, 2011) described an increased activation in response to visuo-tactile stimulation in a set of cortical (premotor and posterior parietal) and subcortical regions matching the neurophysiological literature on multisensory areas in monkeys and humans. Taken together, these results suggested the existence of common neuronal mechanism in humans and nonhuman primates including parietal and premotor cortices for the representation of peripersonal space.

1.2 From the body to its representation(s)

In order to interact with objects in space, in either reaching an interesting stimulus or avoiding potential harm, the human brain needs to concurrently represent not only the position and movements of external stimuli in space, and especially within the PPS, but also the different parts of one's own body potentially interacting with those stimuli. In the following section I will focus on high-level multisensory representation of the body (Body Representation, BR) in the brain, supporting this function.

Our body represents the centre of our sensations and perceptual experiences and at the same time it mediates every physical interaction with the external stimuli. The brain contains several representations of the physical body. It is fair to state that body representation begins with a tactile map of the body surface, since somatosensation is the most basic property that allows every perceptual interaction with the world. One key function of somatosensory representation is the ability to localise the location of tactile stimuli on the body surface. Indeed, as soon as a fly touches our skin, we immediately know where we have been touched in respect to the skin surface. Somatosensory receptors located all over the skin project to the well-known sensory homunculus of the primary somatosensory cortex (SI, Penfield & Rasmussen, 1950) within the post-central sulcus (see Paragraph 1.2.1). Neurons in this area form a characteristically distorted map of the contralateral body surface: each part of this map selectively responds to mechanical and electrical stimulation of a given part of the body, thus supporting perception of where on the skin a sensory stimulus is located. The localisation based on skin receptors can only take account of the localisation of touch in the receptor field surface. However, in order to perform a successful interaction with an external stimulus, for instance to make a motor response towards the source of a tactile stimulation (such as for swatting away an insect that might be about to sting) it is important to know different information exceeding the spatial location of touch on the body. Indeed, localising tactile inputs within the somatotopic map is not sufficient by itself to localise them on the body surface. Since our body and, even more prominently, our limbs are constantly moving in the environment, the relative position of a body part in the external space with respect to the other body parts may vary. So, proprioceptive information about the position of a body parts with respect to each other must be taken into account. Moreover, the body changes continuously in position and dimensions throughout life, so, in order to perform a movement, body representations in the brain need to be continuously updated about shape and dimension of the different body parts in each moment. Surprisingly, no periphery receptors provide information about the dimension of the different body parts in the brain. This body referencing processing is especially true for tactile sensation, but not only for that. For instance, in order to localize of an insect flying around us just through auditory information, our brain needs to compute the distance between the two ears. Similarly, for visual depth perception, the spacing between the two eyes must be taken into account (Serino & Haggard, 2010).

So, it is clear that, in order to entirely account for the different aspects of body experience involved in interaction with the environment, more complex higher-level multimodal representations of the body in the brain must exist, supporting complex perceptual, motor and emotional functions, and, ultimately, underling the experience of having a body and the ability of using that body to interact with the external world.

In the next paragraphs I will review main evidence about the existence of low-level and high-level body representations.

1.2.1 Unimodal low-level body representations

Much is known about unimodal body representations in the primary somatosensory cortex (SI; Kaas, Nelson, Sur, Lin, & Merzenich et al., 1979) and in the primary motor cortex (MI; Penfield, & Boldrey, 1937), each of which contains a tactile and a motor map of the body.

Penfield and colleagues (Penfield & Rasmussen, 1950), using direct cortical stimulation on patients undergoing neurosurgery, first described a somatosensory map in the post-central gyrus. The somatosensory cortex is divided in two parts, the primary somatosensory (SI) and the secondary somatosensory cortex (SII) at the level of the anterior portion of the parietal cortex in the post central gyrus. Somatosensory cortical areas receive a wide range of somatosensory inputs from different peripheral receptors, such as mechanoreceptors, thermoreceptors, and nociceptors, which activation determines an evoked sensation of different nature. And indeed different somatosensory functions are processed by distinct neural pathways: tactile information are transmissed through the dorsal column medial lemniscal pathway, while the anterolateral pathway conveys pain, and temperature information from the periphery to the brain. For sake of clarity, here I will focus mainly on tactile sensation.

Tactile processing is somatotopically organized, meaning that tactile stimuli administered on a given body part elicit a neural response in a specific portion of the somatosensory cortex, matching the same body part. Adjacent neurons on SI surface tend to have adjacent receptive fields on the body. In this representation, known as "somatosensory homunculus" the legs are represented medially, while the face and hands are more laterally.

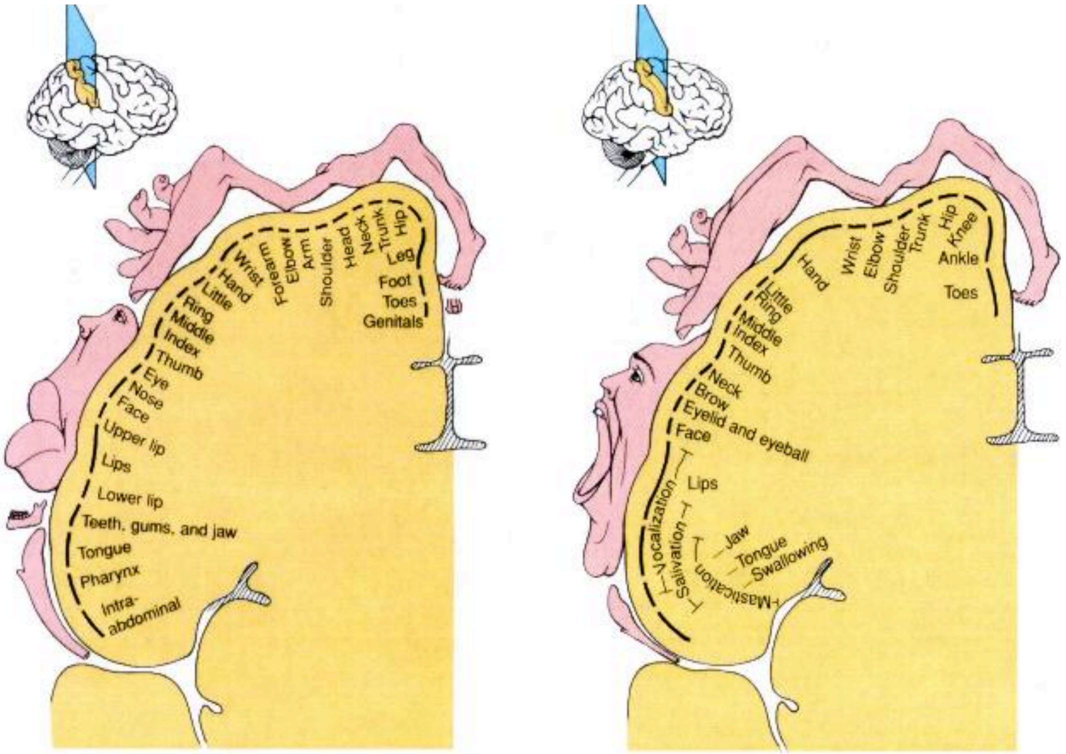

Figure 1.5 Schematic somatosensory (on the left) and motor (on the right) homunculus

In the case of the motor system, as for somatosensory perception, it has been demonstrated that movements of a specific body parts depends on neural activity in a matched region of the primary motor cortex (MI). Indeed, electrical stimulation of specific regions of MI evokes movements of a specific body part (Penfield & Boldrey, 1937; Penfield, 1950). As for SI, also MI is organized in a somatotopic way, with the trunk and legs represented more medially, while face, hands and arms are represented more laterally. Few studies have shown a somatotopic organization also at the level of the Supplemental Motor Area (SMA). Recently, Zeharia and colleagues (Zeharia, Hertz, Flash & Amedi, 2012) investigated movement encoding both in the primary motor cortex and supplementary motor area. Results confirmed that MI and SMA are organized in a somatotopic way, and that SMA activity is more associated with movement suppression as compared to M1.

Finally, functional magnetic resonance imaging (fMRI) studies have identified two separate regions, which specifically process body-related visual information: the extrastriate body area (EBA; Downing, Jiang, Shuman, & Kanwisher, 2001), and the fusiform body area (FBA). These two areas selectively respond to images of the whole body (as well as of non facial body parts) compared to other object categories (Downing et al., 2001; Peelen & Downing, 2005; Taylor, Wiggett, & Downing, 2007; for a review, see Peelen & Downing, 2007). In a recent fMRI study of Orlov and colleagues (Orlov, Makin, & Zohary, 2010), participants were scanned when viewing images of body parts. Results showed a consistent activation at the level of the occipital temporal cortex (OTC), with distinguishable clusters for separate body parts. Moreover the authors tested whether the separate clusters of activation within the body map for particular body parts could depend only on the particular shape of the body parts tested. Results show that separate images of the "hand" and the "elbow", for instance, consistently activated the area that was previously activated for the "upper limb". This suggested that the specificity of activation at the level of OTC for different body parts cannot be explained with a difference in shape only. Finally, this study showed a partial correspondence in the activation of visual and motor (unseen movements or self generated) body parts, suggesting that action related information about the body converge in this area.

Taken together, these low-level unimodal representations process information related to a single body part and single modalities, and thus they are not sufficient to entirely account for the different aspects of body experience involved in interaction with the environment.

In the next paragraph I will review neuropsychological and behavioral evidence about the existence of higher-level body representations in the brain.

1.2.2 Neuropsychological evidence

Several alterations of body representations, without any impairment at the level of primary somatosensory and motor cortices have been described in neuropsychological patients. These deficits result in alteration of body perception, which cannot be ascribed to pure sensory or motor deficits. For instance, the studies of patients suffering from *numbsense*, a tactile deficit with preserved tactually guided movements (de Vignemont, 2010; see also Dijkermann & de Haan, 2007) were especially relevant. Paillard and colleagues (Paillard, Michel, & Stelmach, 1983) reported the case of a patient who suffered from deafferentation after a left posterior cortical lesion. Deafferentation is a clinical condition characterized by a loss of somatosensory information that can affect a portion of the body (Dijkerman & De Haan, 2007). This patient was unable to report a tactile stimulus presented at the contralesional hand, but critically the ability of pointing to the same tactile target was preserved. Rossetti and colleagues (see Rossetti, Rode, & Boisson, 2001) reported a case of a patient, suffering from a lesion at the level of the thalamic nucleus VPL, who presented a similar dissociation: indeed he was able to point with the left hand directly to a tactile target at the impaired right hand, while verbal responses (and pointing responses on a drawing of the arm) were affected. The opposite dissociation was revealed by Paillard and colleagues (1985) in a patient with, instead, preserved ability to report a tactile stimulus, but deficit in pointing to it. These phenomena reviewed above supported the idea of two separate somatosensory pathways for action and conscious perception (see Dijkerman & De Haan, 2007, for a review). This dissociation supported the idea of the existence of different body representations, with a representation of the body that is used for action, more precisely for the guidance of movements, while more perceptual judgements about the spatial relations of the different body parts are supported by a different body representation, as suggested by several authors (see Paragraph 1.2.4 for a discussion on this point).

Other body representation disorders are more properly defined as distortions, like the feeling of having a body of different dimension that its actual size, i.e. *macrosomatoagnosia*, a" distorted awareness of the size of the whole body of body parts", de Vignemont, 2010), or the *Alice in Wonderland Syndrome*, a "distorted awareness of the size, mass, shape of the body or its position in space" (Todd, 1955; see also de Vignemont, 2010).

There are patients exhibiting abnormal belief about their body, not supported by real motor or somatosensory deficits (such as *finger agnosia*, the inability of recognizing their own finger). These abnormal beliefs can be associated with *somatoparaphrenia* (Gerstmann, 1942; see also Vallar & Ronchi, 2009), a pathological denial of ownership of contralesional limb that is felt as not belonging to oneself (Bottini, Bisiach, Sterzi, & Vallar, 2002; Critchley, 1953), sometimes in absence of somatosensory deficits. This phenomenon is often associated to hemispatial neglect (Vallar & Perani, 1986). Neglect patients are characterized by a failure to respond, to attend or to orient voluntarily to objects placed in the contralesional space. Neglect can have different manifestations: patients can exhibit a *personal neglect*, defined as "a lack of attention towards one's side of the body": in this case the patient do not voluntarily attend one side of their body, or also a *motor* manifestation that is the underutilisation of the contralesional side of the body, even in absence of primary motor or somatosensory deficits (Vallar, 1998).

Brain damaged patients with a lesion at the level of the premotor cortices frequently exhibited anosognosia for hemiplegia as a symptom. Anosognosia for hemiplegia is the denial of the contralesional motor deficits that may follow brain damage (Berti, Bottini, Gandola, Pia, Smania, Stracciari et al., 2005; Carruthers, 2008; Pia, Neppi-Modona, Ricci, & Berti, 2004). In this case patients have a motor problem, but they fail in recognizing the severity of their problem, instead they also claim that they do not have any body related problems. These disorders may be accompanied by reports of supernumerary limbs (Halligan & Marshall, 1995), that is the strong awareness of the existence of non-existent limbs.

The phantom limb, that is the strong awareness of an amputated limb, represents a well-known disorder of body representation (Hunter, Katz, & Davis, 2003; Ramachandran & Hirstein, 1998). This strong awareness of the phantom limb includes a series of sensory phenomena that are perceived as originating from the missing body part. The phantom limb phenomena could include tactile sensations, such as the sensation of being touched on the missing body part, as well as more generic somatic sensations such as tingling, itching, pressure, warmth, or cold (Hunter et al., 2003) or also motor sensations. Indeed amputees can report, generally immediately after amputation, being able to move their missing limb voluntarily, with this ability decreasing over time. These sensations are frequently accompanied by painful sensation originating from the missing limb. Importantly, in this case patient are aware of their amputation and that these sensations are not veridical (Serino & Haggard, 2010; see also Chapter 2). Interestingly, phantom limb phenomena are not limited to a sensory or motor percepts originating from the missing body part (Hunter et al., 2003; Kooijman, Dijkstra, Geertzen, Elzinga, & van der Schans, 2000), but are often referred by patients as conscious awareness of the presence - implying position, shape and size - of the missing limb (Flor, Nikolajsen, & Staehelin Jensen, 2006; Hunter et al., 2003). The complexity and richness of these phantom limb phenomena is hardly explainable as resulting only from cortical reorganization in unimodal primary cortices. Rather, they suggest an involvement of multisensory body representations, which integrate the continuous flow of information from different sensory modalities in order to give raise to the experience of the body and its parts (Blanke & Metzinger, 2009; Petkova, Bjornsdotter, Gentile, Jonsson, Li, & Ehrsson, 2011a; Ionta, Gassert, & Blanke, 2011; see Paragraph 7.4).

These studies on neuropsychological patients suggested that the experience of the body could be affected independently from primary somatosensory or motor deficits. The diversity and variety of bodily disorders suggested the existence of multiple and more complex body representations that account for a complete body experience.

1.2.3 Behavioural evidence

Different effects of interaction between multisensory body-related signals support the existence of multisensory body representation. For instance, in a study Kennet and colleagues (Kennet, Taylor-Clarke, & Haggard, 2001) showed that tactile information was improved by viewing the body tactilely stimulated, although visual information was totally uninformative about tactile stimulation (tactile stimuli were hidden from view). The authors measured tactile acuity by means of the 2-point discrimination thresholds on the forearm, while participants were looking either at the arm or at a neutral object, presented at the same location of the arm. Results demonstrated that spatial resolution of touch was better when participants could view the arm as compared to when participants viewed the neutral object. These results clearly show that viewing the body boosts tactile processing. The fact that participants did not see any information about the tactile stimulation during the task suggests that the visual information specifically related to the body offers a special context, that is the body itself, to which tactile information is referred to.

Tactile and proprioceptive inputs also interact to build and update high-level BRs: this is revealed for instance through some spectacular illusions, such as the Pinocchio illusion (Lackner, 1988; de Vignemont, Ehrsson & Haggard, 2005). In this illusion, participants held the tip of their nose with the thumb and the index finger while the tendon of the biceps muscle was vibrated. Vibration of this tendon normally elicited the sensation of the arm moving away from the body. When the nose and the finger were in direct contact, in order to solve the mismatching information about constant tactile sensation and dynamic proprioception, participants felt like their nose was elongating. De Vignemont and colleagues (2005) used the Pinocchio illusion to experimentally demonstrate that proprioceptive information is used to update body representation. In this experiment participants held their right index finger with the left index finger while the tendons of either the biceps or the triceps muscles of the right arm were vibrated. When the tendon of the biceps was vibrated, the arm was perceived as extending and it elicited the sensation that the left index finger was elongating. During the vibration participants received a couple of tactile stimuli at the finger and at the forehead as a reference body part, and they were asked to judge whether the tactile distance felt on the finger or the forehead was longer or shorter. Participants perceived the tactile distance as longer when the finger was perceived as elongating (that is, in case of the vibration of the tendon of the biceps of the forearm). The contrary effect, that is the perception of the tactile distance as shorter when the arm was perceived as contracting (so the finger was perceived shortening) was not found. These results suggested that proprioceptive information is used to update Body Representation: the internal representation of the body, such as the perceived body size, affected the perception of an external object. Critically the effect on the perceived tactile distance was evident only in the case of the perceived elongation, but not contraction, of the arm.

In a different study, Taylor-Clarke and colleagues (Taylor-Clarke, Jacobsen & Haggard, 2004) demonstrated the relevance of visual information in updating body representation. According to an illusion originally provided from Weber (1978), the same tactile distance is perceived larger when presented on a zone with higher tactile acuity, as compared to a zone with low tactile acuity. This illusion suggested that tactile information is processed with reference to tactile receptors density. In the study of Taylor Clarke and colleagues, participants performed a tactile distance perception task for two tactile stimuli presented simultaneously to the finger or the arm after a period of visual experience of these body parts. When subjects viewed an enlarged version of their arm (but not of the hand), the tendency to underestimate tactile distances on the arm relative to the hand was significantly reduced, while the tactile acuity remained unaffected. They demonstrated that perceptual judgements about an object touching the skin depend not only on the primary tactile sensations, but also on the perceiver's representation of the body part that the object touches. Indeed, in this case the *visual size* of the body is shown to affect the *tactile size* of an object touching the skin. These results suggest that tactile signals are processed with reference to an implicit representation of the body (see also Medina & Coslett, 2010). Finally, in a recent study Tajadura-Jimenez and colleagues (Tajadura-Jimenez, Väljamäe, Toshima, Kimura, Tsakiris, & Kitagawa, 2012) demonstrated that also auditory information contributes to update body representation. In their study participants performed an audio-tactile tapping task. They were asked to tap on a surface with the right arm and, in synchrony with the tap they produced, they listened to a tapping sound that originated at different distances from where they performed the tapping. After the task, in order to assess the perceived arm length, participants underwent a tactile distance task on the right arm. Results showed that when the sound originated at double the distance at which participants actually tapped, tactile distances on the test right arm, as compared to distances on the reference left arm, felt bigger than those before the exposure. These results are interpreted as an increase in the perceived arm length. Results from the present study provided an evidence of the contribution of self-produced sounds to body-representation, revealing an auditory-dependent plasticity of body-representation (Tajadura-Jimenez et al., 2012).

Finally, the probably most known and surprising phenomena revealing how multisensory inputs provide important inputs to high-level body representation is the so-called Rubber Hand Illusion (RHI). In RHI experiments, a realistic fake hand can be perceived as a part of one's own body if concurrent visuo-tactile stimulation is seen on the fake hand and felt on one's own hand, hidden from view (Botvinick & Cohen, 1998; see Tsakiris, 2010). This effect has been originally interpreted as vision dominating over proprioception and touch under conditions of multisensory conflict. If visual and tactile stimuli are presented asynchronously, the illusion does not occur, such as the visual and tactile stimuli appear to originate from different objects.

In order for the RHI to take place, however, the synchronicity between visual and tactile inputs is a necessary, but not a sufficient condition: indeed the fake hand needs to be lateralized as the real hand (Tsakiris & Haggard, 2005), oriented as the real hand (Costantini & Haggard, 2007) and placed in a spatial configuration compatible with body structure (Pavani et al., 2000). This means that for the RHI to be effective, tactile and visual information should be integrated in a realistic model of the physical body. The subjective feeling of ownership for the rubber hand is associated with physiological changes in the way bodily-related signals are processed. If participants experiencing the RHI observed a syringe stabbing in, they increased skin conductance response, indicating distress, and increased activity in anxiety-related brain areas (Ehrsson, Wiech, Weiskopf, Dolan, & Passingham, 2007). These kinds of behavioural, physiological and neural responses are usually associated to threat or damage to the real body. In addition, experience of ownership for the rubber hand also results in dropping of temperature of the real hand, such as that were disembodied (Moseley, Olthof, Venema, Don, Wijers, Gallace, & Spence, 2008), and increased immunity responses to inflammatory agents, such as an estranger organism has entered one's own body (Barnsley, McAuley, Mohan, Dey, Thomas, & Moseley, 2011). Thus, results from these studies suggested that under a condition of synchronous visuo-tactile stimulation the fake hand was integrated into body representation, inducing a change in body ownership: an object that is not part of the body is processed as an already existing part.

Such illusion has been demonstrated not only for the hand, but also per the entire body, i.e., the so-called Full Body Illusion (Lenggenhager, Tadi, Metzinger, & Blanke, 2007). In such illusion, by using a modified version of the RHI in a virtual reality context, participants viewed the back of their body from a distance of 2 m and projected onto a three-dimensional display. Under a condition of synchronous visuo-tactile stimulation perceived on their back and seen on their virtual body, participants mislocalised themselves toward the virtual body and feel ownership for the virtual body (see also the Out-of-body experience illusion, Ehrsson, 2007 and the body-swap illusion, Petkova, Khoshnevis, & Ehrsson, 2011b).

In summary, different results from the literature have revealed that, in humans, visual (Taylor-Clarke et al., 2004), auditory (Tajadura-Jimenez et al., 2012) somatosensory

(Kennet et al., 2001; see Serino & Haggard, 2010 for a review) and proprioceptive information (de Vignemont et al., 2005) is integrated in order to represent the perceived size of different body parts and of objects touching the skin (see also Longo, Azañòn, & Haggard, 2010a) in an high-level multisensory representation of the body in the brain.

1.2.4 Taxonomies of BR

There is little agreement in literature about the number and types of body representations in the brain. The first distinction was proposed by Head and Holmes (1911), by studying impairments in tactile perception in a brain damaged patient suffering from a surgical ablation of part of the precentral gyrus. Head and Holmes found that the brain lesion affected patient's ability to localise the position of his hand in space, leaving unaffected the ability to localise, by naming it, a tactile stimulus at the hand. Head and Holmes introduced a dyadic distinction between a Postural Schema, a representation of the position of the body parts in space, used for action execution and updating of postural changes, and Superficial Schema, a model of the skin surface used for localising bodily and tactile sensations.

After this seminal paper, different taxonomies of body representations have been proposed, based on the different kinds of body-related information. The currently most accepted taxonomy poses a dyadic distinction between Body Schema and Body Image. Body Schema is generally defined as a constantly updated representation of the position of different body parts in space in relationship with each other, derived from multiple sensory (proprioceptive, vestibular, tactile, visual, auditory, kinaesthetic) inputs. It is commonly accepted that Body Schema interacts with the motor system in the genesis of *actions*. The Body Image instead is an abstract and stable representation of the body for *perception*, more related to semantic or affective processes, and mainly influenced by visual inputs (de Vignemont, 2010; Gallagher, 2005; Schwoebel & Coslett, 2005). This action-perception duality reminds that originally shown in the visual domain (Goodale & Milner, 1992; Mishkin & Ungerleider, 1982), and more recently in the auditory (Belin & Zatorre, 2000) and somatosensory domains (Kammers, Longo, Tsakiris, Dijkerman, & Haggard, 2009; see Dijkerman & De Haan 2007 for a review).

Other authors (Schwoebel & Coslett, 2005) extended the original dyadic distinction between Body Schema and Body Image, adding a third component. This taxonomy maintained the concept of Body Schema as a sensorimotor representation based on afferent and efferent information and split the concept of Body Image in two different representations: the Body Structural Description and the Body Semantic. With the term Body Structural Description, they refer to a static description of the relationship between the different body parts in a fixed map of the body as it should normally be (e.g. with a head, which is above two arms, which in turn are above two legs). Instead with the concept of Body Semantics, authors refer to a more conceptual body representation, interfacing with language, aimed at describing the functional purpose of the different body parts and a categorical relationship between them (de Vignemont, 2010).

Other distinctions have been proposed based on different characteristics of body representation, such as the temporal dynamics. Some authors distinguished between online and offline body representation (Carruthers, 2008). With the term online representation, for instance, Carruthers refers to a representation of the body as it currently is, constructed and updated moment by moment by the different incoming multisensory inputs. Instead an offline representation refers to a more stable representation of what the body is usually like, made of the multiple, everyday life experiences concerning one’s own body and stored in memory. Given the different role of Body Schema for action and Body Image for perception, the concept of online body representation applies more to the former, whereas that of offline body representations applies to the latter.

More recently, Longo and colleagues (2010a) proposed a general body model that distinguishes between two major classes of high-order body representations, named *somatoperception* and *somatorepresentation*. The first term refers to the process of perceiving the body itself, while the second one is more related to abstract knowledge, beliefs and attitudes towards one’s own body.

However, at the moment, the exact number and functions of different body representations is matter of debate (see Kammers, Mulder, de Vignemont, & Dijkerman, 2010). Different attempts have been made to distinguish between different body representations. So far, the problem has not been solved yet. For this reason, hereafter I will adopt the neutral term Body Representation to define high-level, multisensory representations of the body, supporting perceptual and motor functions more complex that those implemented in the unimodal homunculi in the primary sensory and motor cortices.

1.2.5 Neural basis

In monkeys, neurons in the superior parietal cortex, particularly in area 5 (Laquiniti, Guigon, Bianchi, Ferraina, & Caminiti, 1995; Graziano, Cooke, & Taylor, 2000; Sakata, Takaoka, Kawarasaki, & Shibutani, 1973) are thought to encode the position and movement of the hand in body-centered coordinates. These neurons have both sensory and motor properties, since they receive projections from the primary somatosensory cortex and they project to the primary motor and premotor cortex.

These neurons vary their responses as function of the seen and felt position of the monkey's arm, with a preference for particular postures of the limb, thus integrating visual and proprioceptive information in encoding the spatial location of a limb. Neurons of area 5 are also active immediately before and during reaching movements and object manipulation (Snyder, Batista, & Andersen, 1997), independently from somatosensory stimulation (Mountcastle, Lynch, Georgopoulos, Sakata, & Acuna, 1975; Seal, Gross, & Bioulac, 1982; see also Graziano & Botvinick, 2002 for a review). Finally, neurons in this area also respond to visual information concerning arm position, being their firing rate modulated by the vision of a fake monkey arm (Graziano et al., 2000).

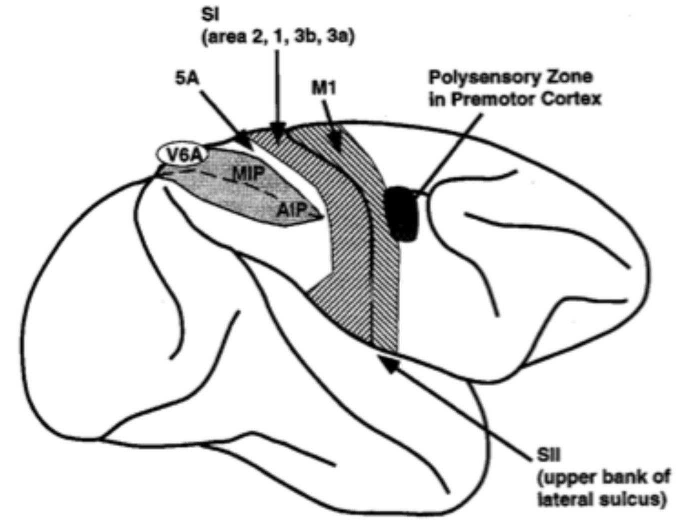

Figure 1.6 Side view of the macaque monkey brain showing some of the cortical areas involved in representing the physical configuration of the body. The intraparietal sulcus is shown opened up to expose the buried cortex. MIP= medial intraparietal area, AIP=anterior intraparietal area, 5A=anterior area, M1=primary motor cortex, SI=primary somatosensory cortex, SII=secondary somatosensory cortex. **Adapted from Graziano & Botvinick, 2002.**

In an fMRI study, Lloyd and colleagues (Lloyd, Shore, Spence, & Calvert, 2003) identified regions involved in the encoding of limb position in the human brain.

Participants received a tactile stimulation at the right hand with the hand either placed in the right or in the left hemispaces. In absence of vision, authors found an increased activation at the level of the right parietal cortex when the hand was in the right hemispaces. This activation shifted to the left parietal cortex when participants performed the task with the eyes open and with the left hand across the body midline in the left hemispace. They showed also activation at the level of the left ventral premotor cortex, left medial intraparietal sulcus and the junction of the left angular and supramarginal gyrus. These results are in line with results in non-human primate, showing that a parieto frontal circuit has been shown to mediate multisensory representation of limb position (Graziano, 1999; Rizzolatti, Fogassi, & Gallese, 2002). Bolognini and Maravita (2007) further investigate the role of the posterior parietal cortex in the spatial remapping of touch. With the terms we refer to the process of converting tactile location from a somatotopic map to an external frame of reference. Participants received TMS stimuli at the primary visual cortex for the inducement of phosphenes and were asked to verbally report any perceived visual sensation. Unpredictable tactile stimuli were presented at the hands. Results showed that visual sensitivity (the number of phosphenes reported) was enhanced when a tactile stimulus was spatially aligned with the reported location of the phosphenes in the external space. This facilitation was maintained when participants performed the task crossing the hands over the body midline, suggesting the existence of spatial remapping of these visual-tactile spatial effects across postures. When the activity of PPc was disrupted after repetitive TMS, in the hand crossed condition phosphenes detection was enhanced by tactile stimuli misaligned in external space, suggesting that the disruption of PPC activity has affected the ability of updating body parts position in space. Thus, the present study provided evidence for the important role of the posterior parietal cortex in maintaining visual and somatosensory maps in the brain updated. These results have been confirmed by a study of Azanon and colleagues (Azanon, Longo, Soto-Faraco, & Haggard, 2010). In this study participants were asked to compare the elevation of tactile stimuli administered on the arm suspended and oriented vertically, lateral to the face, as compared to tactile stimuli presented at the forehead, in absence of vision. The arm position (upper or lower) was passively manipulated trial by trial. Single pulse TMS stimulation over the PPc was applied every trial after every tap at the arm. Results showed that TMS over PPc impaired participants' performance, as compared to a control condition in which TMS was applied over the vertex. Authors did not observe any impairment in proprioceptive judgements or in tactile localisation *per se*, suggesting a role of PPc specifically in the tactile remapping of space, a process that involves the integration of tactile localisation on the skin with proprioceptive localisation of body parts in space.

Integration of body-related multisensory information that underlies the feeling of body ownership, as shown by the so-called Rubber Hand Illusion (see Paragraph 1.2.3) is associated with a modulation of neural activity in ventral premotor cortex and in the posterior parietal cortex (Ehrsson, Spence, & Passingham, 2004; Ehrsson, Holmes & Passingham, 2005; Ehrsson et al., 2007). Interestingly, these areas are thought to play an important role in the representation of the peri-hand space, suggesting that the multisensory integration of tactile stimuli at the hand and visual stimuli presented close to the hand plays an important role in eliciting the RHI. Indeed, according to Makin and colleagues (Makin, Holmes, & Ehrsson, 2008), the posterior parietal cortex seems to integrate multisensory information with respect to the rubber hand. Makin and colleagues suggested that illusory body parts ownership might involve trimodal neurons, at the level of the premotor and parietal cortices, which integrate tactile stimuli on a specific body part (head, face neck, trunk or shoulders) with visual and/or auditory stimuli close to the same body part (see Paragraph 1.1.1 for a full description). It has been proposed that during the Rubber Hand Illusion, but also during the Full Body Illusion (see Blanke, 2012, for a review), just seeing the fake body being stimulated and experiencing a synchronous tactile stimulation may lead to a shift of the receptive field of multisensory neurons towards the fake body parts.

Taken together these studies suggest that somatosensory, proprioceptive, visual and kinaesthetic inputs are integrated in parietal and premotor areas, in order to represent the shape and position of different body parts in space (see also Dijkermann & de Haan, 2007 and Medina & Coslett, 2010 for reviews), this suggesting that a fronto-parietal circuit seemed is involved in representing the body in the brain.

"Anything which participates in the conscious movement of our bodies is added to the model of ourselves and becomes part of those schemata: a woman's power of localization may extend to the feather of her hat."

Head and Holmes, 1911

CHAPTER TWO: PLASTIC PROPERTIES OF PERIPERSONAL SPACE REPRESENTATION AND BODY REPRESENTATIONS

2.1 Plastic properties in Peripersonal Space representation

A critical property of Peripersonal Space representation is that it is dynamically modified through experience: using a tool to reach objects in far space extends the limits of PPS representation. Indeed, near and far space are separately represented, but what is near or far is not defined a priori, but functionally depends upon movements that allow the body to interact with objects in space. Here I will review neurophysiological studies on primates and neuropsychological and behavioural studies in humans revealing tool-dependent modifications in PPS representation.

2.1.2 Neurophysiological evidence

In monkeys, Iriki and colleagues (Iriki, Tanaka, & Iwamura, 1996) showed that hand-centred visual RFs of neurons located in the intraparietal sulcus elongated after a training period of using a rake to retrieve pieces of food placed at a distance. Critically after a period of inactivity the size of the visual RFs came back to the normal size. In a different study, Iriki and colleagues (Iriki, Tanaka, Obayashi, & Iwamura, 2001; see also Maravita & Iriki, 2004, for a review) trained a monkey to use a tool under visual feedback of their hand provided through video-captured images projected on a monitor in the far space. After tool-use, the visual receptive field of the neuron recorded in the intraparietal sulcus were shown to extend up to the image of the hand holding the rake in the monitor. These results suggested that the visual image of the hand (and its 'virtual' equivalent in the monitor in this case) was treated by the monkeys as an extension of their own body. These pioneering studies have been usually taken as an evidence of Peripersonal Space extension after tool-use in primates.

2.1.2 Neuropsychological evidence

Evidence for corresponding dynamic properties also in humans came from neuropsychological studies on brain damaged patients. Berti and Frassinetti (2000) examined the effect of tool-use on a brain damaged patient suffering from a form of neglect selective for the space close to the body, exhibiting a classic rightward bias in a bisection line task only when the task was performed in peripersonal space (see also Chapter 1, paragraph 1.1.2), and not in the extrapersonal space. Authors showed that when a long stick was used to perform the same bisection task in far space, the patients showed a similar rightward bias. These results suggest that when the stick made the far space "reachable", this became automatically coded as it was near space.

Further neuropsychological studies on extinction patients demonstrated that after using a tool to retrieve distant objects for five minutes, crossmodal extinction for a tactile stimulus presented at the contralesional hand increased when a visual stimulus was presented at the tip of the tool, as compared to before tool-use (Farnè, Iriki & Làdavas, 2005; Farnè & Làdavas, 2000; see also Maravita, Husain, Clarke, & Driver, 2001 and Làdavas, 2002). Peripersonal space expansion lasted only few minutes after tool use: after five minutes of resting period the extent of crossmodal extinction at the tip of the tool regained a pre tool-use level, suggesting that patient's peripersonal space contracted backwards, in close similarity with monkeys studies. The peri-hand space extension produced by tool-use was not perfectly coincident with the length of the tool. Indeed, Farnè and colleagues (Farnè et al., 2005) compared the compared the extent of crossmodal extinction after the use of two different tools, one longer (60 cm) and the other shorter (30 cm). Cross modal extinction was assessed at two different positions of space, specifically at 60 cm and 30 cm. They found that in the case of the short tool-use, a weaker – but still present - extension effect was found even at 60 cm of distance. These results suggested that the extension area of peripersonal space did not perfectly correspond to the tip of the tool, but partially extended beyond it. Critically in the same study the effect of a 60 cm long tool, but with the functional part located at 30 cm, on peripersonal space representation was tested. By using this tool indeed was possible to dissociate the effective length of this tool from its functional properties. Results showed the level of crossmodal extinction was more severe at 30 cm, at the spatial area corresponding to the functional part of the tool. These results are compatible with other studies suggesting that an active experience with the tool is critical in promoting an extension effect, since a prolonged but passive exposure to the tool failed to elongate the peri-hand space (Maravita et al., 2001).

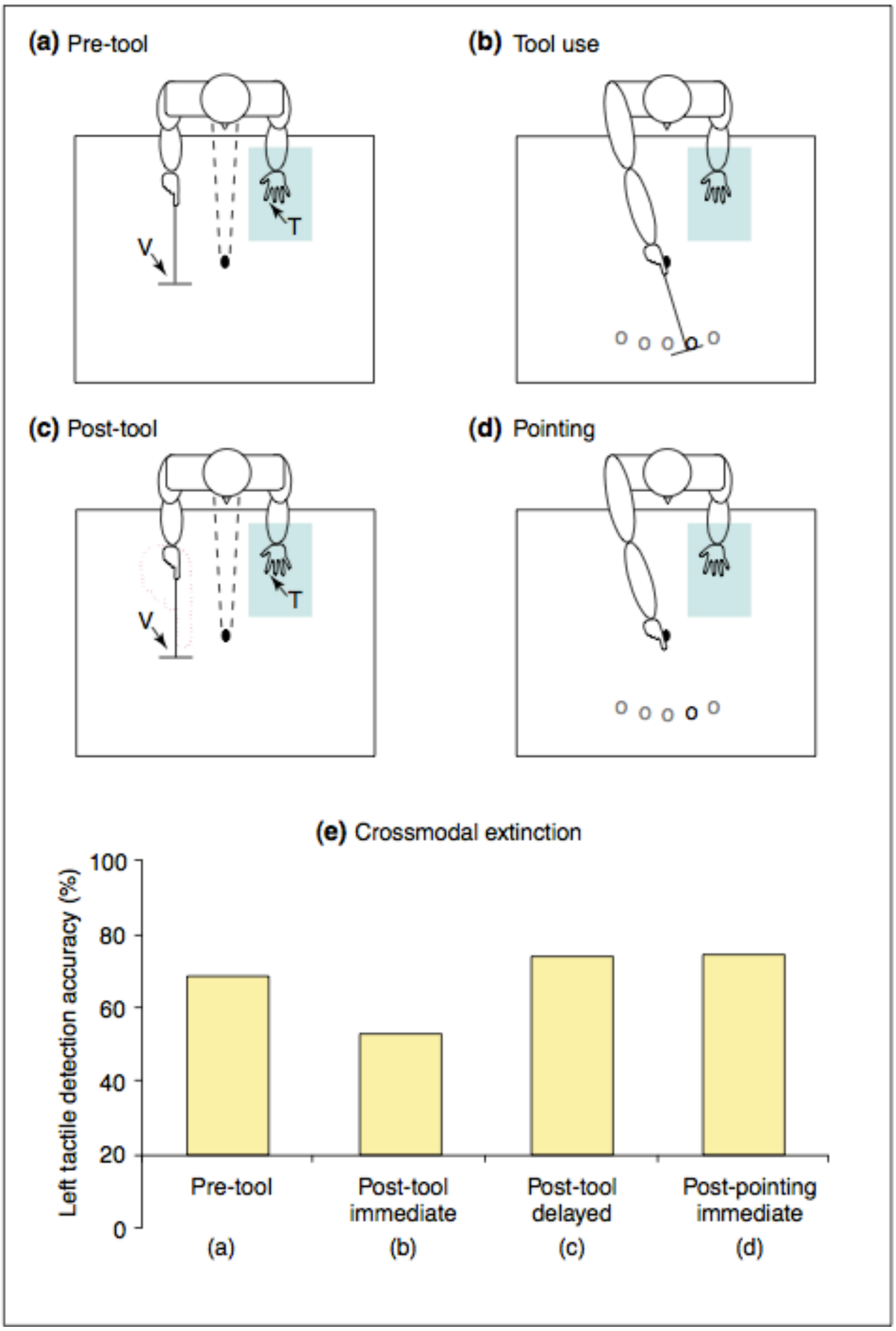

Figure 2.1 Schematic drawings of the experimental set-up in a study to assess the spatial extension of peripersonal space. (a). The location of visual (V) and tactile (T) stimulation is indicated by arrows. Crossmodal extinction was assessed before (a) and after (c) the patient used a rake to retrieve distant fishes (b, open circles) or pointed towards them (d). The patient's left hand was always occluded from view by a cardboard shield (shaded area). The large dotted red hand symbolically represents the extension of the reaching space of the patient's hand. (e) Mean percentage correct detection of the left tactile stimulus in each experimental condition. **(Modified from Farnè & Làdavas, 2000; adapted from Làdavas, 2002).**

Different studies have focused on whether this plastic modification of peripersonal space was more compatible with a proper extension effect encompassing the entire length of the tool or rather with a shift of this integrative space to the tip of the tool. Farnè and colleagues (Farnè, Serino, & Làdavas, 2007; Bonifazi, Farnè, Rinaldesi, & Làdavas, 2007) tested the severity of crossmodal extinction in different positions along the tool axis, showing that the level of extinction significantly increased both at the middle and the tip of the tool, but with no effect at the tool handle. These results strongly supported the idea that tool-use promote an incorporation of the entire tool in its representation (see also Holmes, 2012 for a discussion of this hypothesis).

Taken together these results suggested that using a tool created a connection between the hand holding the tool and visual stimuli coming from a portion of space including the tip of the tool in the far space. This suggested that, following tool-use, the multisensory peri-hand area where visual and tactile stimuli were integrated was pushed farther in space up to include the entire tool length, in order to allocate processes multisensory stimuli where the goal of the action was.

2.1.3 Behavioural evidence

Tools

An extension of the limits of tactile, visual and/or acoustic stimulus integration has been shown also in healthy subjects after short term (Holmes, Calvert & Spence, 2004; Maravita, Spence, Kennett and Driver, 2002; but see also Holmes, Calvert, & Spence, 2007a; Holmes, 2012) and long term (Bassolino, Serino, Ubaldi, & Làdavas, 2010; Serino et al., 2007a) tool-use.

To investigate peripersonal space extension after tool-use in healthy subjects, Maravita and colleagues (Maravita et al., 2002) took advantage from the crossmodal congruency task (see Chapter 1 for a detailed description of the task). In this experiment participants held two sticks (more precisely two golf clubs) in their hands. Their task was to detect a vibrotactile stimulation administered at the two hands while visual stimuli were presented at the tips of the tools. Participants performed the task either with the two tools crossed or uncrossed. When the tools were uncrossed, the visual distractors at the tip of one tool interfered more strongly with vibrotactile stimuli administered at the ipsilesional hand as compared to the contralateral hand, suggesting that stimuli coming from the same side of space interacted more effectively. Instead, in the crossed condition, the visual stimuli presented at the tip of the tool in the right hemispace interacted more effectively with the tactile stimulus administered at the left hand, because they interacted within the same hemispace. These results suggested that the tool created a link between the hand and the far space where the tool was used, promoting a remapping of this far space as close to the body. In a series of experiment, Holmes and colleagues (Holmes et al., 2007a) further investigated the hypothesis that tool use modifies peripersonal space (see also Holmes et al., 2004; Holmes, Sanabria, Calvert, & Spence, 2007b; see Holmes, 2012, for a review). Authors tested crossmodal interactions in the peri hand space by interleaving trials of the crossmodal congruency task with an active tool use task (that is using the tool to push a small button located in the far space). This way, the effect of tool-use could be studied in moments immediately preceding and following active tool movements. In this study participants performed the crossmodal congruency task while holding a tool in the left and right hand. Tactile stimulation was administered at the hands, while the visual distractors were presented either close to the participants hands', at the middle of the tool or at the tip of the tool. Results showed an increased interaction between tactile stimuli and visual distractors at the hands and at the tip of the tool. Interestingly, when participants were asked to shift from the right to the left tool in a predictable way (i.e. every 4 trial), multisensory integration increased as a function of the number of trial. Instead, in a random condition (where the shift between right and left was unpredictable), the level of crossmodal interaction remained constant for the entire duration of the task. Results from the present study demonstrated an effect of tool-use movement preparation on the extent of crossmodal interaction, showing that multisensory interactions change trial-by-trial basis, depending on the predictability of the next movement.

The PPS expansion effect has been described mainly after a brief training with a tool, resulting in short term expansion of peripersonal space that lasted only for short time intervals. Interestingly, two different studies from Serino and colleagues investigated whether a daily experience with a tool could promote a long-term extension effect on PPS representation. In a first study Serino and colleagues (Serino et al., 2007) investigated audio-tactile interaction in blind participants. The paradigm used was an audio-tactile interaction task (see Chapter 1, Paragraph 1.1.4). In this paradigm participants received tactile stimuli at their index finger, while a concurrent sound was presented. The sound position in space was manipulated, so that in different trials it was presented either close to the participant's hand (near condition) or far from it, at a distance of around 125 cm (far condition). Participants were asked to verbally respond to the tactile stimulation as quickly as possible, by saying TAH in a microphone while ignoring the auditory stimuli during the task. By using this paradigm was possible to compare audio-tactile interaction at the hand and at the tip of the tool. Participants performed the task while holding either their cane or a short handle. Results showed that when holding the handle, participants tactile RTs were faster when the sound was presented in the peri-hand space, as compared to the far sound condition. Their performance in this condition was totally comparable to the performance of a group of blindfolded healthy subjects in the same experimental condition. When healthy participants performed the task after a brief training with the long tool, the facilitation of tactile stimuli associated with near sound disappeared, revealing an extension of auditory peri hand space up to the tip of the tool, as described for visual peri-hand space. After a period of inactivity, the extent of peripersonal space came back to the pre-training level. Interestingly, when blind participants, selected for a long experience of using a cane, performed the task just holding the cane, without any previous training, the pattern of response was completely reversed: blind cane users were faster in responding to tactile stimuli at the hand associated with far auditory stimuli (i.e. coming from the space at the tip of the cane) as compared to near stimuli (see also Figure 2.2). Results from the present study suggested that the modulation of auditory peri-hand space is highly plastic, varying as a function of experience: a short training can result in a limited extension of peripersonal space, while long-term experience, as in the case of blind cane users, result in a durably extended representation of peripersonal space.

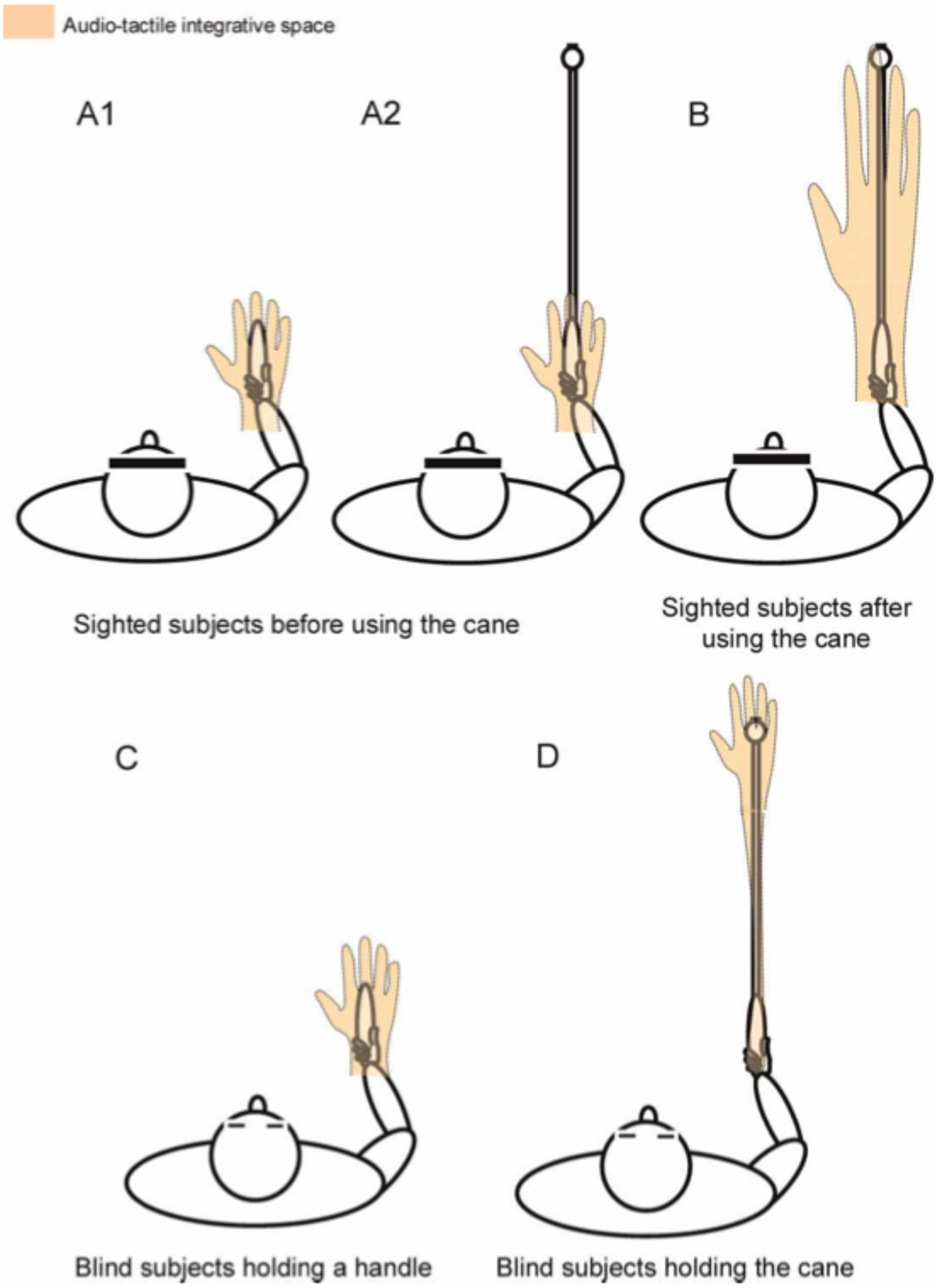

Figure 2.2 Schematic drawing of the effects of short-term versus long-term experience of tool use, as assessed by Serino and colleagues **(Serino et al., 2007).**
Upper panel: audio-tactile integrative space (metaphorically represented by the transparent hand) around the hand before and after tool use in sighted participants. Before using a cane, audio-tactile integration is limited around the hand, independently from the length of the cane yielded by the participants (A1 and A2). After a training with the cane, the auditory peri-hand space expands to include the cane (B). Lower panel: audio-tactile integration in the space around the hand in blind cane users. When blind participants hold the cane (D), but not a short handle (C), the auditory peri-hand space shifts to the tip of the cane. **Adapted from Làdavas & Serino, 2008.**

These results were confirmed and extended by a further work from Bassolino and colleagues (2010), where they studied the extent of auditory peripersonal space in mouse users in three different conditions: using the mouse to perform a task in the far space, passively holding the mouse in the hand, or no mouse condition. They showed an extension of peripersonal space while participants performed the audio-tactile interaction task both actively using and passively holding the mouse. These extension effects was selective for the effector used, since when participants performed the task with the left hand, that was rarely used to control the mouse, peripersonal space extended only in the active condition, but not in the passive one.

Body mirrors and shadows

All the studies previously described focused on a remapping of far space as near one due the use of a tool that allowed them to reach far object. However, there are other situations whereby stimuli presented far from the body could be related to tactile stimuli presented on the body surface, as in the case of mirrors and shadows of the body. The efficacy of mirrors in binding personal space and extrapersonal space has been demonstrated both in right brain damaged patients and in healthy subjects.

Maravita and colleagues (Maravita, Spence, Clarke, Husain, & Driver, 2000) assessed cross-modal extinction for tactile stimuli administered at the contralesional hand of patients, when ipsilesional visual stimuli were delivered close to a mirror reflection of the patient's hand. The visual stimuli, even if actually far from the patient's hand, increased tactile extinction at the patients' hand. Similar results were obtained by using the cross modal congruency task in healthy subjects (Maravita et al., 2002). These results suggested that a portion of far space, corresponding to the portion of space surrounding the hand's reflection in the mirror was remapped as the space immediately close to the hand, thus creating a connection between near and far space through the mirror. Similar results were obtained in experimental studies on body shadows (Pavani & Castiello, 2004). Body shadows represent a body shaped visual stimulus that generally follows body movement and adapts to every change of the physical body across the entire life. Pavani and Castiello (2004) used a visuo-tactile crossmodal congruency task (see above) to investigate possible cross modal interaction between tactile stimuli presented at the hand and visual stimuli presented close to shadows of the hand, in a far portion of space. Results showed visual stimuli presented around the shadow of the hand interacted with tactile stimuli at the hand, demonstrating that the hand shadow was able to create a connection between the peri-hand space and the far space, promoting a remapping of far space as it was near (see also Pavani & Galfano, 2007). Critically, this effect was specific for the hand shadow, because when a non-body shaped shadow was used (with participants wearing a particular glove that projected a polygonal shape), authors did not replicate the same effect as for the body shadow. This study suggested that the body shadow could share with the tool the possibility to extend peripersonal space to the far space. This property would give a small advantage in detecting a potentially harmful stimulus that is approaching the body. For instance when we are walking in a sunny day and we see the shadow of a potential dangerous stimulus close to our body shadow, it is necessary to immediately process information presented close to our shadow as close to the body, in order to plan an appropriate motor reaction.

2.1 Plastic properties in Body Representations

As the body changes continuously in position and dimensions throughout life, its brain representations need to be updated in order to correctly interact with the external world. Body representations take in account every perceptual input related to the body. So it is reasonable to think that body representation should be plastic enough to update accordingly to slow and fast changes the body undergoes with time.

2.1.1 Plastic changes in unimodal Body Representations

A series of studies demonstrated a relationship between changes in the physical body structure and unimodal body representations. One of the best examples revealing a link between primary cortical activity at the level of the primary somatosensory cortex and body representation is represented by deafferentation. Deafferentation is a clinical condition characterized by a loss of somatosensory information that can affect a portion of the body (Dijkerman & De Haan, 2007). A possible cause for deafferentation is a nerve resection or anaesthesia. Studies on monkeys (Jenkins, Merzenich, & Recanzone, 1990; Pons, Garraghty, Ommaya, Kaas, Taub, & Mishkin, 1991) demonstrated that the deafferentation of peripheral inputs from a body part induces a plastic reorganization at the level of the somatosensory cortex. After deafferentation, a part of somatosensory cortex that previously responded to inputs coming from the deafferented body part started to respond to afferent stimuli coming from adjacent portions of skin. In humans (Rossini, Martino, Narici, Pasquarelli, Peresson, Pizzella, et al., 1994a), it has been demonstrated that cortical responses coming from unanaesthetized fingers were increased following a relatively brief period of anaesthesia of the adjacent finger, providing another example of short term plasticity effects in the brain due to the loss of afferent somatosensory information (see Serino & Haggard, 2010, for a review). This cortical reorganization follows a somatotopic principle, since, for instance, it has been demonstrated that anaesthesia of a foot does not imply a cortical reorganization at the level of the area of the face, since these two body parts are not adjacent at the level of the SI. These deafferentation effects could be explain with the unmasking of existing synaptic connections between adjacent areas of SI (Buonomano & Merzenich, 1998; see Serino & Haggard, 2010).

The phantom limb syndrome represents one of the stronger examples revealing a link between unimodal cortex activity and the body experience. The phantom limb experience results from limb amputation or deafferentation, and includes a general awareness of the existence of the missing body part. Patients, although being aware of the fact that the missing limb is not present, report a series of somatic sensations that could be also strongly painful originating from the missing limb. One interesting feature of phantom limb is represented by referred sensation, i.e., sensation localized to a phantom body part after tactile stimulation of another part of the subject's body (Ramachandran, Rogers-Ramachandran, & Stuart, 1992). In amputees patients indeed it is frequent that a touch on the face elicited a tactile sensation on the missing body part. Critically, at the level of primary somatosensory cortices, the representation of face and arm are adjacent. So, these referred sensations have been interpreted as a sign of cortical reorganization of primary sensory cortices that dynamically adapt to the change in the physical body structure. Indeed, the deprivation of the afferent inputs that normally come from the amputate body part leads the neighbouring portions of the SI map to ''invade'' the cortical territory previously representing the amputated body part. As a consequence, that part of the cortex that was previously responding to the arm now responds to the face, leading to an activation of two different percepts. This form of plasticity at the level of SI after amputation has been explicitly investigated in humans. Farnè and colleagues, by studying the case of an upper limb amputee who underwent a hand transplant, showed that amputation-induced remapping, however, reverses after transplantation, as the grafted hand regains its sensorimotor representation (Farnè, Roy, Giraux, Dubernard, & Sirigu, 2002; see also Giraux, Sirigu, Scheneider, & Dubernard, 2001). Borsook and colleagues (Borsook, Becerra, Fishman, Edwards, Jennings, Stojanovic, et al., 1998) in an fMRI studies experimentally investigated whether these plastic phenomena at the level of SI after amputation depend on the unmasking of synaptic connections between adjacent areas of SI in an fMRI study. They tested an upper limb amputee within 24 hours following an above the elbow amputation of his left arm and they observed that tactile stimulation at the ipsilateral face elicited precise sensations at the phantom limb. These elicited phantom sensations activated the contralateral posterior cingulate gyrus, supplemental motor area and the post central gyrus, in close proximity with the part of the primary somatosensory cortex where the hand is represented. These activations in the hand area when participant was touched on the face 24 hours after amputation suggested that the process of plastic that take place in SI followed a somatotopic principle and happened rapidly.

Di Russo and colleagues (Di Russo, Committeri, Pitzalis, Spitoni, Piccardi, Galati et al., 2006) investigated changes in the primary somatosensory cortex in case of elongation of a limb in a group of achondroplastic dwarfs. The elongation technique offers the possibility to study a change in the physical body structure that usually takes place extremely slowly during our life. Two patients, submitted to progressive elongation of lower limbs were tested both with somatosensory evoked potentials (SEPs), fMRI and behavioral testing. Coherent results from SEPs and fMRI data indicated a functional reorganization in SI for foot stimulation immediately after the elongation ending.

It has been demonstrated that not only the deprivation of afferent inputs from the physical body could affect the somatosensory body representation in SI, but also the quantity of the tactile inputs. In monkeys, Recanzone and colleagues (Recanzone, Merzenich, Jenkins, Grajski, & Dinse, 1992) demonstrated that when the monkey underwent a tactile training with one digit, the cortical representation of this digit expanded in SI. Braille readers represent a well-known example of the same concept in humans. These people have a greater tactile ability, since they have a long-term experience in using tactile information to read. Interestingly, it has been demonstrated that only the right index finger, that is used to read, but not the left one, had an increased representation in SI (Pascual-Leon & Torres, 1993; see also Braun et al., 2000 for similar results in case of active tactile stimulation and Godde et al., 2000, for passive tactile stimulation; see also Serino & Haggard, 2010, for a review).

Taken together these experiences provided evidence for strong plasticity effects in unimodal body representation due to a change in the physical body structure and in the amount of afferent information projecting to unimodal somatosensory cortices.

2.1.2 Plastic changes in multisensory Body Representations

The representation of the body in the brain is a rather complex phenomenon. As previously reviewed in Chapter 1 a complete experience of the body is possible because multisensory (proprioceptive, tactile, visual and auditory inputs body related) are continuously integrated in order to update body perception. A series of studies, extensively reviewed in Chapter 1 (see Paragraph 1.2.3) demonstrated how stimuli presented in different sensory modality dynamically update a multisensory high-level body representation (see Taylor-Clarke et al., 2004; de Vignemont et al., 2005; Tajadura-Jimenez et al., 2012). A further study of Gandevia and Phegan (1999) demonstrated how incoming tactile information affected body size perception. In their study, participants were asked to draw the size of their thumb before and after a digital anaesthesia following three different interventions: nerve block, cutaneous topical application or cooling. Results show that participants reported an increase in the perceived size of the anaesthetized thumb. The same effect was found also for the lips, which are represented closer to the hand at the level of the somatosensory homunculus in SI, while the perceived size of both index fingers was not affected.

The most striking phenomena of plasticity in high-order BR remains the Rubber Hand Illusion: a series of evidence, previously reviewed in Chapter 1, demonstrated that the perception of what is part of the body can be dynamically updated under certain conditions: the illusory ownership of a fake hand can be induced under a condition of synchronous visuo-tactile stimulation. This body-ownership of an object that is not part of the body arises as an interaction between current multisensory input and internal models of the body (see also Tsakiris, 2010, for a review).

Tool-use

Since a long time now it has been suggested that body representation is plastic and can incorporate external objects that have a systematic relation to the body itself, such as clothes, ornaments and tools (Berlucchi & Aglioti, 1997; 2010). Benjamin Beck (1980) defined tool-use (and thereby those objects that one could consider as a ‘tool’) as follows:

“...tool use is the external employment of an unattached environmental object to alter more efficiently the form, position, or condition of another object, another organism, or the user itself when the user holds or carries the tool during or just prior to use

and is responsible for the proper and effective orientation of the tool."

Under appropriate circumstances, hand-held tool, for instance, may become so familiar that it feels as if it is a natural extension of the hand. Such changes however, are usually temporary and contingent to the duration of the relationship between the body and the tool used.

Three recent papers demonstrated a specific change in BR following tool-use. Cardinali and colleagues (Cardinali, Frassinetti, Brozzoli, Urquizar, Roy, & Farnè, 2009a) showed that kinematics of arm movements during hand grasping changed after pincers were used to grasp objects. This effect did not depend on a fatigue effect due to handling the tool, since a training with a weight identical to the tool weight did not change in any of the kinematic parameters. This effect was also associated with a change in the localisation of tactile stimuli on the arm. Taken together these results showed that tool-use affected arm motor behaviour and at the same time the somatosensory representation of the body part used to perform the motor action.

In a recent study, the same group (Cardinali, Brozzoli, Urquizar, Salemme, Roy, & Farnè, 2011) tested whether the effects of tool-use on body representation was specific for a representation of the body used for action (i.e., the so-called Body Schema) and not for a more perceptual body representation (i.e., the so-called Body Image; see paragraph 1.2.4). To this aim, participants were tested after tool-use using tasks that required a motor response (pointing to a body part) or a perceptual judgement (localising a body part on a ruler). According to their hypothesis, tool use should specifically affect only a motor response. Moreover, they also investigated whether the incoming information provided to subjects during the task may play a role in determining which body representation is used. They found that perception of forearm length increased after tool-use for both tasks, but only when the input for the task (which body part was to localise) was given tactilely (by touching the target body part) and not verbally (by naming the target body part). Finally, Sposito and colleagues (Sposito, Bolognini, Vallar, & Maravita, 2012) demonstrated a change in the internal representation of body part size (i.e. the forearm) following a training with a functional tool. In a first experiment, participants performed a task with a 60cm long tool used in order to retrieve objects placed in the far space. Before and after the training, participants were asked to perform a bisection task, in which they had to indicate the midpoint of their right upper limb segment, considering the elbow and the tip of the middle finger as the two extremities. Results showed that after the training participants located the midpoint of their forearm used during the training more distally. This result is compatible with an extension of the perceived length of the arm after the tool. In a second experiment, participants performed the same training with a 20cm long tool. In this case, any change in forearm midpoint was observed. Finally, in a third experiment, participants performed the task with the 60cm long tool both with the dominant and non-dominant arm. Results from this experiment showed an increased in the perceived forearm's length after tool-use, as for the first experiment. These results are in line with results from Cardinali and colleagues, showing that body-space interactions requiring the use of tools that extend the natural range of action resulted in measurable dynamic changes in body perception.

Summary

A series of evidence, coming from neurophysiological studies on monkeys, neuropsychological studies on brain damaged patients and behavioural studies in healthy volunteers confirms that the limits of multisensory integration, normally occurring in the space around the body, shift to the far space if a tool is used to increase the body action space (see Paragraph 2.1). These studies show that the extent of PPS representation can be dynamically shaped as a function of where subjects act upon external objects, i.e. their action-space (Gallese & Sinigaglia, 2010). Moreover, some studies demonstrated that tool-use affected upper the limb kinematics, the somato-motor representation of the arm (Cardinali et al., 2009a; Cardinali et al., 2011; Sposito et al., 2012) and the perceived dimension of the arm used to perform the training.

Some authors (i.e. Iriki et al., 1996; Maravita & Iriki 2004) have proposed that the extension of PPS after tool-use reflects a plastic modification in BR, such that the tool is incorporated as a part of the body (Berlucchi & Aglioti, 1997; Critchley, 1979; Head & Holmes, 1911; Holmes & Spence, 2006; Maravita, 2006). Interestingly in the majority of these studies, tool incorporation has been only indirectly demonstrated through perceptual changes in PPS representations.

CHAPTER THREE: NEURAL BASIS OF PERIPERSONAL SPACE REPRESENTATION

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3.1 Introduction

As previously described in Chapter 1, seminal studies in monkeys have suggested that neurons in the ventral premotor cortex (vPMc), specifically in area F4 (Graziano et al., 1997a; Fogassi et al., 1996; Graziano et al., 1994; Rizzolatti et al., 1981a, 1981b), and in the intraparietal sulcus, specifically in the ventral intraparietal area (VIP; Avillac et al., 2005; Duhamel et al., 1998), may underlie multisensory representation of PPS.

Neuroimaging studies have tried to identify brain areas underlying PPS representation in the human brain (Bremmer, Duhamel, BenHamed, & Graf, 2002; Sereno & Huang, 2006; Makin et al., 2007; see also Paragraph 1.2.5), suggesting that in humans, as in monkeys, a network of brain areas located in the premotor and parietal cortices might underlie a multisensory representation of the PPS. However, imaging studies do not reveal a direct causal link between brain structures and function. The aim of the present study is to test the necessary role of vPMc and PPc in multisensory representation of PPS. To this aim, we applied low-frequency (1 Hz) repetitive TMS (rTMS) to transiently interfere with vPMc and PPc processing. When applied to the motor cortex, this rTMS protocol induces a transient suppression of cortical excitability (Avenanti, Bolognini, Maravita, & Aglioti, 2007; Boroojerdi, Prager, Muellbacher, & Cohen, 2000; Chen, Classen, Gerloff, Celnik, Wassermann, & Hallet, 1997). Administration of 1-Hz rTMS to other cortical areas also results in behavioral effects consistent with transient suppression of cortical excitability (Balslev, Christensen, Lee, Law, Paulson, & Miall, 2004; Hilgetag, Théoret, & Pascual-Leone, 2001). Thus, this rTMS protocol can be used to induce transient "virtual lesions" in neurologically intact participants (Ziemann, 2010; O'Shea & Walsh, 2007; Pascual-Leone, Walsh, & Rothwell, 2000).

Here we test whether the representation of PPS was altered by rTMS-induced virtual lesions to vPMc and PPc in comparison with a baseline condition of no rTMS administration. In addition, rTMS was also applied over primary visual cortex (V1), serving as a control site, to exclude possible effects due to a generic administration of TMS, rather than to a specific inhibition of the target areas.

The present study comprises two experiments. We first replicate and validate a behavioral task previously used (Serino et al., 2007; Bassolino et al., 2010) to measure PPS representation around the hand in humans (Experiment 3.1A and 3.1B). We applied this paradigm to test the effects rTMS over vPMc, PPc, and V1 on PPS representation (Experiment 3.2).

3.2 Experiment 3.1A

To assess PPS representation around the hand, we used an audio–tactile task developed by our own group (see Bassolino et al., 2010; Serino et al., 2007). Participants were asked to verbally respond as fast as they could to either a weak electrical stimulus or strong electrical stimulus on their right index finger. Tactile stimuli were either administered unimodally or together with concurrent task-irrelevant auditory stimuli. Auditory stimuli were to be ignored and were presented either near the stimulated hand (NEAR sound) or at a distance of about 100 cm from the hand (FAR sound). The rationale of the task is that stimuli from different sensory modalities interact more effectively with one another when presented within the same spatial representation (Stein & Meredith, 1993). This implies that, in normal conditions, the response to tactile stimuli administered on the hand should be more strongly affected by sounds presented near the hand (i.e., within the PPS) than by sounds presented far from the hand. Hence, we predict that the presentation of sounds should speed up tactile RTs in comparison with the unimodal tactile condition. More importantly, tactile stimuli associated with near sounds should be processed faster than tactile stimuli associated with far sounds, in line with previous results (Serino et al., 2007).

We also tested whether the intensity of the tactile stimulus is critical for audio–tactile interaction. Because stimuli from different sensory modalities interact more strongly when unimodal information is weak (i.e., inverse effectiveness law of multisensory integration; Stein & Meredith, 1993), stronger audio–tactile effects can be predicted in response to a weaker rather than a stronger tactile stimulus. For this reason, we compared RTs for three stimulation conditions when subjects were asked to respond either to a weak or strong tactile target.

3.2.1 Methods

Participants

Twelve healthy subjects (all women, mean age=26 years) participated in the study. All participants were right-handed and had normal hearing and touch. All subjects were students at the University of Bologna and gave their informed consent to participate in the study, which was approved by the local ethics committee in accordance with the Declaration of Helsinki.

Procedure and Materials

Tactile stimuli were delivered from two constant-current electrical stimulators (DS7A, Digitimer, Hertfordshire, U.K.) via two pairs of neurological electrodes (Neuroline, Ambu, Ballerup, Denmark) placed on the dorsal surface of the index finger. The electrical stimulus was a single, constant voltage, rectangular monophasic pulse (duration = 100 sec). One pair of electrodes delivered weak stimuli, and the other pair delivered strong stimuli. Stimulus intensity was calibrated for each subject in a pretest session as follows: the experimenter began by administering a very low intensity stimulus (10 mA) and progressively increased the stimulus intensity until the subject reported detection. Normally, the weak stimulus was perceived around 50–80 mA, but this value was highly variable between subjects, seemingly dependent upon the placement of electrodes, the subject's skin, and individual sensitivity. After the initial detection report, the intensity was further increased by 10 mA. At that point, to ensure that the weak stimulus was actually perceived, 10 weak stimuli interspersed with 10 catch trials were administered. If the subject correctly reported the weak stimulus at least in 9 of 10 stimulations (90% of the time), the intensity of the weak stimulus was set at that value. Otherwise, the intensity of the weak stimulus was further increased and the procedure repeated. The intensity of the strong stimulus was then set at a factor of 1.5 of the intensity of the weak stimulus. The experimenter then administered 10 strong stimuli interspersed with 10 catch trials, ensuring that the strong stimulus was perceived 100% of the time. At the end of this procedure, the experimenter administered a series of five weak and five strong stimuli, in random order, and asked the subject to indicate, after presentation of each stimulus, whether it was strong or weak. If the discrimination was not perfect, the intensity setting procedure was repeated.

Auditory stimuli were 100-msec bursts of white noise. The intensity of the near and far sounds was set to be equal (≈70 dB) as measured by a sound meter above the subject's head (over the vertex). Sounds were generated by two identical loudspeakers, placed either near the subject's hand (NEAR sound, i.e., at ≈5 cm from the hand, at ≈50 cm from the subject's torso, and at ≈60 cm from the subject head) or in a far position (FAR sound, i.e., at 100 cm away from the near position, at ≈150 cm from the subject's torso, and ≈160 cm from the subject's head). Inspection of phonon spectral waves (recorded by a computer) from the two loudspeakers ensured that the sounds were equal at their origin for emitted frequencies.

The experimental setup is illustrated in Figure 3.1A. On each trial, participants received either a weak or a strong electrical stimulus on their right index finger. Tactile stimuli were presented alone (NO sound) or together with a concurrent task-irrelevant sound, arising from either the near (NEAR sound) or the far loudspeaker (FAR sound). The tactile and near acoustic stimuli were delivered simultaneously. Far sound onset preceded tactile stimulus onset by 5 msec to compensate for the delayed arrival of the far sound relative to the near sound because of the difference in distance. A total of 128 trials were administered: 20 weak tactile stimuli with no sound, 20 strong tactile stimuli with no sound, 20 weak tactile stimuli with near sounds, 20 weak tactile stimuli with far sounds, 20 strong tactile stimuli with near sounds, 20 strong tactile stimuli with far sounds, and 8 catch trials (i.e., trials on which only sounds, 4 near and 4 far, were presented). Each trial lasted about 3 sec.

The task was performed in two experimental conditions, run in separate blocks, whose order was counterbalanced between subjects. In the weak target condition, subjects were asked to respond as fast as possible (saying "TAH") only to the weak electrical stimulus and to refrain from responding to the strong electrical stimuli; vice versa, in the strong target condition, they were asked to respond to the strong and not to the weak electrical stimulus.

Subjects were explicitly instructed to ignore the sounds when present. RT was measured by means of a voice-activated relay. A computer running XGen (www.sph.sc.edu/comd/rorden/xgen.html) software was used to control the presentation of the stimuli and record responses. Before the experiment, 30 trials were administered to familiarize subjects with the task. Subjects performed the task blindfolded.

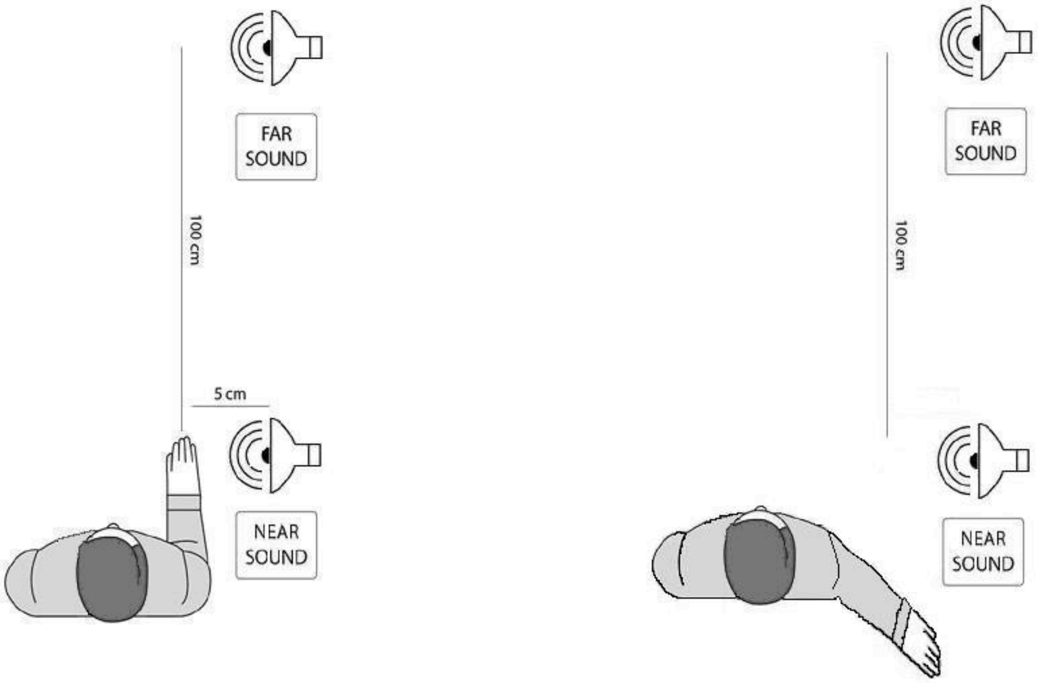


Figure 3.1 Experimental setup. (A) Experimental setup for Experiment 3.1A and Experiment 3.1B in the hand forward condition. (B) Experimental setup for Experiment 3.1B in the hand backward condition.

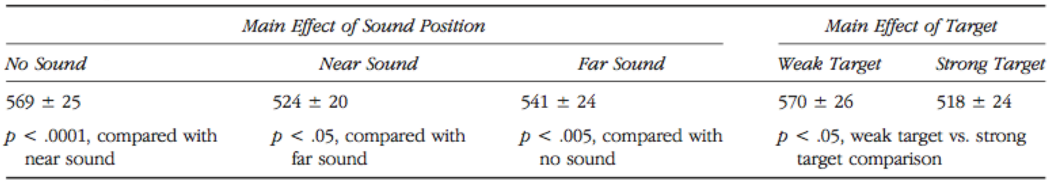
Data analysis

Mean RT to weak and strong tactile targets presented unimodally, with task-irrelevant near and far sounds, were calculated. RTs exceeding more than 2 standard deviations from the mean RT were considered outliers and trimmed from the analyses (4% of trials). Raw RTs in the different conditions were analyzed using a Sound (no sound, near sound, and far sound) by Target (weak and strong) ANOVA.

3.2.2 Results

The Sound by Target ANOVA on mean RT revealed a main effect of target [F(1,11)=7.67, $p<0.05$; $\eta^2=.41$] with faster RTs to strong relative to weak tactile targets and a main effect of sound [F(2,22)=15.07, $p<0.0000$; $\eta^2=.58$]. Newman–Keuls post hoc comparisons indicate that RTs to tactile targets were faster when a near or a far sound was presented, in comparison with when no sound was presented ($p<0.01$). Moreover, RT-to-tactile targets associated with near sounds were faster than those associated to far sounds ($p<0.05$; Table 3.1). The differences due to sound presentation were comparable for the weak and the strong target, as indicated by the lack of a significant two-way interaction ($p=0.92$).

Percentage of omissions (no response to the target stimulus) and false alarms (wrong response to the non target stimulus) were very low and comparable across all conditions (omissions are 2%, 3%, and 2% for near sound, far sound and no sound conditions, and for both weak and strong target conditions, respectively; false alarms are <1% in all conditions). These results demonstrated that sounds boost the processing of tactile stimuli presented to the hand. Critically, the audio–tactile interaction effect is stronger when sounds are presented in the space around the hand rather than in the far space. The same effect occurs for processing both relatively weaker and relatively stronger tactile stimuli.



Main Effect of Sound Position			*Main Effect of Target*	
No Sound	*Near Sound*	*Far Sound*	*Weak Target*	*Strong Target*
569 ± 25	524 ± 20	541 ± 24	570 ± 26	518 ± 24
$p < .0001$, compared with near sound	$p < .05$, compared with far sound	$p < .005$, compared with no sound	$p < .05$, weak target vs. strong target comparison	

Table 3.1 Experiment 3.1A results

3.3 Experiment 3.1B

To ensure that the audio-tactile interaction effect of Experiment 3.1A is related to a hand-centered representation of the PPS and not to a general proximity of the sound to the body, in Experiment 3.1B we manipulated the relative distance between the hand and the sound sources. The task was performed in two within-subject conditions: in the hand forward condition, the subjects' right hands were placed next to the near loudspeaker, as in Experiment 3.1A; in the hand backward condition, subjects rotated their arms so that it was off to their side, pointing slightly backward. This way, sound-to-head spatial distance was kept constant, but both near and far sounds were in far space with respect to subjects' hands. If audio–tactile interaction is coded in a hand-centered reference frame, no difference between RTs associated with near and far sounds is expected in this condition.

3.3.1 Methods

Participants

Eighteen new healthy subjects (13 women, mean age=26 years) participated in Experiment 3.1B. All participants were right-handed and had normal hearing and touch. All subjects were students at the University of Bologna and gave their informed consent to participate in the study, which was approved by the local ethics committee in accordance with the Declaration of Helsinki.

Procedure and Materials

The experiment was conducted with the same materials as for Experiment 3.1A, with the following exceptions: (a) only near and far sounds conditions were administered and (b) the tactile target was always the weak stimulus.

The experimental setup is illustrated in Figure 3.1A and B. The task was performed in two experimental conditions and run in separate blocks, with order counterbalanced between subjects. Arm position was manipulated across conditions. In the hand forward condition, the subject's right hand was placed close to the near loudspeaker; therefore, the distance between the hand and the sound sources was ≈5 cm for the near loudspeaker and ≈100 cm for the far loudspeaker. In the hand backward condition, the subject's right arm was rotated and pointed slightly backward; therefore, the subject's right hand was placed at ≈80 cm from the near loudspeaker and ≈180 cm from the far loudspeaker. A total of 140 trials were administered: 30 target trials with the near sound, 30 target trials with the far sound, 30 non target trials with the near sound, 30 non target trials with the far sound, and 20 catch trials (i.e., trials on which only a sound, 10 near and 10 far, was presented). Each trial lasted about 3 sec.

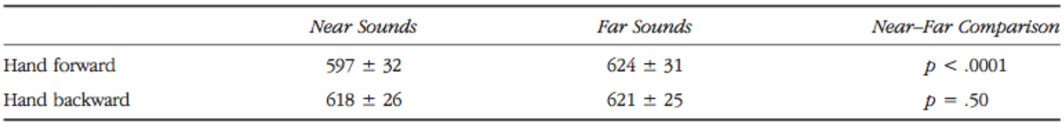
Data analysis

Mean RT-to-tactile targets presented with task-irrelevant near and far sounds were calculated for the two experimental conditions of arm position. RTs exceeding more than 2 standard deviations from the mean RT were considered outliers and trimmed from the analyses (3.9% of trials). Raw RTs in the different conditions were analyzed using a Sound by Hand position ANOVA.

3.3.2 Results

The Sound by Hand position ANOVA on mean RTs showed both a main effect of sound [$F(1,17)=28.42$, $p<0.0001$, $\eta^2=.30$] and, most importantly, a two-way interaction [$F(1,17)=20.75$, $p<0.0005$, $\eta^2=.18$]. In the hand forward condition, RTs to tactile targets were significantly shorter when task-irrelevant sounds were presented near the hand in comparison with when sounds were presented far from the hand ($p<0.0005$). No similar advantage was found in the hand backward condition ($p=0.40$; Table 3.2).

Percentage of omissions and false alarms were very low and comparable across all conditions (omissions are 2% and 3% for near sound and 2% and 2% for far sound for hand forward and hand backward conditions, respectively; false alarms are 1% and 2% for near sound and 1% and 3% for far sound for hand forward and hand backward conditions, respectively).



	Near Sounds	*Far Sounds*	*Near–Far Comparison*
Hand forward	597 ± 32	624 ± 31	$p < .0001$
Hand backward	618 ± 26	621 ± 25	$p = .50$

Table 3.2 Experiment 3.1B results

3.3.3 Discussion

Results from Experiment 3.1A and 3.1B confirm that, in normal conditions, the processing of tactile stimuli on the hand interacts with the processing of sounds presented in the environment: RT-to-tactile targets associated to sounds were faster than RT-to-unimodal tactile stimuli. Importantly, this effect is modulated by sound position in space: RTs were shortened by a concurrent sound presented near the hand compared with far from the hand (Bassolino et al., 2010; Serino et al., 2007). The audio–tactile temporal advantage was sensitive to the hand's location: when subjects placed their arm backward, thus moving the hand away from the source of near sounds, while keeping the distance between the sounds and the rest of their body constant, RTs associated to near and far sounds were comparable. Hence, the sound's proximity to the hand (and the tactile stimulus), not to the subject in general, was critical for modulating tactile processing. We propose that this behavioral effect arises from the summation of multisensory inputs within the same spatial representation, that is, within representation of PPS around the hand. This effect is reminiscent of the functional properties of multimodal neurons in vPMc and PPc, as also formalized in a neural network model for PPS representation (see Magosso, Serino, di Pellegrino, & Ursino, 2010a; Magosso, Ursino, di Pellegrino, Làdavas, & Serino, 2010b; Magosso, Zavaglia, Serino, di Pellegrino, & Ursino, 2010c).

3.4 Experiment 3.2

In Experiment 3.1, we showed a specific form of audio–tactile interaction near the hand as a sign of a multisensory representation of the PPS around the hand. A second experiment was conducted to investigate the neural basis of such representation in the human brain. We tested whether the audio–tactile interaction effect around the hand was affected by suppression of neural activity in fronto-parietal regions by means of rTMS. To this aim, the same auditory–tactile interaction task was delivered in four experimental blocks performed either within the inhibitory window created by 15 min of 1-Hz rTMS (post-rTMS blocks) or outside the influence of rTMS (baseline block).

In two critical post- rTMS blocks, rTMS was applied to vPMc or PPc to test their role in PPS representation. In another post-rTMS block, rTMS was also administered on V1, serving as an active control site. As for Experiment 3.1, during the task, subjects received either a weak or a strong tactile stimulus on the right hand, presented concurrently with task-irrelevant sounds presented either near the hand or in far space. Subjects were instructed to respond as fast as possible to weak tactile stimuli, ignoring sounds. Because we measured the spatial modulation of audio–tactile interaction around the right hand, rTMS was delivered to critical and control areas of the contralateral left hemisphere. The choice of the left hemisphere as a target for TMS interference is also in keeping with the finding that motor excitability in the left hemisphere shows a space-dependent modulation because of auditory (Serino et al., 2009) or visual (Makin et al., 2009) stimuli presented either near or far from the right hand.

The following predictions were tested. In the baseline condition with no rTMS, PPS representation should be intact, and therefore, subjects are expected to respond faster to tactile targets associated with near sounds than to those associated with far sounds. In contrast, rTMS over vPMc and PPc should interfere with brain processes representing the PPS, resulting in a reduction of the speeding effect due to near sounds when the task was administered after these two critical post-rTMS conditions. If the reduction of the speeding effect was specifically because of interfering with two putative nodes of the network underlying the PPS and not to a generic effect of rTMS, then suppression of V1 should not affect multisensory interaction within the PPS, and thus, decreased RT associated with near sounds is expected, as for the baseline condition.

To test these critical predictions, we used the same task as in Experiment 3.1B, but with participants' arms always placed close to the near loudspeaker. This ensured the entire task lasted for about 7–8 min, so that in each post- rTMS block all the responses were collected well within the inhibitory effect created by 1-Hz rTMS.

3.4.1 Methods

Participants

Ten new subjects, all students from University of Bologna, participated in Experiment 3.2. All participants were right- handed and had normal hearing and touch. They gave their informed consent to participate in the study, which was approved by the local ethics committee in accordance with the Declaration of Helsinki.

Procedure and Materials

The experiment was conducted with the same method as for Experiment 3.1A, with the exception that only forward arm position was included in the present design. Therefore, subjects received a two (tactile, weak, and strong) by two (auditory, near, and far) combination of stimuli. A total of 140 trials were administered: 30 target trials with the near sound, 30 target trials with the far sound, 30 non target trials with the near sound, 30 non target trials with the far sound, and 20 catch trials (i.e., trials on which only a sound was presented and no response was required). Each trial lasted about 3 sec; thus, each block lasted about 7 min in total.

Participants performed the audio–tactile task in four blocks, run over 2 days. Three of four blocks were performed immediately after 15 min of 1-Hz rTMS (post-rTMS blocks) over a target area (vPMc, PPc, and V1). Studies suggest that this low-frequency rTMS protocol disrupts functions related to the targeted area for at least half the stimulation time (Pascual-Leone et al., 2000; Chen et al., 1997). Thus, all the post-rTMS blocks were performed under the interfering influence of 1-Hz rTMS. To minimize carryover effect of rTMS, in each session the interblock interval was at least

1 hr. This way, we ensured that all interferential effects of one rTMS train had faded away at the time of the following block. The very same interblock interval was used when a post-rTMS block was preceded by a baseline block (no rTMS preconditioning). Baseline blocks were performed either as the very first (in six participants) or as the last block (in the remaining subjects). The order of the post-rTMS blocks was counterbalanced.

Transcranial Magnetic Stimulation

In the preliminary part of the experiment, single-pulse TMS was used to set the intensity of low-frequency rTMS. To this aim, motor-evoked potentials (MEPs) to left motor cortex stimulation were recorded in the right first dorsal interosseous (FDI) with MP-150 Biopac EMG equipment (Biopac Corp., Goletta, CA). Pairs of Ag-AgCl surface electrodes were placed in a belly–tendon montage on the FDI muscle, with further ground electrodes on the wrist. EMG signals were band-pass filtered (30–500 Hz) and sampled at 5 kHz. A figure-of-8 coil connected to a Magstim Rapid2 Transcranial Magnetic Stimulator (Magstim, Whitland, U.K.) was placed over the left motor cortex with the handle pointing backward at 45° from the midline. In this way, the current induced in the neural tissue was directed approximately perpendicular to the line of the central sulcus, optimal for trans synaptic activation of the cortico-spinal pathways (Brasil-Neto, Cohen, Panizza, Nilsson, Roth, & Hallet, 1992; Mills, Boniface, & Schubert, 1992). By using a slightly suprathreshold stimulus intensity, the coil was moved over the left hemisphere to determine the optimal position from which maximal amplitude MEPs were elicited in the FDI muscle.

In the three post-rTMS blocks, the behavioral audio–tactile task was preceded by 15 min of continuous low- frequency 1-Hz rTMS over a target area (900 stimuli in total).

Stimulation intensity was set at 90% of the resting motor threshold, defined as the lowest level of stimulation able to induce MEPs of at least 50 μV in the right FDI with 50% probability (Rossini, Barker, Berardelli, Caramia, Caruso, Cracco, et al., 1994b). In the 5 min preceding rTMS, subjects were asked to rest quietly with eyes closed. Moreover, they were asked to keep this state throughout the rTMS train, as muscle contraction may reduce the effect of rTMS (Touge, Gerschlager, Brown, & Rothwell, 2001).

Coil position was identified on each participant's scalp with the SofTaxic Navigator system (Electro Medical Systems, Bologna, Italy) as in previous studies (Bertini, Leo, Avenanti, & Làdavas, 2010; Bolognini, Miniussi, Savazzi, Bricolo, & Maravita, 2009; Avenanti et al., 2007; Bolognini & Maravita, 2007). Skull landmarks (nasion, inion, and two preauricular points) and about 100 points providing a uniform representation of the scalp were digitized by means of a Polaris Vicra digitizer (Northern Digital, Inc., Ontario, Canada). Coordinates in Talairach space (Talairach & Tournoux, 1988) were automatically estimated by the SofTaxic Navigator from an MRI-constructed stereotaxic template. Figure 3.2 illustrates site reconstructions displayed on a standard template from MRIcro (v1.40; www.mricro.com).

The vPMc was targeted in the ventral aspect of the pre- central gyrus bordering the posterior part of the inferior frontal gyrus (coordinates: x=-52, y=8, z=25, corresponding to Brodmann's area 6/44). The PPc was targeted within the anterior part of the intraparietal sulcus (x=-39, y=-40, z=43, corresponding to Brodmann's area 40). These locations were chosen by averaging the coordinates of vPMc and PPc sites found in previous neuroimaging studies on PPS in humans (Makin et al., 2007; Bremmer et al., 2001). In the active control block, we identified the scalp location that corresponded best to the visual cortex (x=19, y =-98, z=1, Brodmann's area 17, in the middle occipital gyrus; Figure 3.2).

Data Analysis

Mean RT-to-tactile targets presented concurrently with near and far sounds was calculated for the four experimental blocks. Similar to Experiment 3.1, RTs exceeding more than 2 standard deviations from the mean RT were considered outliers and, thus, trimmed from the analyses (2.7% of trials). Raw RTs were analyzed using a mixed model ANOVA with the within-subjects factors "stimulation" (no-TMS, vPMc, PPc, V1) and "sound" (NEAR and FAR); moreover, because half the subjects performed the no-TMS baseline condition at the beginning of the experiment and half at the end, we included the between-subjects factor "time of baseline" (initial and final) in the ANOVA to control for potential effects of order of baseline presentation (see Table 3.3).

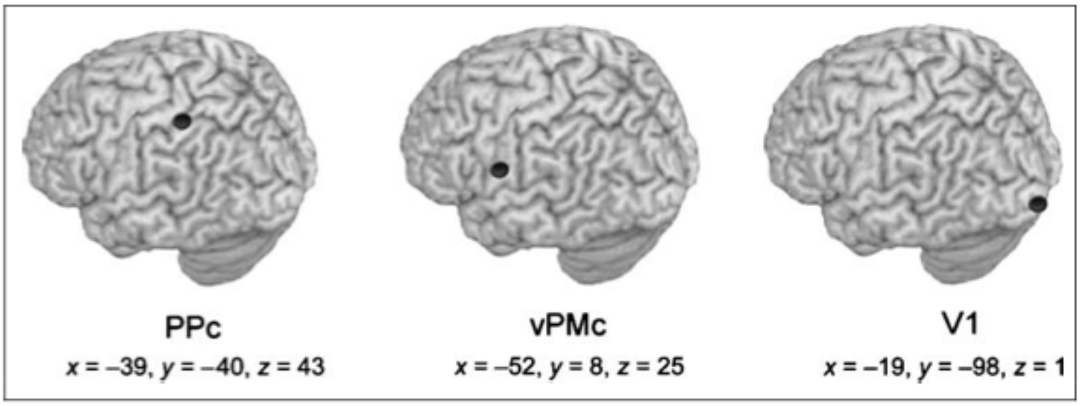


Figure 3.2 Brain locations and mean Talairach coordinates of the coil position to induce virtual lesion by means of rTMS.

3.4.2 Results

The Stimulation by Sound by Time of Baseline ANOVA on RTs revealed only a significant Stimulation by Sound interaction [$F(3,24)=6.18$, $p<0.01$; $\eta^2=.44$). Newman–Keuls post hoc comparisons showed that, in normal physiological conditions (baseline block), we replicated the integrative effect found in Experiment 3.1: RTs were significantly shorter when task-irrelevant sounds were presented near the hand in comparison with when sounds were presented far from the hand (p<0.01). A similar speeding effect due to near sounds was also found after the inhibition of V1 (p<0.05). In contrast, the speeding effect completely disappeared after the suppression of vPMc or PPc (p>0.29; see Table 3.3 and Figure 3.3).

	Near Sounds	*Far Sounds*	*Near–Far Comparison*
Baseline	583 ± 32	600 ± 34	p = .01
Post-rTMS vPMc	607 ± 31	603 ± 33	p = .45
Post-rTMS PPc	614 ± 24	602 ± 25	p = .29
Post-rTMS V1	612 ± 26	626 ± 25	p = .04

Table 3.3 Experiment 3. 2 results

These findings indicate that temporal advantage of tactile processing due to the presentation of near sounds typically found in normal physiological condition (baseline block) was disrupted by suppression of vPMc and PPc, but not by suppression of V1.

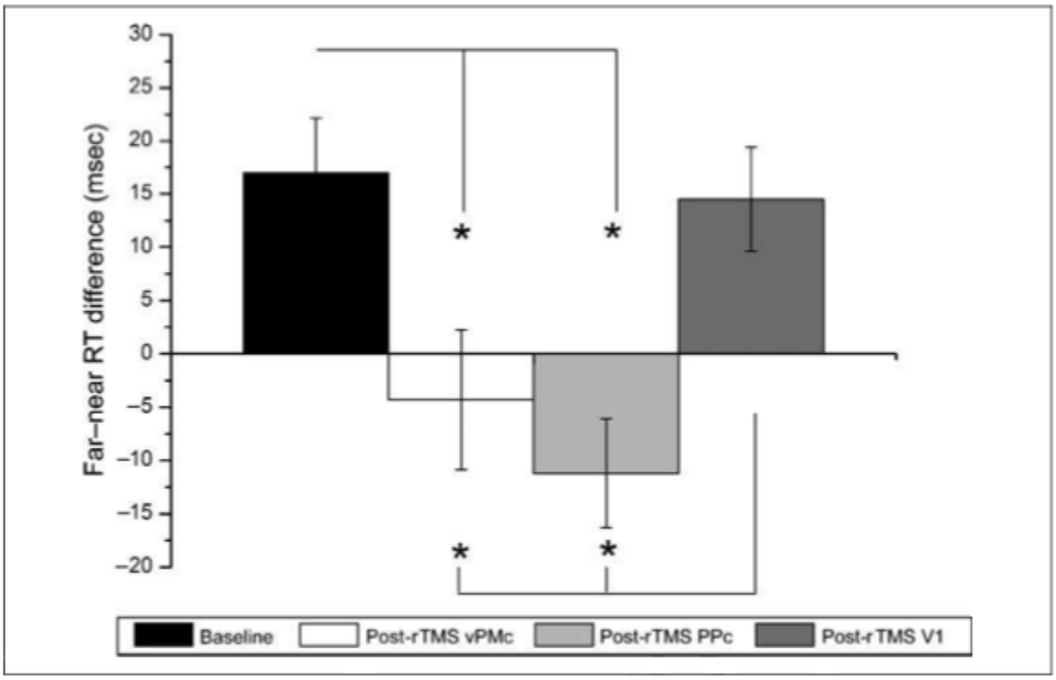


Figure 3.3 Experiment 3.2 results. The graph shows the far–near RT difference (RT for far sounds − RT for near sound) in the baseline condition (no rTMS) and after rTMS over the vPMc (post-rTMS vPMc), the PPc (post-rTMS PPc), or the primary visual cortex (post-rTMS V1). Error bars denote S.E.M.

Percentage of omissions and false alarms were infrequent and comparable across conditions (omissions are 4%, 5%, 4%, and 4% for near sound and 4%, 2%, 3%, and 3% for far sound for baseline, post-rTMS vPMc, post-rTMS PPc, and post-rTMS V1, respectively; false alarms are <1% in all conditions).

3.5 Discussion

In the present study, we directly tested whether vPMc and PPc play a necessary role in audio–tactile representation of the PPS around the hand. Subjects performed a rapid response discrimination task to tactile stimuli administered on their right hand while concurrent task-irrelevant sounds were presented either close to the hand or in far space. When no TMS was applied, as in Experiment 3.1 and in the baseline condition of Experiment 3.2, RT-to-tactile targets were reduced if the auditory stimulus was presented near the hand rather than in far space. This audio–tactile effect, anchored by hand-centered reference frames is indicative of a specific multi- sensory interaction within the boundaries of PPS.

Critically, the speeding effect associated to near sounds disappeared when the same task was performed after transient suppression of neural activity in vPMc or PPc: in these conditions, RT-to-tactile targets were not different when near and far sounds were administered. The absence of any difference between the effect induced by near and far sounds was not an unspecific consequence of rTMS. For when stimulation was administered over V1, RT-to-tactile target was again faster when near instead of far sounds were presented, thus showing an intact audio–tactile interaction within the space around the hand. These findings suggest that virtual lesions to vPMc and PPc, but not to V1, disrupt PPS representation mechanisms around the hand.

The vPMc and PPc regions targeted in the present experiment were found to be active in two recent imaging studies during processing of tactile, visual, or auditory stimuli close to the head (Bremmer et al., 2001) or the hand (Makin et al., 2007). In addition, interference with PPc activity impairs the integration of proprioceptive information, defining upper limbs postures, with visual information presented near (Bolognini & Maravita, 2007) or tactile information presented on (Azanon et al., 2010) the arm. These results suggest that PPc plays a critical role in discerning whether external stimuli are near or far from a part of the body, depending on the position of body parts. However, no previous studies have tested the critical role of PPc or vPMc in audio–tactile interaction near and far from the body. Bremmer and colleagues (2001) proposed a strong homology for vPMc and PPc areas of the human brain and multisensory regions in the vPMc and in the VIP of the macaque brain (see also Sereno & Huang, 2006; Grefkes & Fink, 2005). According to this view in humans as in monkeys, populations of cells within vPMc and PPc constitute two critical nodes of a fronto-parietal network underlying a multisensory representation of the space around the body. Our study expands on this by showing that interference of vPMc and PPc processing disrupts audio–tactile interactions in the peri hand space, thus suggesting that fronto-parietal networks are necessary for PPS representation in humans.

Another line of evidence indicates that vPMc and PPc also play a critical role in action representation. These areas are highly interconnected (Lewis & Van Essen, 2000) and send projections to the motor cortex (Davare, Lemon, & Olivier, 2008; Koch, Fernandez Del Olmo, Cheeran, Schippling, Caltagirone, Driver, et al., 2008; He, Dum, & Strick, 1995). Several studies indicate that vPMc and PPc are involved in action execution, observation, and imagery (Avenanti et al., 2007; Grèzes & Decety, 2001; Binkofski, Dohle, Posse, Stephan, Hefter, Seitz, et al., 1998). The role of vPMc and PPc in action representation is well in keeping with the present evidence that these areas are involved in multisensory PPS representation. Studies suggest that sensory representations of space and motor representations of actions coexist within the same fronto-parietal network, which provides multimodal representation of the PPS for action (Gallese & Sinigaglia, 2010). Indeed, in monkeys, multimodal cells in F4 and VIP, beside sensory responses, also discharge during movements of the body part where their tactile receptive fields are allocated (Rizzolatti et al., 1981a). Moreover, prolonged electrical stimulation of F4 and VIP results in complex movements of the monkeys' head and arm, resembling defensive motor responses to threatening stimuli approaching the body (Cooke & Graziano, 2004; Cooke, Taylor, Moore, & Graziano, 2003; Graziano et al., 2002; see also Stepniewska et al., 2005). The strong link between action and PPS representations in humans was supported by recent single-pulse TMS studies showing that auditory (Serino, Annella, & Avenanti, 2009) or visual (Makin et al., 2009) stimuli presented either near the hand or in far space differentially activate hand representation in the motor cortex. Taken together, these data suggest that vPMc and PPc represent multisensory stimuli in the space around the hand for the purpose of planning appropriate motor responses.

Finally, also their role in space and action representation, an apparently alternative view, conceives of the PPc and vPMc as two key regions in controlling spatial attention. Extensive investigations have revealed that these areas interact in shifting the focus of spatial attention both endogenously (Yantis, Schwarzbach, Serences, Carlson, Steinmetz, Pekar, et al., 2002; Hopfinger, Buonocore, & Mangun, 2000) and exogenously (Arrington, Carr, Mayer, & Rao, 2000; Corbetta, Kincade, Ollinger, McAvoy, & Shulman, 2000). Such attentional control mechanisms in vPMc and PPc act cross-modally, because both endogenous and exogenous orienting in one sensory modality affects information processing in other sensory modalities (see Macaluso & Maravita, 2010; Macaluso & Driver, 2005, for reviews). On this view, the role of vPMc and PPc in the present experimental paradigm might be that of shifting spatial attention toward or away from the hand, depending on the location of the auditory stimulation, respectively, accelerating or slowing tactile processing at the hand. However, in contrast to classic cue-to-target experimental designs normally used to study exogenous cross-modal attention, in the present study, auditory stimulation was actually administered simultaneously to the tactile stimulation. Thus, it is unlikely that auditory stimulation acted as an attentional cue. To make a more general argument, the fact that nearly identical fronto-parietal areas are considered critical by studies both on cross-modal spatial attention and on multisensory integration within the PPS does not appear to be contradictory. In fact, it is in line with the view that vPMc and

PPc might participate in representing PPS for action. According to the premotor theory of attention (Rizzolatti, Riggio, Dascola, & Umiltá, 1987), attentional control is conceived as implicit shifts of spatial representations to prepare actions. In keeping with this view, Andersen and colleagues (see Andersen & Buneo, 2002, for a review) propose a central role for the PPc in representing intentional maps, defined as cognitive plans for movements (see also Hu, Bu, Song, Zhen, & Liu, 2009), suggesting that pure attentional effects possibly found in PPc would be related to planning movements. A multisensory representation of the space where actions can be immediately implemented is necessary for motor intention and action planning. Therefore, it is not surprising to find overlapping spatial, motor, and attentional functions in a unique fronto-parietal network, encompassing PPc and vPMc.

In conclusion, results from the present study provide the first empirical evidence for a necessary role for vPMc and PPc in representing multisensory PPS around the hand.

CHAPTER FOUR: DYNAMIC SOUNDS CAPTURE THE BOUNDARIES OF PERIPERSONAL SPACE REPRESENTATION

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4.1 Introduction

Previous studies both on neuropsychological patients and healthy subjects, as described in Chapter 1, have revealed spatial constraints of multisensory interaction between visual/auditory and tactile stimuli. Results from Study 1 of the present work (see Chapter 3, Experiment 3.1) specifically confirmed that in healthy subjects audio-tactile information are strongly integrated when stimuli occurred in the space close to the body, i.e. within the PPS.

The vast majority of the previously cited behavioural studies on PPS representation (see Chapter 1) compared the effects of visual or auditory stimuli, presented at two fixed locations – far or close to the body - on tactile perception. Interestingly, neural systems representing PPS both in humans and in monkeys show response preference for moving stimuli, over static stimuli. Indeed, neurophysiological studies in monkeys showed that bimodal and trimodal neurons, both in the premotor cortex (Graziano et al., 1994; 1997a; 1999; Fogassi et al., 1996) and in the ventral intraparietal area (Duhamel, Bremmer, BenHamed, & Graf, 1997; Colby et al., 1993), are more effectively activated by presenting three dimensional objects approaching toward and receding from the animal’s body, compared to static stimuli. Some of these neurons also show direction-selective and velocity dependent response patterns, as firing rates in certain cells increase as a function of the velocity of approaching stimuli (Fogassi et al., 1996). Finally, in humans, Bremmer and colleagues (2001) demonstrated an increased neural activity in the depth of the intraparietal sulcus and in the ventral premotor cortex evoked by approaching visual, auditory and tactile stimuli (see also Makin et al., 2007).

Given the high relevance of moving objects to the PPS system, we propose that using dynamic, instead of static stimuli could be a more powerful way to study PPS representation in humans. Moreover, this approach more directly resembles ecological contexts, where external stimuli continuously move in the environment. Finally, this approach is closer to the experimental conditions used in monkeys’ neurophysiology, thus allowing a more direct comparison across species. For these reasons, in the present study we presented a new paradigm, which involves carrying out a dynamic audio-tactile interaction task in order to assess the extension of PPS in a more functionally and ecologically valid condition. We measured reaction time (RTs) to a tactile stimulus at the hand while dynamic sounds were presented, giving the impression of a sound source either approaching, or receding from the subject’s hand. Tactile stimulation was delivered at different temporal delays from the onset of the sound, such that it occurred when the sound source was perceived at varying distances from the body. Subjects were asked to respond as rapidly as possible to the tactile stimulation, trying to ignore the sound. Since we have repeatedly demonstrated that sounds boost tactile RTs when presented close to the body, and not at a distance (Serino et al., 2007; Serino, Canzoneri, & Avenanti, 2011), we predicted that RTs to tactile stimuli would progressively decrease as a function of the sound source’s perceived approach; and conversely, that they would increase as a function of the sound source's perceived recession. The function describing the relationship between tactile RTs and the perceived position of sounds in space at the occurrence of the tactile stimulation can be used to study the shape of PPS representation and to locate its boundaries along a continuum between near and far space.

4.2 Experiment 4.1

4.2.1 Methods

Participants

Seventeen healthy subjects (16 females, mean age 23.2 years, range: 20-26) participated in the study. All participants were right-handed and had normal hearing and touch. All subjects (students at the University of Bologna) gave their written informed consent to participate in the study, which was approved by the Ethical Committee of Department of Psychology, University of Bologna, and was performed in accordance with the Declaration of Helsinki.

Procedures and materials

Audio-tactile interaction task

During the task, subjects were blindfolded and sat down with their right arm resting palm down on a table beside them. During each trial, a sound (pink noise) was presented for 3000 ms. Two types of sound were used, which we term from here onwards as *IN* and *OUT* sounds. The sounds were generated by two loudspeakers: one was placed on the table in the proximity of the hand, while the other one was placed on the floor, at a distance of ~100 cm from the near loudspeaker (i.e. far from the hand). Auditory stimuli were samples of pink-noise, at 44.1 kHz. Sound intensity was manipulated by using the SOUNDFORGE 4.5 software (Sonic Foundry, Madison, WI), so that IN sounds had exponentially rising acoustic intensity from 55 to 70 dB Sound Pressure Level (SPL) as measured with an audiometer at the position of subjects' ears, while OUT sounds had exponentially falling acoustic intensity from 70 to 55 dB. Each sound is a combination of two identical samples of pink noise, one of increasing (for the IN sound) and the other one of decreasing (for the OUT sound) intensity, emitted by the near and the far loudspeaker. Both loudspeakers were activated simultaneously, but in case of the IN sound the far loudspeaker activated at the maximum intensity and then its intensity decreased up to silence along the trial, whereas the near loudspeaker activated at the minimum intensity (not perceived), and then its intensity increased up to the maximum value along the trial. In order to generate the OUT sound, the same setting was used, with reversed intensities and timing for the near and far loudspeaker. In this way, IN sounds gave the impression of a sound source moving from the far to the near loudspeaker, i.e., towards the subject's body, while OUT sounds gave the impression of a sound source moving in the opposite direction. Although other cues, such as frequency spectrum, reverberant energy and inter-aural level differences, are normally used by the auditory system to determine the spatial position of a sound, dynamic change in sound intensity seems to provide the most critical information for determining the position and direction of a moving auditory source (Seifritz, Neuhoff, Bilecen, Scheffler, Mustovic, et al., 2002; Middlebrooks & Green, 1991).

Along with the auditory stimulation, in the 60% of trials subjects were also presented with a tactile stimulus, delivered by means of a constant-current electrical stimulator (DS7A, Digitimer, Hertfordshire, United Kingdom), via a pair of neurological electrodes (Neuroline, Ambu, Ballerup, Denmark) placed on the hairy surface of the right index. The electrical stimulus was a single, constant voltage, rectangular monophasic pulse. Before the experiment, the intensity of the tactile stimulus was set to be clearly above thresholds, individually for each subject, as follows: intensity of the stimulator was set at the minimum value and then progressively increased until the subject referred to clear perceive the stimulation. Then, the subject was presented with a series of 10 stimuli, at that level of stimulation, intermingled with 5 catch trials, and asked to report when he/she felt the tactile stimulus. If the subject did not perfectly perform (i.e. if he/she omitted some stimuli or answered to catch trials), intensity was further increased by 5 mA, and the procedure was repeated. Intensity for the tested subjects ranged between 60 and 90 mA, depending on subjects' individual thresholds. Stimulus duration was equal to 100 µsec. Along the experiment, the remaining trials (40% out of total) were catch trials with auditory stimulation only. Subjects were asked to respond vocally to the tactile target, when present, saying "TAH" as fast as possible, trying to ignore the auditory stimulus. Tactile RTs were recorded by means of a voice-activated relay. A PC running C.I.R.O. software (www.cnc.unibo.psice.unibo/ciro) was used to control the presentation of the stimuli and to record responses.

For each trial, the sound was preceded and followed by 1000 ms of silence. Temporal delays for the tactile stimulus were set as follows: *T1*, tactile stimulation administered at 300 ms after the sound onset (corresponding to 1300 ms from the beginning of the trial); *T2*, at 800 ms from sound onset (at 1800 ms from trial beginning); *T3*, at 1500 ms from sound onset (at 2500 ms from trial beginning); *T4*, at 2200 ms from sound onset (at 3200 ms from trial beginning); and *T5*, at 2700 ms from sound onset (at 3700 ms from trial beginning). Thus, the critical manipulation was that the tactile stimulus was delivered at different temporal delays (from T1 to T5) from the onset of the auditory stimulus, for both IN and OUT sounds. In this way, tactile stimulation occurred when the sound source was perceived at different locations with respect to the body: i.e., close to the body, at high temporal delays for the IN sound and at low temporal delays for the OUT sound; and far from the body, at low temporal delays for the IN sound and at high temporal delays for the OUT sound.

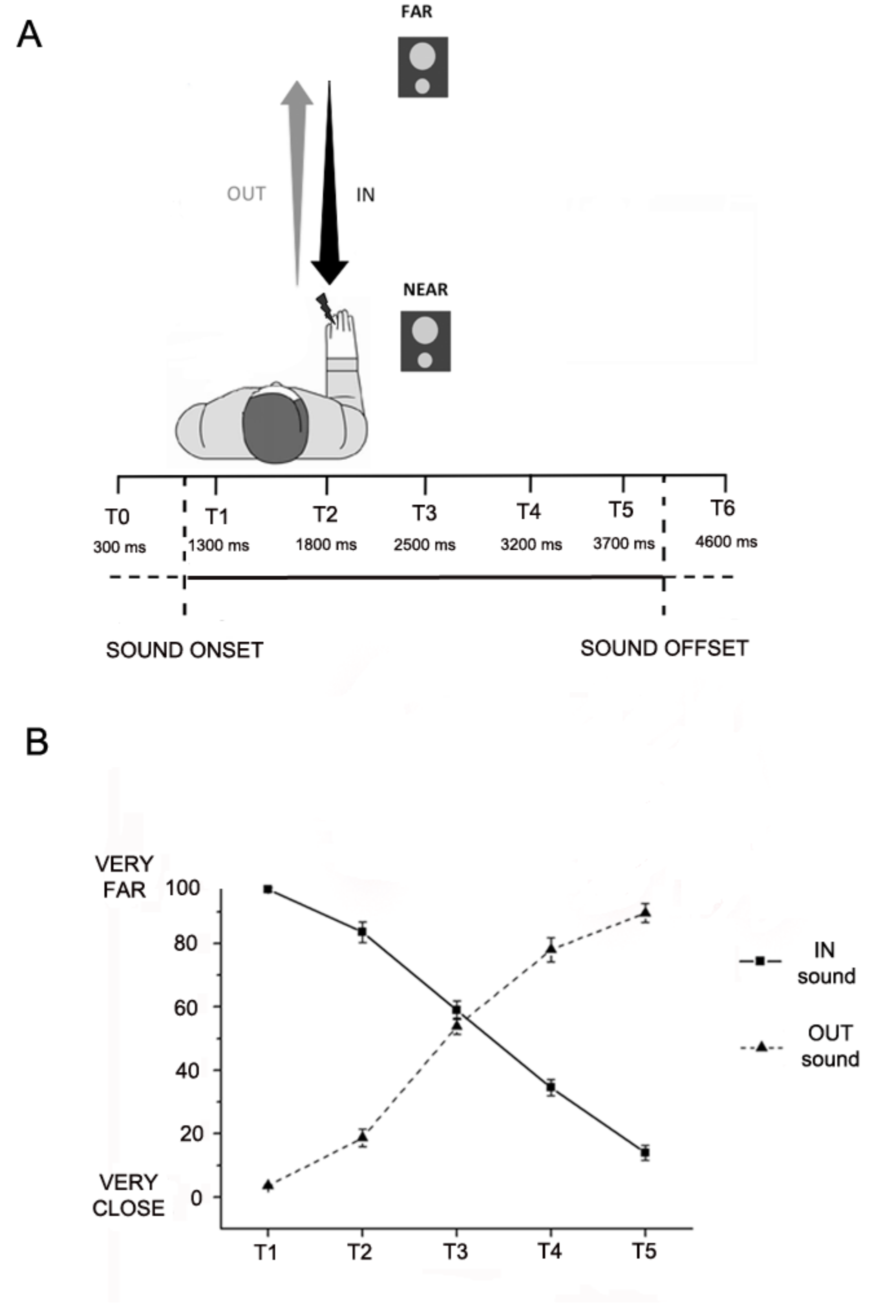

Figure 4. 1
A. *Experimental set up.* Subjects received a tactile stimulus at their hand while task-irrelevant sounds either approached to or receded from the hand. Tactile stimuli were delivered at different temporal delays from sound onset (from T1 to T5), so that they were processed when sounds were perceived at a different distance from the hand.
B. *Sound localisation experiment results*. The graph shows subject's mean responses indicating the perceived position of sound in space when they receive a tactile stimulus at different temporal delays from sound onset, from T1 to T5. Filled line refers to IN sound condition, hatched line refers to OUT sound condition. Error bars denote S.E.M. A repeated measure ANOVA with Sound (IN, OUT) and Temporal Delay (from T1 to T5) confirmed that IN and OUT were perceived as an approaching and receding auditory stimuli, respectively, as clearly shown by the significant two-way interaction [F(4,24)=304.30, p <0.00001].

Finally, in order to measure RTs in unimodal tactile condition (without any sound), tactile stimulation could be also delivered during the silence periods, preceding or following sound administration, namely at 300 ms (*T0*) and at 4600 ms (*T6*) after the beginning of the trial (see Figure 4.1A). The total experiment consisted in a random combination of 8 target stimuli for each temporal delay, for the IN and OUT sounds, resulting in a total of 112 trials with a tactile target, randomly intermingled with 76 catch trials. Trials were equally divided in two blocks, lasting about 8 minutes each.

In order to demonstrate that subjects actually perceived the sound source at different locations according to different temporal delays (from T1 to T5) for the IN and the OUT sound, we ran a sound localisation experiment on 7 naïve subjects. During the sound localisation experiment subjects were blindfolded and sat down with their right arm resting palm down on a table beside them. They received a tactile stimulation on the forearm at one of the different temporal delays in a series of 80 trials, randomly presented. At the end of each trial, they were asked to verbally indicate the perceived position of the sound in space when they had felt the tactile stimulus, on a scale from 1 (very close) to 100 (very far). Participants were explicitly invited to use the entire range between 1 and 100, taking in account also for small differences in the perceived position of sound. Subjects' responses and statistical analyses, reported in Figure 1B, clearly show that for the IN sound, subjects progressively perceived the sound closer to their body when the tactile stimulus was administered at successive temporal delays from T1 to T5. The pattern of responses was reversed for the OUT sound, when the sound was perceived in spatial positions progressively farther from the body from T1 to T5. The results of this control experiment confirmed that IN and OUT sounds were perceived respectively as approaching and receding auditory stimuli, and that, when subjects received tactile stimulation at different temporal delays, the sound was perceived at a different distance from their body.

4.2.2 Results

Since tactile stimuli were administered well above threshold, subjects were extremely accurate in performing the task, as rate of false alarms and omissions was very low, i.e., 0.25% and 1.75% respectively. Thus, the performance was analysed in term of reaction time only. Mean RTs to tactile targets were calculated for every temporal delay, from T0 to T6, separately for IN and OUT sounds. RTs exceeding more than 2 standard deviations from the mean RT were considered outliers and trimmed from the analyses (1.6% of trials on average in all conditions). The relationship between RTs to the tactile target and the different temporal delays at which the tactile stimulus was administered (from T0 to T6) is represented in Figure 4.2 for the IN (filled line) and the OUT (hatched line) sound. Two different effects are visible: for the IN sound, RTs progressively decreased as temporal delays increased, i.e. as the perceived sound approached the body; and vice versa for the OUT sound: RTs progressively increased as temporal delays increased, i.e. as the perceived sound receded from the body. However, the shape of the relationship between RTs and Sound position does not appear exactly the same for the two classes of sounds.

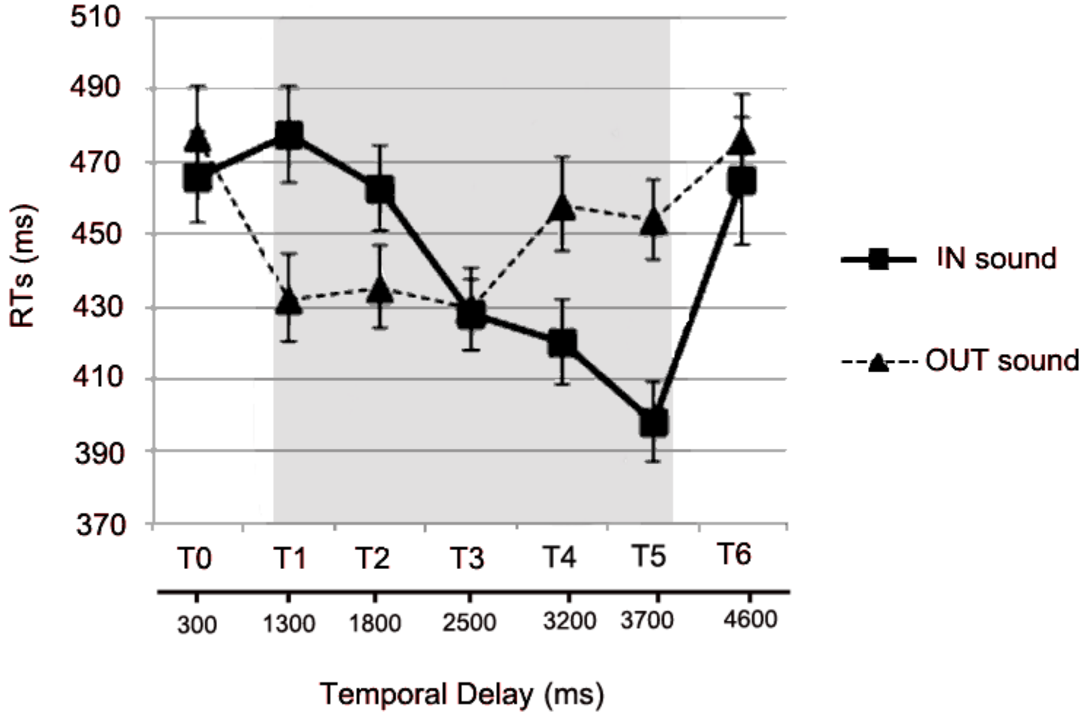

Figure 4.2. *Effects of IN and OUT sounds on tactile processing.* Mean RTs (and S.E.M.) to the tactile target at different temporal delays (from T0 to T6) for IN (filled line) and OUT (hatched line) sounds. The shaded region indicates the duration of the sounds.

These effects were confirmed by an ANOVA on tactile RTs with the within subjects factors of Sound (IN, OUT) and Temporal Delay (T0, T1, T2, T3, T4, T5, T6). The two-way interaction Sound x Temporal Delay was significant [F(6,96)=7.88; p<0.0001]. In order to analyse this interaction, we performed two separate ANOVAs for IN and OUT sounds with Temporal Delay as within-subjects factor. In case of the IN sound, the ANOVA revealed a significant main effect of Temporal Delay [F(6,96)=8.46, p<0.0001]. Newman-Keuls post-hoc tests showed that RTs at T1 (when sounds were perceived far from the body; mean RTs=478 ms, S.E.M.=±18) and T2 (463 ms±15) were significantly slower compared to RTs at T3 (when sounds were perceived close to the body; 428 ms±14), T4 (420 ms±15) and T5 (398 ms±15; all p_s<0.05). RTs at T1 and T2 were not significantly different from each other (p=0.73), as well RTs at T3, T4 and T5 were not significantly different from each other (all p_s>0.10). RTs in the unimodal conditions (i.e., when tactile stimuli were delivered at T0, before sound onset and at T6, after sound offset) were significantly slower as compared to RTs at T3, T4 and T5 (all p_s<0.05), i.e. when the sound was perceived close to the body. In addition, RTs at T0 and T6 were not different from each other (RTs at T0=467 ms±17 and T6=465 ms±23, p=0.95), therefore excluding the possibility that subjects were generically faster at late delays in each trial just because they paid more attention as the probability of receiving a stimulation increased along the trial duration.

In the case of the OUT sound, the main effect of Temporal Delay was significant [F(6,96)=5.97, p<0.0001], as it was for the IN sound. RTs at T5 (454 ms±15), and T4 (458 ms±17) - when the sound was perceived far from the body - were slower than RTs at T3 (429 ms±15), T2 (435 ms±15) and T1 (432 ms±16) - when sounds were perceived close to the body. The pattern of results therefore showed a similar trend as for the IN sound. However, the differences between RTs at higher temporal delays (T5 and T4) and RTs at lower temporal delays (T1-T3) were statistically significant with simple comparisons (two-tailed t-tests, p_s<0.05), but did not resist to Newman-Keuls corrections for multiple comparisons (all p_s>0.16). RTs in the two unimodal conditions were not different from each other (RTs at T0=477 ms±18 and T6=476 ms±17, p=0.55), but were significantly slower as compared to the other conditions (all ps <0.05, Newman-Keuls corrected).

Taken together, these results suggest that tactile processing is modulated by co-occurrence of dynamic sounds, depending on the position of sounds in space, as far as sounds were perceived at a limited distance from the body, and such distance can be considered as the boundary of PPS representation around the hand. In addition, the relationship between the spatial position of sounds in space and their effect on tactile RTs seems stronger when an approaching, rather than when a receding sound, was presented.

In order to further investigate the differential effects of the two types of dynamic sounds on tactile processing, we studied mathematical functions describing the relationship between tactile RTs and timing at which tactile stimuli were delivered. We compared two possible functions, a sigmoidal function and a linear function. In order to compute the mathematical functions, the time of tactile stimulation was referred to the sound onset for both types of sounds (IN and OUT sounds), so that experimental time T1 corresponds to 300 ms, T2 to 800 ms, T3 to 1500 ms, T4 to 2200 ms and T5 to 2700 ms. The sigmoidal function was described by the following equation: $y(x) = \frac{y_{min} + y_{max} \cdot e^{(x-x_c)/b}}{1 + e^{(x-x_c)/b}}$ where x represents the independent variable (i.e., the timing of touch delivery in ms), y the dependent variable (i.e., the reaction time), y_{min} and y_{max} the lower and upper saturation levels of the sigmoid, x_c the value of the abscissa at the central point of the sigmoid (i.e., the value of x at which $y = (y_{min} + y_{max})/2$) and b establishes the slope of the sigmoid at the central point. The linear function was described by the following equation: $y(x) = y_0 + k \cdot x$; where x and y have the same meaning as above, y_0 represents the intercept at $x = 0$ and k is the slope of the linear function. For each subject, the two functions were fitted to the averaged tactile RTs at the five timing of tactile delivery, separately for the IN and the OUT sound, in the least-squares sense. In the linear model, the estimated parameters were the intercept (y_0) and the slope (k). In the sigmoidal model, we analogously limited the estimated parameters to two, as in the linear function, in order to directly compare the root mean square error (RMSE), as an index of best fit between the two models. To this end, for each set of data, values of the parameters y_{min} and y_{max} were assigned a priori equal to the minimum and maximum values of the data set (independently calculated for each subject), and the estimated parameters were the central position of the sigmoid (x_c) and the slope of the sigmoid at the central point (b). For the IN sound, RMSE was significantly lower for the sigmoidal function (19.60 ms) than for the linear function (22.54 ms; $t(16)=-2.43$, $p<0.05$), indicating that the empirical data were better represented by the former than by the latter function (see Table 4.1). This finding suggests that the effect of IN sounds on tactile processing did not increase linearly along a continuum from far to near space as the sound approaches the body. Instead, there was a critical spatial range, located between T2 and T3, after which auditory stimuli from the outside began interacting with tactile stimuli on the body surface, fastening tactile RTs. We can consider such spatial range as the boundary of audio-tactile PPS representation around the hand (see Figure 4.3).

In the case of the OUT sound the function linking tactile RTs and the perceived position of sounds in space did not fit the data as well as that for the IN sound. Indeed, RMSE for the sigmoidal function (20.59 ms) were not significantly different from those for the linear function (20.70 ms; $t(16)=-0.19$; $p=0.85$). Moreover, the slope of the sigmoidal function computed for the OUT sound was significantly flatter (0.03 ms) compared to that computed for the IN sound (-0.15 ms; $p<0.05$). These results suggest that the effect of sound on tactile RTs depends not only on the perceived position of sound in space, but also on the perceived direction of sound motion, with a stronger effect for IN sounds than for OUT sounds.

	SIGMOIDAL FUNCTION			LINEAR FUNCTION		
	CENTRAL POSITION (ms)	**SLOPE**	**RMSE (ms)**	**INTERCEPT (ms)**	**SLOPE**	**RMSE (ms)**
IN	1439.22	-0.15	19.60	486	-0.03	22.54
OUT	1425.02	0.03	20.59	426	0.02	20.70

Table 4.1 Estimated parameters and Root Mean Square Errors for the sigmoidal function (central position and slope, on the left) and the linear function (intercept and slope, on the right) fitting the relationship between tactile RTs and timing of touch delivery - 300 ms, 800 ms, 1500 ms, 2200 ms, 2700 ms, corresponding to the five different perceived positions of the sounds - both for IN and OUT sound.

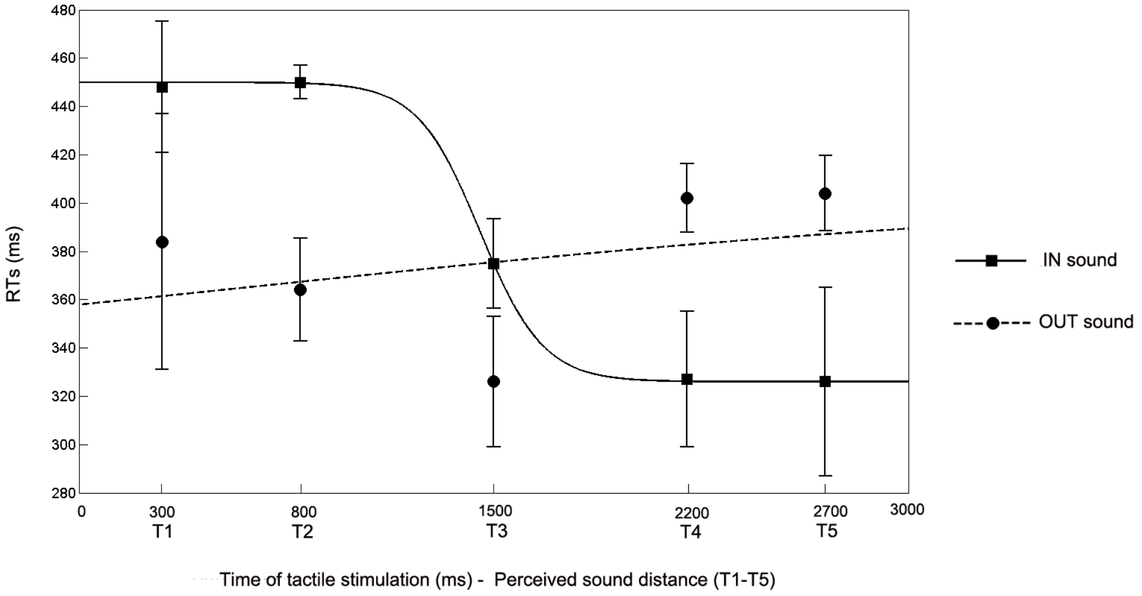

Figure 4.3. *Best fitting function for the relationship between sound position in space and tactile processing.* Data from a paradigmatic subject are reported. Figure 4.3 plots mean RTs (and S.E.M.) at different times of tactile stimulus delivery and the best fitting sigmoidal functions for IN (filled line) and OUT (hatched line) sounds.

4.3 Discussion

In this study, we developed a new dynamic paradigm to study PPS representation. Our results show that an auditory stimulus speeds up the processing of a tactile stimulus at the hand, if the sound is administered within a limited distance from the hand. By using dynamic sounds we were able to study such critical distance along a continuous spatial range, spanning near and far space, thus estimating the boundaries of PPS representation.

Previous studies have shown that auditory stimuli affect the perception of tactile stimuli, both in terms of detection ability (Ro, Hsu, Yasar, Elmore, & Beauchamp, 2009) and RTs (Zampini et al., 2007; Tajadura-Jimenez et al., 2009; Serino et al., 2007; Bassolino et al., 2010). However, whether, and to what extent audio-tactile interactions are modulated by the spatial features of the stimuli is still a debated issue. Some studies (Zampini et al., 2007; Lloyd, Merat, Mc Glone, & Spence, 2003; Murray et al., 2005; Zampini et al., 2005) have suggested that the spatial links between auditory and tactile signals may be weaker than those existing between other modality pairings involving vision, such as audio-visual (Spence & Driver, 1996) and visuo-tactile (Spence, Pavani, & Driver, 2000; 2004) interactions. Indeed, some authors reported a facilitation effect not only when auditory and tactile stimuli are delivered to the same location, but also when they are widely separated (Zampini et al., 2007; Murray et al., 2005; see also Yau, Olenczak, Dammann, & Bensmaia, 2009; Gillmeister & Eimer, 2007). In contrast, other studies have supported the hypothesis that spatial factors, such as the stimulus distance from the body, are also important in auditory-tactile interactions, as they showed stronger auditory–tactile effects for stimuli arising from the same sector of space (Tajadura-Jimenez et al., 2009; Kitagawa et al., 2005; Occelli, O’Brien, Spence, & Zampini, 2010).

The auditory system has a lower spatial acuity than the visual system, thus the modulation of tactile processing in relation to auditory stimuli might be less sensitive to spatial factors, compared with visual stimulation. However, if spatial features of auditory stimulation are stressed by using dynamic sounds, as in the present experiment, spatially dependent auditory-tactile interactions can be revealed. It is worth also noting that most previous evidence of space-dependent modulation of auditory-tactile interactions in monkeys (Graziano et al., 1999; Schlack, Sterbing-D'Angelo, Hartung, Hoffmann, & Bremmer, 2005) concerns stimuli administered close to the head, and especially in the rear space. Also in humans, evidence concerning spatially dependent audio-tactile interactions is more common for the peri-head space than in the peri-hand space (see Occelli et al., 2011, for a review), although a number of studies reported different forms of audio-tactile interaction around the hand (Bruns & Roder, 2010; Soto-Faraco & Deco, 2009; see also Serino et al., 2011, as reported in Chapter 3). This might have occurred because localisation of auditory stimuli with respect to the head is simpler and more precise than that with respect to the hand, due to the nature of computation required to localize sounds in space. Nevertheless, localisation of sounds around the hand is necessary under specific conditions. For instance, when you hear a bee approaching your right hand you do not withdraw your head or your left hand, but you do withdraw your right hand. In cases such as this, auditory-tactile interaction in the peri-hand space is likely to be modulated as a function of the position of sounds in space, as we demonstrated in the present study.

Here we proposed that the speeding effect on RTs due to sounds processed in the near space might arise from the integration of multisensory (auditory and tactile) inputs within the same spatial representation (i.e. within PPS around the hand), as previously shown with a different paradigm in the previous study (see Chapter 3). A similar mechanism can explain results from the present study.

The novelty of the present approach is that by using dynamic stimuli, approaching or receding from the body, we could measure multisensory interaction around the body along a continuum between far and near space, rather than as a comparison between a series of fixed locations. This approach offers a series of advantages in comparison to previous behavioural approaches, which compared the effects on tactile processing of visual (Macaluso & Maravita, 2010) or auditory (Occelli et al., 2011) stimuli presented in two fixed locations. First, we measured the extension of PPS in a more ecologically valid condition, mimicking dynamic stimulations of everyday life. Second, this paradigm directly resembles the stimulations used in monkey neurophysiology to study PPS bimodal or trimodal neurons, where a visual or an auditory stimulus was presented, as approaching to or receding from the animal's body part where the neuron's tactile receptive field was located (Fogassi et al., 1996; Graziano et al., 1999; Duhamel et al., 1997; Schlack et al., 2005). Our approach also fits well with the notion that bimodal and trimodal neurons in monkeys' premotor (Graziano et al., 1994; 1997a; 1999; Fogassi et al., 1996) and parietal cortices (Duhamel et al., 1997; Colby et al., 1993) and multisensory responses in human homologues areas (Bremmer et al., 2001; Makin et al., 2007) are particularly sensitive to dynamic stimuli.

Interestingly, the present results also suggest that, among dynamic stimuli, approaching sounds have a stronger spatially-dependent effect on tactile processing, compared with receding sounds. Indeed, the sigmoidal function, describing the relationship between tactile RTs and timing at which tactile stimuli were delivered, had a better fit and was significantly steeper for the IN sound than for the OUT sound.

These findings fit perfectly with the sensory-motor function of PPS representation (Graziano & Cooke, 2006): a stimulus possibly colliding with the body implies faster and more accurate processing, as it is likely to require a rapid motor response, in order to avoid a potential harm. This notion is supported by electrophysiological evidence in monkeys showing that direct electrical stimulation of the areas containing bimodal and trimodal PPS neurons evokes in anesthetized animals fast motor responses, resembling defensive and avoidance reactions to threatening stimuli in everyday life contexts (Graziano et al., 2002; Cooke et al., 2003; Stepniewska et al., 2005). The existence of a similar sensory-to-motor coding of PPS in humans is supported by two recent TMS studies showing that processing visual (Makin et al., 2009) or auditory (Serino et al., 2009) stimuli within or outside the PPS around the hand differently affects the representation of hand muscles in the cortico-spinal tract.

In sum, the present study provides an effective and ecologically valid approach to measure the extent of PPS representation. The function describing the relationship between tactile processing and the position of sounds in space along a spatial continuum can be used to localize the boundaries of PPS representation. This method can be used to study plasticity of PPS representation in different contexts and following different types of short-term and long-term experiences (Longo & Serino, 2012). In the next studies included in this thesis, we will show how this task has been applied to study changes in PPS representation following tool-use (Chapter 5), multisensory stimulation (Chapter 6), amputation (Chapter 7) or social interaction (Chapter 8).

CHAPTER FIVE: PLASTIC MODIFICATION OF BODY AND PERIPERSONAL SPACE REPRESENTATION AFTER TOOL USE

[Canzoneri, E., Ubaldi, S., Rastelli, V., Finisguerra, A., Bassolino, M., & Serino, A. Tool-use reshapes the boundaries of body and peripersonal space representations. Under revision]

5.1 Introduction

In order to interact with objects in space, in either reaching an interesting stimulus or avoiding potential harm, the human brain needs to integrate information about the position and shape of body parts and information about the position and movements of objects in relation to the body. This bodily and spatial information are strictly linked, since the brain needs to represent the space around us mainly with reference to the body.

On the one hand, the brain holds an accurate multisensory representation of the body (Body Representation - BR). On the other hand, the representation of the space immediately surrounding the body (Peripersonal Space - PPS) is enabled by integration of tactile and proprioceptive information concerning specific body parts and visual and/or acoustic inputs related to objects presented in a limited portion of space surrounding the same body parts (see Chapter 1).

A critical property of PPS representation is that it is dynamically modified through experience: using a tool to reach objects in far space extends the limits of PPS representation. In monkeys, Iriki and colleagues (1996) showed that hand-centred visual RFs of neurons located in the intraparietal sulcus elongated after a training period of using a rake to retrieve pieces of food placed at a distance. Further neuropsychological studies on extinction patients demonstrated that after using a tool to reach distant objects, crossmodal extinction for a tactile stimulus presented on the contralesional hand increased when a visual stimulus was presented at the tip of the tool, as compared to before tool-use (Farnè et al., 2005b; Farnè & Làdavas, 2000; see also Maravita et al., 2001). In healthy subjects, tool-use may increase the impact of far visual distracters on tactile discrimination (Holmes et al., 2004; Maravita et al., 2002). An extension of the limits of multisensory integration from the PPS to the tool's action space has been shown also in healthy subjects after short (Serino et al., 2007) and long-term (Serino et al., 2007; Bassolino et al., 2010) tool-use experiences. Taken together these studies show that the extent of PPS representation is dynamically shaped as a function of where subjects act upon external objects, i.e. their action-space (Gallese & Sinigaglia 2010; but see Holmes et al., 2007b, and Holmes 2012, for a different interpretation of these effects).

Some authors (i.e. Iriki et al., 1996; Maravita & Iriki, 2004) have proposed that the extension of PPS after tool-use reflects a plastic modification in BR, such that the tool is incorporated as a part of the body (Berlucchi & Aglioti, 1997; Critchley, 1979; Head & Holmes, 1911; Holmes & Spence, 2006; Maravita, 2006). BR indeed should be plastic enough to update accordingly to slow and fast changes the body undergoes with time. However, the majority of these previous studies testing the effects of tool-use showed a modification in the effect of visual and/or auditory stimuli presented near or far from the body (at the tip of the tool) on processing of simultaneously presented tactile stimuli; they did not directly show a change in the representation of the body itself after tool-use. Instead, in these studies, tool incorporation has been only indirectly demonstrated through perceptual changes in PPS representations. Three recent papers demonstrated a specific change in BR following tool-use. Despite the little agreement in literature about the number and types of body representations in the brain (see also Chapter 1, Paragraph 1.2.4), in line with the dyadic view of body representations (that opposes Body Schema and Body Image) there is a general consensus in defining the Body Schema as the body representation for action: this representation stores the information about the body that is relevant for appropriate motor control, as the position of different body parts in space and relative to each other, and their size, by integrating multiple sensory inputs. The Body Image instead is generally defined as a Body Representation for perception. The existence of two separated body representations for action and perception is supported also by recent behavioral data showing that the different body representations could be selectively updated according to the nature of a task (motor VS perceptual; Kammers et al., 2009; Kammers, Kootker, Hogendoorn, & Dijkerman, 2010). In line with this view in a recent study, Cardinali and colleagues (Cardinali et al., 2011) tested whether the effects of tool-use on body representation was specific for tasks requiring a motor response (pointing to a body part) or a perceptual judgements (localising a body part on a ruler) to indirectly estimate the represented length of their arm, in order to investigate whether plasticity after tool-use occurred on a representation of the body used for action (i.e., the so-called Body Schema) or for perception (i.e., the so-called Body Image; see Dijkerman & de Haan, 2007; de Vignemont, 2010; Gallagher, 1986; see also Chapter 2). They found that perception of forearm length increased after tool-use for both tasks, but only when the input for the task (which body part was to localise) was given tactilely (by touching the target body part) and not verbally (by naming the target body part). Results from the present study provided evidence of a selective update of body representation after tool-use depending on the appropriate combination between the task modality (motor VS perceptual) and the sensory modality of the input, revealing that a critical role is played by tactile information in updating the Body Schema. Interestingly, these findings also suggest that although their functions and properties are different, Body Schema and Body Image are interconnected and might influence each other (Cardinali et al., 2011).

Sposito and colleagues (Sposito et al., 2012) demonstrated a change in the internal representation of body part size (i.e. the forearm) following a training with a functional tool. Interestingly, the length of the tool and the extent to which action capability was influenced affected the occurrence of plastic changes in body representation, resulting in an increased in the perceived forearm's length after tool-use. Cardinali and colleagues (2009a) showed that also kinematics of arm movements during hand grasping changed after pincers were used to grasp objects. This effect was also associated with a change in the localisation of tactile stimuli on the arm.

The motor and somatosensory effects of tool-use here reviewed suggested that tool-use could influence the perceived representation of the internal size of body parts. However, these findings cannot demonstrate a direct link between the effects of tool-use on PPS representation and the modification in body representation, because in the cited literature these tasks have been specifically designed to investigate changes in body metrics only.

The aim of the present study is to directly test whether using a functional tool to act upon objects at a distance concurrently affects both space and body representation in the same sample of subjects, using different tasks that specifically tap into PPS representation and body representation, by considering features that mainly define these representations. In order to assess the extension of the multisensory PPS representation in a functionally and ecologically valid condition, we used a new *audio-tactile interaction task* recently developed by our group (Canzoneri, Magosso, & Serino, 2012; see Chapter 4). In order to measure the extension of Body Representation, we assessed the perceived dimensions of the forearm by using two different tasks. In a *tactile distance perception task*, participants received two pairs of tactile stimuli, one on the forehead (as a reference body part) and one on the forearm (target body part), and they were asked to judge whether the distance between the two stimuli was larger on the forehead or on the forearm. This task allowed assessing implicitly the internal representation of body part size. In a *body-landmarks localisation task,* instead, participants were asked to localise two anatomical landmarks, specifically the wrist and the elbow, by verbally indicating when a moving marker overlapped with the felt position of these occluded body parts. This task explicitly assesses a representation of the arm metric properties without involving any tactile signals or a comparison between two different body parts (see also Longo & Haggard, 2010; Cardinali et al., 2011; Lopez, Schreyer, Preuss, & Mast, 2012). In line with the dyadic view of body representations, the perception of body parts size is considered a component of Body Schema, in that information about the dimensions of the different body parts is critical in order to control the body in interaction with the environment. We are aware that, in the view of the triadic taxonomy of body representations (i.e. Body Schema, Body Structural Description and Body Semantics, see Schwoebel & Coslett, 2005; Sirigu, Grafman, Bressler, & Sunderland, 1991), some authors propose that this kind of information is processed by the so-called Body Structural Description, i.e. a visuo-spatial map of the body. In addition, Longo and Haggard (2010; 2011) proposed that there is a specific model of the body in the brain (i.e. body-model, see Longo & Haggard, 2010; 2011), containing information about the size and dimension of body parts. However, since at the moment, the exact number and functions of different body representations is matter of debate (see Kammers et al., 2010), in the present work I will adopt the more neutral term Body Representation (BR).

In Experiment 5.1, participants performed the audio-tactile interaction task and the tactile distance perception task, before and after a training session with a tool. In Experiment 5.2, in order to provide further evidence for a change in the internal representation of the arm size, participants performed the tactile distance perception task and the body-landmarks localisation task after the same training with a tool as the one used in Experiment 5.1. Finally, in order to demonstrate that any change in PPS and BR was actually due to tool-use, and not to a generic effect of movement, attention, or simply to repetition of the tasks, in Experiment 5.3 we evaluated both PPS representation and BR with the same tasks used in Experiment 5.1 before and after a control training, consisting in pointing to objects placed in different positions in far space.

5.2 Experiment 5.1

In this experiment we measured PPS representation by means of the audio-tactile interaction task, and BR, by means of the tactile distance perception task, before and after a training session, consisting in using a tool with the right arm to retrieve objects placed in different positions in far space for 20 minutes (Tool-use training).

5.2.1 Methods

Participants

Twelve healthy subjects (11 females, mean age 25 years) participated in the study. All subjects were right-handed and had normal hearing and touch. All subjects, students at the University of Bologna, gave their informed consent to participate in the study, which was performed in accordance with the Declaration of Helsinki.

Materials and procedures

Audio-tactile interaction task

Procedures for this task were the same to those previously explained in Chapter 4, Paragraph 4.2.1, except for the tactile stimulation that was administered on the hairy surface of the forearm.

Tactile distance perception task

Blindfolded subjects were lain down with their right arm resting in a prone position. In order to set the spatial distance between stimuli administered on the forehead and on the forearm, we initially measured the two-point discrimination threshold (2pdt) on the forearm, both for transversal and longitudinal orientations by using a staircase method. Subjects were tactilely stimulated with needles (diameter 5 mm) mounted on a calliper. Either double (67%) or single posts (33%) were administered at random. Only double posts were used to compute the staircase. The starting double posts separation was 40 mm, clearly above the 2pdt. The separation was then reduced progressively by 50% after each set of three successive correct responses. When subjects made an error, the separation was subsequently increased to midpoint of the current (erroneous) trial and the immediately preceding (correct) trial. This procedure was terminated at the shortest separation at which subject clearly perceived two posts. We then confirmed this 2pdt estimate by delivering five double posts at this separation randomly intermixed with five single posts. If subjects scored between 7/10 and 9/10 correct, the threshold estimate was accepted for experimental testing. Otherwise, the procedure was repeated. For each subject, 2pdts were measured both for transversal and longitudinal orientation on the forearm, and the corresponding individual 2pdt was used to set the distance between the pairs of posts used during the tactile distance task. Three different inter-point distances were used: at the 2pdt, 1.5 the 2pdt, and twice the 2pdt.

On each trial of the tactile distance perception task, subjects were touched with a pair of posts on the forehead and immediately later with a pair of posts on the forearm. Subjects made un-timed two-alternative forced-choice judgments of whether the two posts felt farther apart on the forehead or on the forearm, responding verbally. The task comprised a total of 36 trials: for 12 trials, the inter-point distance for the pair of posts on the forehead and on the forearm was the same (i.e., at the 2pdt, at 1.5 the 2pdt or twice the 2pdt); for 12 trials, the inter-point distance was longer for the pair of posts on the forearm; vice-versa for the remaining 12 trials (i.e., the difference between the two distances could be half the forearm threshold or equal to the threshold). An experimenter administered stimuli manually for approximately one second, with an inter-stimulus-interval of one second between taps on the forehead and the forearm (See Figure 5.1B). Subjects were blindfolded throughout the procedure. In order to assess both the perceived width and the perceived length of the forearm, tactile stimuli were applied in two different orientations, transversally and longitudinally to the forearm axis. Subjects performed the task for transversal and longitudinal orientations, before and after tool-use, in blocked sessions, run in counterbalanced order.

Tool use training

The tool-use training was adapted from Serino and colleagues (2007). The tool used was a 1 mt wooden stick of a 2.5 cm diameter plus a 10 cm handle. A 21 x 10 x 1 cm plastic plate was fixed on the distal part of the tool. The tool's weight was around 1 kilo. The training consisted in using the tool to find and retrieve 10 x 3 x 3 cm parallelepiped targets randomly placed in each trial in one out 30 different locations on the floor. Possible locations were chose on two a 3 by 5 matrix, one for each side of space: there were 3 possible longitudinal distances from the body (at 50 cm, at 80 cm and at 110 cm), and 5 transversal positions on the left and 5 on the right of the participants, covering a space ranging from 50 to 110 cm in front of the subject and up to 140 cm to the right and to the left of the subject's feet. Participants performed the task blindfolded. They comfortably sit on a chair in the middle of the experimental room. They hold the tool with the right hand and they were asked to place the left arm on the leg during the training. On each trial, participants hold the tool in a starting position, with the tip of the tool placed on the floor close to their feet. At the beginning of the trail the experimenter placed one of the target objects on the floor, avoiding making any sound that could cue the subjects toward the object location. Participants were instructed to explore the space around them, making a continuous fluid movement starting from the left to the right space until they found the object. Once they found it, they drag it until their foot. Then the experimenter removed the target object and positioned another one. Participants were instructed to place the arm back on the initial position at the end of each trial, until the following trial started.

The experimenter monitored the correct execution of tool-use training. On average, during each session of 20 minutes training, participants retrieved 65 target objects.

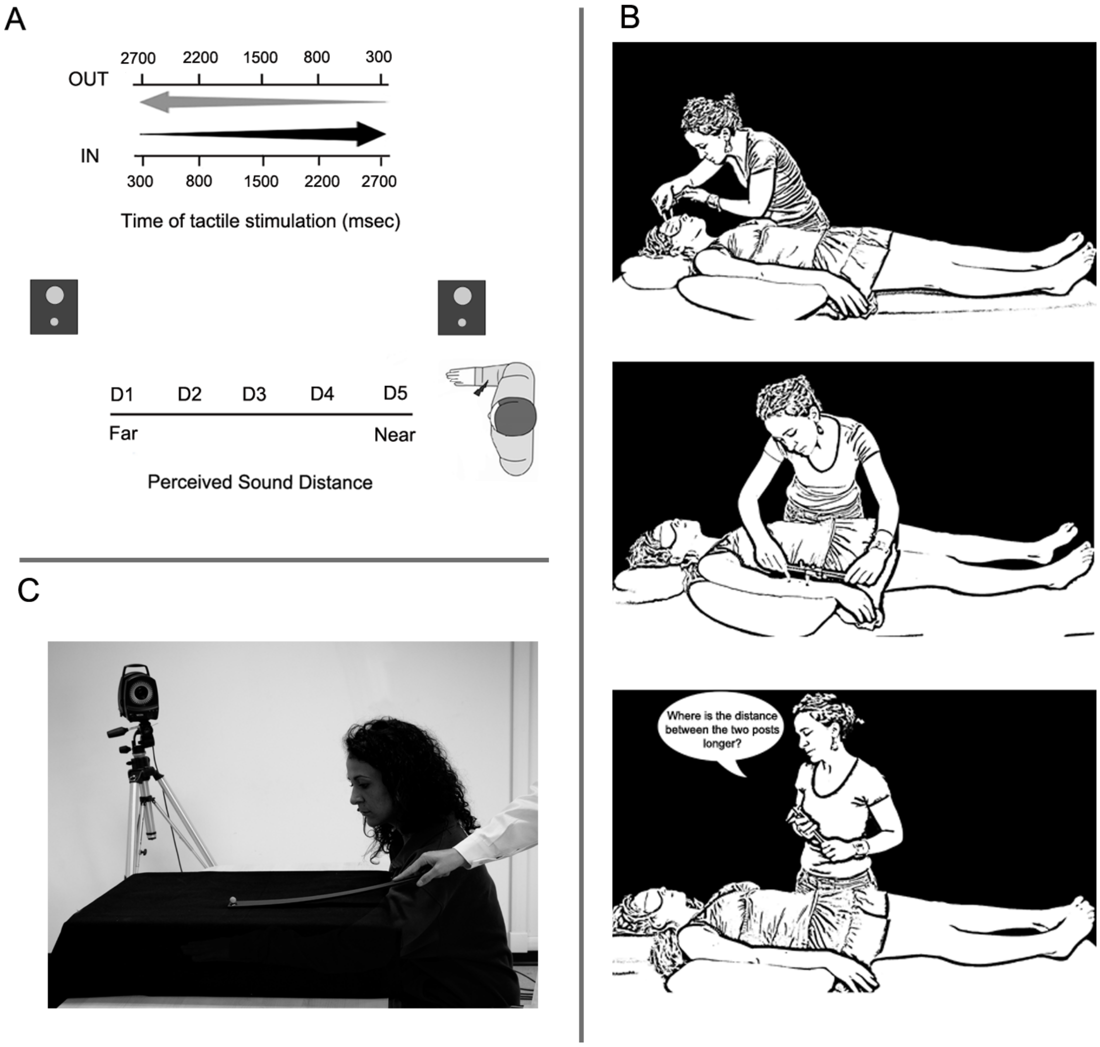

Figure 5.1
A. Experimental set up for the audio-tactile interaction task.
B. Experimental set up for the tactile distance perception task.
C. Experimental set up for the localisation task.

Design

We measured PPS representation and BR before and after a training session, consisting in using a tool with the right arm to retrieve objects placed in different positions in far space for 20 minutes The PPS assessment was intermingled with BR assessment. The order of task administration was as follows. Before tool-use, half subjects performed the audio-tactile interaction task first and then the tactile distance perception task, and vice versa for the remaining subjects. Then each subject performed two sessions of 20 minutes training with a 1 m long stick, consisting in using this tool to find objects placed on the floor at various locations (within a space from 50 to 110 cm in front of the subject and up to 140 cm to the right and to the left of the subject's feet). Each session was intermingled with an assessment session. In the assessment performed after the first training session, half subjects were tested with the audio-tactile interaction task and the other half with the tactile distance perception task. In the assessment performed after the second training session, subjects previously tested with the audio-tactile interaction task were tested with the tactile distance perception task; vice-versa for the second half of subjects. In this way, each post-tool-use assessment with the PPS representation and the BR task was immediately preceded by the same amount of tool-use (i.e. 20 minutes), and the order of PPS or BR assessment after tool-use was counterbalanced between subjects. Subjects were blindfolded during both the experiment and the training.

5.2.2 Results

Audio-tactile interaction task

In order to study the relationship between RTs and the different perceived positions of sound in space as a proxy of PPS extension, we calculated tactile RTs both for IN and OUT sounds at the different temporal delays at which tactile stimulation was administered. RTs exceeding more than 2 standard deviations from the mean RT were considered outliers and trimmed from the analyses (1.5% of trials). At every temporal delay, from T1 to T5, sound is perceived in a different position of space with respect to the stimulated body part. Given the equivalent segmentation of the different temporal delays (see Canzoneri et al., 2012) from T1 to T5, there was a spatial correspondence between the perceived position of IN and OUT sounds at T1 IN and T5 OUT (farthest distance from the body) and at T2 IN and T4 OUT (far distance), T3 IN and T3 OUT (intermediate distance), T4 IN and T2 OUT (close distance), T5 IN and T1 OUT (closest distance). This assumption was confirmed by a sound localisation experiment run with the same set up and published in Canzoneri and colleagues (2012; see Chapter 4). We averaged tactile RTs for these couples of delays and analysed RTs as a function of the five possible perceived distances, from D1, farthest distance, to D5, closest distance, in a unique function.

Since tactile stimuli were administered well above threshold, subjects were extremely accurate in performing the task, as rate of false alarms and omissions was very low, i.e., 0.06% and 2.88% respectively. Thus, the performance was analysed in term of reaction time only. The ANOVA conducted on RTs with Condition (Before tool-use, After tool-use) and Distance (from D1 to D5) as within subjects factors showed a significant two-way interaction [F(4,44)=3.15, p<0.05]. As Figure 5.2 shows, before tool-use, the function describing the relationship between tactile RTs and the position of sound in space shows that tactile RTs progressively sped up as the perceived sounds' distance from the body decreased. In particular, RTs at D1 (mean RTs ±S.E.M, 477 ms ±30) and D2 (481 ms ±28) - when sounds were perceived far from the body - were significantly longer compared to RTs at D3 (450 ms ±29), D4 (444 ms ±27) and D5 (444 ms ±30; all $p_s<0.02$, Newman-Keuls corrected) - when sounds were perceived close to the body. This spatial modulation of tactile perception due to sound position captures the boundaries of PPS representation before tool-use (see Canzoneri et al., 2012 for similar results). Those boundaries were extended after tool-use, as shown by a change in the shape of the function describing the relationship between sound position and tactile RTs. After tool-use, RTs at D2 were no more significantly different than RT at D3, D4 and D5 (all $p_s > 0.72$). Thus, the critical spatial range where sounds became effective in modulating tactile RTs shifted to include positions more distant from the forearm, i.e. around D2, whereas it was located around D3 before tool-use. Indeed, RTs at D2, and not at any other distance, were significantly faster after tool-use compared to before tool-use ($p < 0.05$).

Results from the present experiment are in line with several pieces of evidence in the literature, showing that using a tool affected PPS representation. Previous studies in monkeys (Iriki et al., 1996), healthy human subjects (Maravita et al., 2002; Serino et al., 2007; Bassolino et al., 2010) and neuropsychological patients (Farnè & Làdavas, 2000; Farnè et al., 2005a; Maravita et al., 2002) have shown that after tool-use, visual or auditory stimuli presented in the far space, at the tip of the tool, interact with somatosensory stimuli on the hand holding the tool (see Farnè & Làdavas, 2000; Làdavas & Serino, 2008; Maravita, 2006; Maravita & Iriki, 2004). These effects have been interpreted by the majority of the authors as evidence of extension of PPS representation to envelop the space in which the tool is used (see Maravita, Spence, & Driver, 2003). Alternatively, some authors interpret similar effects as a consequence of a shift of crossmodal spatial attention (maybe due to motor preparation, see Holmes et al., 2007a; Yau et al., 2009; see also Holmes, 2012), from the space around the body to that around the tip of the tool, rather than as a change in PPS representation. In order to exclude that the present results were due only to a generic shift of attention towards the far space we conducted Experiment 5.3 (see below).

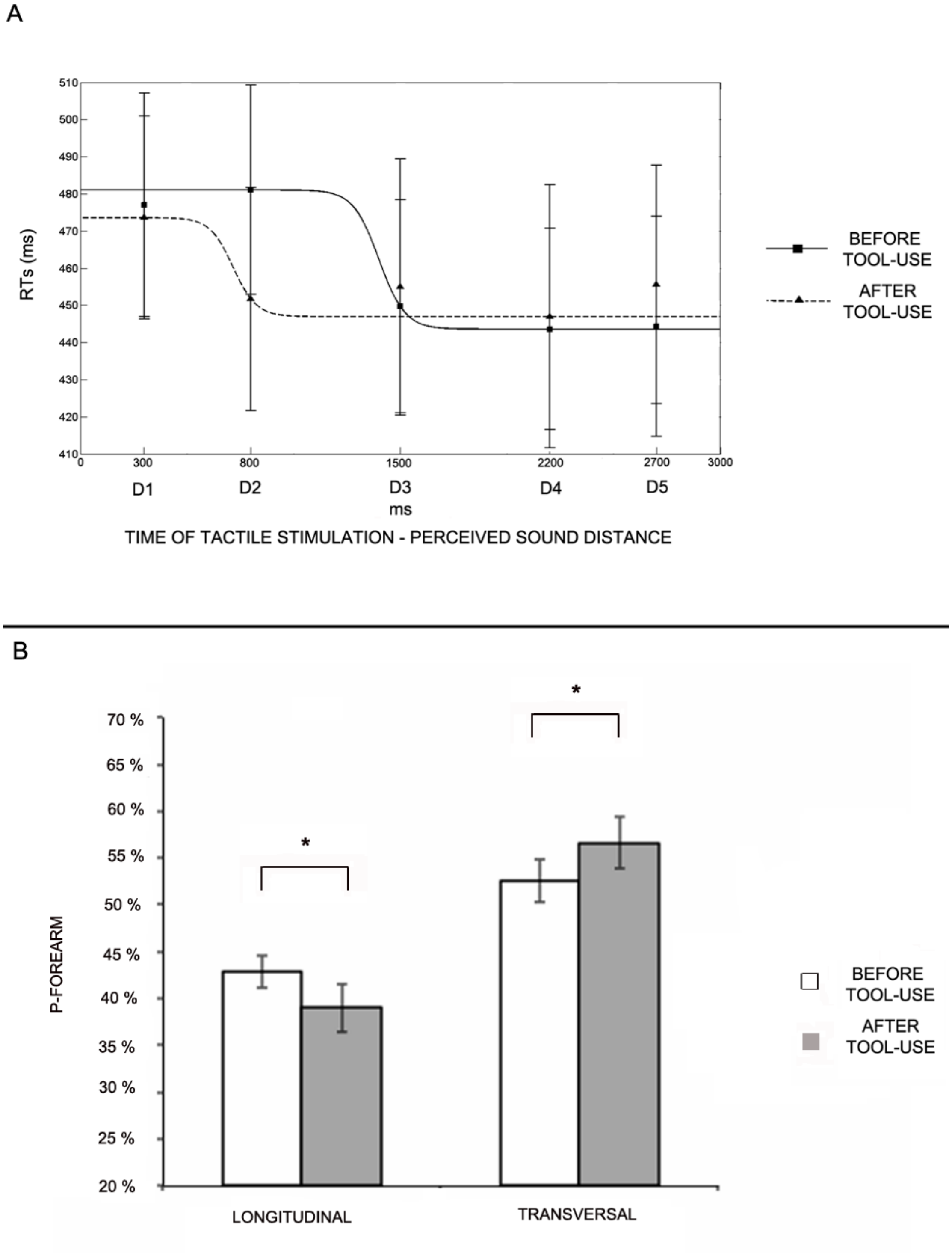

Figure 5.2. Experiment 5.1 results.

A. Tool-use extends PPS representation.

Audio tactile interaction task results. Mean (and S.E.M.) RTs at different perceived sound distances from D1- farthest - to D5- closest - (corresponding to different times of tactile stimulus delivery), and best fitting sigmoidal functions describing the relationship between RTs and sound distance, Before tool-use (filled line) and After tool-use (dotted line).

Individual data were averaged and the mean RTs were fitted with a sigmoidal function with least squares regression; the parameters estimated in the best-fitting procedure were the central point of the sigmoid and the slope of the sigmoid at the central point. The central point of the sigmoidal function shifted towards the far space (715 ms) after tool-use as compared to before tool-use (1399 ms), showing that, after tool-use, auditory signals affected tactile processing at earlier temporal delays, i.e.

at farther distances from the subject's body. The Figure reports the sigmoidal function fitted after averaging RTs at each distance from individual subjects.

B. Tool-use affects the internal representation of arm shape.

Tactile distance perception task results. The graph shows mean P-Forearm (and S.E.M.) both for longitudinal and transversal orientations, Before tool-use (white columns) and After tool-use (grey columns).

Tactile distance perception task

For each subject we calculated the mean probability of reporting the distance on the forearm as longer for all the combinations of inter-point distances (P-Forearm). All these probabilities were compared before and after tool-use, for longitudinal and transversal orientations, in order to assess the respective perceived length and width of the forearm. Since an equal number of stimuli on the forearm and on the forehead had greater relative inter-stimulus distance, a-priori P-Forearm of an unbiased perceiver was expected to equal 50%. We predicted, instead, that P-Forearm would vary depending on the perceived size of the stimulated forearm,

The ANOVA conducted on the mean P-Forearm with Condition (Before tool-use and After tool-use) and Orientation (Longitudinal and Transversal) as within-subjects factors showed a significant main effect of Orientation [F(1,11)=24.06, p<0.01]. Subjects systematically perceived greater distance between the two stimuli on the forearm in the Transversal (P-Forearm mean ±S.E.M, 55% ±2) than in the Longitudinal orientation (41% ±2), showing that subjects normally underestimate tactile distance along the longitudinal axis of the forearm. This effect is already known and it is probably due to the organization and shapes of tactile receptive fields along the forearm surface (Longo & Haggard, 2011). More importantly, for the aim of the present experiment, the pattern of responses changed when P-Forearm was compared before and after tool-use, as revealed by the significant two-way interaction [F(1,11)=11.79, p<0.01]. In the Longitudinal orientation, P-forearm decreased after tool-use (38% ±2) as compared to before tool-use (44% ±2, p<0.05). Conversely, in the Transversal orientation, P-Forearm significantly increased after tool-use (57% ±3) as compared to before tool-use (53% ±2, $p<0.05$). Since the effect of tool-use training was opposite for Transversal and Longitudinal orientation, the main effect of Condition was not significant [$F(1,11)=0.3$, $p=0.59$].

In summary, the present results show that after tool-use subjects perceived the distance between the two stimuli as shorter in the longitudinal orientation and longer in the transversal orientation. It is currently accepted that tactile signals are processed with reference to an implicit representation of the body (see Longo et al., 2010; Medina & Coslett, 2010). Some authors also showed that such representation can by modified by manipulating visual (Taylor-Clarke et al., 2004), proprioceptive (de Vignemont et al., 2005) or acoustic (Tajadura-Jiménez et al., 2012) body-related inputs. Accordingly to these studies, an increase in perceived tactile distances is interpreted as an increase in the represented size of the body part tactilely stimulated. A different body of literature in the field of haptic perception, however, offered an opposite interpretation of similar effects. Other authors have indeed shown that the size of graspable objects is scaled relative to the size of the hand used to grasp them, such that the hand is used as a "perceptual ruler" to measure object's size: the larger the hand is perceived as being, the smaller the object placed in the hand is judged; a "complementary" effect, so to speak (Action Specific Perception perspective; Linkenauger, Ramenzoni, & Proffitt, 2010; Linkenauger, Witt, & Proffitt, 2011). This kind of effect is reminiscent of experiences reported by individuals with a neurological condition, called "Alice in Wonderland" syndrome, in which patients experience, for instance, growth of their body followed by shrinkage of the world around them (Todd, 1955; Linkenauger et al., 2010). Effects of re-scaling distance perception as a function of the perceived body size have been also recently shown after illusions of ownership of virtual bodies: when participants experienced a tiny body as their own, they perceived objects to be larger and farther away and, conversely, when they experienced a large-body illusion, they perceived objects to be smaller and nearer (van der Hoort, Guterstam, & Ehrsson, 2011).

We are inclined to interpret the results from the present experiment more in line with this last account, proposing that perception of the distance between two tactile stimuli is rescaled on the basis of the context in which they are presented, accordingly to a context dependent bias: the same distance is perceived as wider when presented in a smaller context as compared to when presented in a wider context. This context-dependent effect is well documented in the field of visual perception, such as, for instance, in the Ebbinghaus illusion (1897), where the same central circle is perceived as smaller or bigger when presented against a background of bigger or smaller surrounding circles, respectively. In order to demonstrate such a context-dependent bias in the case of distance perception, we conducted a visual-analogue and a tactile-analogue of the present tactile distance perception task. In the visual distance experiment, 9 naïve subjects underwent a computerized visual task. During the experimental sessions patients sat in a dimly lit and sound attenuated room in front of a 17” PC monitor (refresh rate 60 Hz) at a distance of 57 cm. Stimulus presentation and response recording was controlled by a PC running C.I.R.O software (http://www.cnc.unibo.psice.unibo/ciro). Participants were presented with two red dots on a white background rectangle projected on the computer screen for 300 ms, followed by a black screen lasting 500 ms. Then a second pair of red dots on a white rectangle appeared for 300 ms. Subjects were asked to judge whether the distance between the two red dots was longer in the first or in the second visual stimulus, ignoring the background rectangle and responding verbally. The distance between the two dots was systematically manipulated so as to mimic the tactile distance perception task. The length of the background rectangle was also manipulated so as to mimic the perceived dimensions of the forearm. In this way, in different trials subjects were asked to compare two dots whose distance was actually different, or two dots whose distance was equal, but which were placed on a different context (see Figure 5.3 legend for details on the experimental procedure). If the context-dependent bias applies as we predicted, subjects' responses should be influenced by the dimension of the background rectangle so that the inter-point distance between a pair of dots presented on a shorter rectangle should be perceived longer than the same inter-point distance between a pair of dots presented on a longer rectangle. The results confirmed this prediction. For each subject we calculated the probability of reporting a longer distance between the two dots in the second stimulus (P-Second) when: a) the Inter-point Distance was kept constant and the length of background rectangle was manipulated (being longer in the first visual stimulus, longer in the second visual stimulus, or equivalent in the two visual stimuli); b) the size of the background rectangle (Background Size*)* was kept constant and the inter-point distance was manipulated (being longer in the first visual stimulus, longer in the second visual stimulus, or equivalent in the two visual stimuli). The ANOVA with Inter-point Distance and Background Size as within-subjects factors showed a significant two-way interaction [F(1,8)=397.72, p<0.01)]. Even when the inter-point distance was equal for the two visual stimuli, P-Second was lower when the background rectangle of the second visual stimulus was longer (P-Second mean ±S.E.M, 58% ±6), than when the background rectangle of the second visual stimulus was shorter (75% ±7, p<0.01). Instead, when the inter-point distance was actually manipulated, and the size of the background rectangle was constant, P-Second was correctly higher when the inter-point distance was longer in the second visual stimulus (97% ±1) than in the first visual stimulus (3% ±1, $p<0.01$), confirming that subjects were correctly performing the task. Thus, the dimension of the background rectangle clearly affects distance perception, as predicted by the context dependent bias, replicating the results obtained by Taylor-Clarke and colleagues (2004) in a visual analogue of the tactile distance perception task.

In order to demonstrate that the context-dependent hypothesis applies also in the case of tactile stimulation, we also run a tactile distance experiment, in which 16 new participants were tactilely stimulated by two posts, longitudinally applied on their left forearm (reference body part) and, 2 seconds later, by two posts longitudinally applied on their right forearm (target body part). In two-thirds of trials, target stimuli on the right arm was preceded by a “context stimulation” in which the borders of a rectangular box was applied on the right arm for 1 second and then removed, just before administration of the target stimuli. Target posts were administered in the middle of the skin surface previously framed by the rectangular box (see Figure 5.3 legend for details on the experimental procedure). The experiment was conducted in 3 randomized conditions of context stimulation, i.e., by using a short (12 cm long X 5 cm wide) rectangular box, a long (18 cm long X 5 cm wide), or no box. The short and the long rectangular boxes were used to differently prime the space on the forearm where tactile posts were referenced. Participants made un-timed two-alternative forced-choice judgments of whether the two points felt farther apart on the reference or on the target forearm, responding verbally, while being asked to ignore the context stimulation. An experimenter administered the stimuli manually and recorded the response. Participants were blindfolded throughout the procedure.

For each subject we calculated the probability of reporting a longer distance between the two posts in the second stimulus of the target forearm (P-Second). An ANOVA on P-Second with the factors Context Stimulation (short, long or no rectangle) and Inter-point Distance, showed a significant two-way interaction [F(4,60)=4.13, $p<0.01$]. In line with the context-dependent bias hypothesis, and with the results of the visual analogue task, we found that in case of uncertainty about the inter-point difference between stimuli applied on the two arms (in conditions of no inter-point difference), the administration of the rectangular box biased subjects' perception so that distance between posts applied on the target arm was underestimated (P-Second mean ±S.E.M, 18% ±3.3), when the stimuli were preceded by the long rectangular box, priming a longer arm surface, and over-estimated (24% ±4, $p<0.05$), when the stimuli were preceded by the short rectangular box, priming a shorter arm surface. As for the visual distance experiment, subjects' perception was accurate, when inter-point distance was actually manipulated: P-Second was correctly higher when the inter-point distance was longer on the target (68% ±6) than on the reference (40% ±6, $p<0.01$) arm.

Therefore, the results of the two control experiments on visual and tactile distance perception support the context-dependent bias hypothesis.

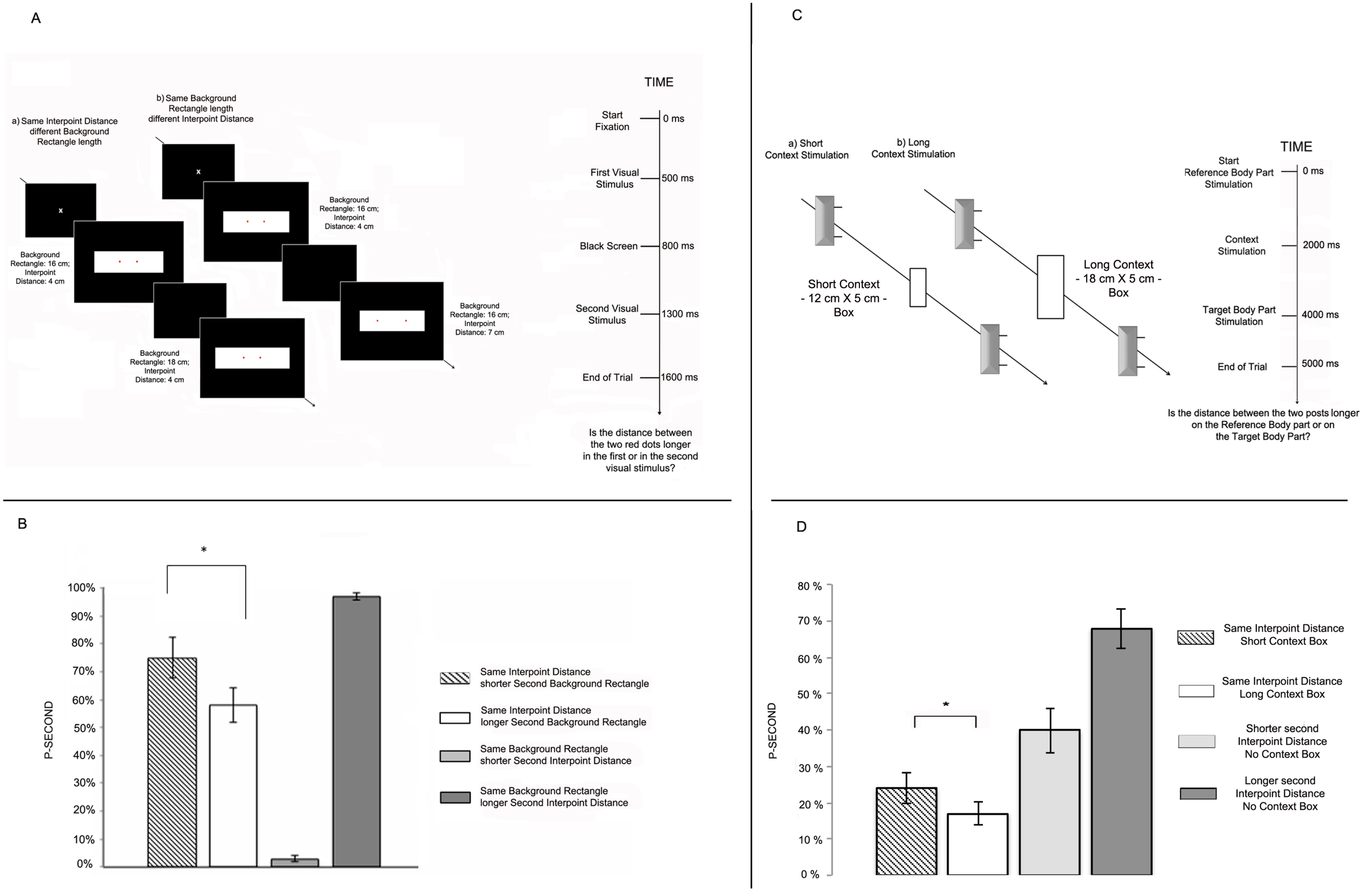
A
a) Same Interpoint Distance different Background Rectangle length
b) Same Background Rectangle length different Interpoint Distance
x
x
Background Rectangle: 16 cm; Interpoint Distance: 4 cm
Background Rectangle: 16 cm; Interpoint Distance: 4 cm
Background Rectangle: 18 cm; Interpoint Distance: 4 cm
Background Rectangle: 16 cm; Interpoint Distance: 7 cm
TIME
Start Fixation
0 ms
First Visual Stimulus
500 ms
Black Screen
800 ms
Second Visual Stimulus
1300 ms
End of Trial
1600 ms
Is the distance between the two red dots longer in the first or in the second visual stimulus?
B
*
P-SECOND
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Same Interpoint Distance shorter Second Background Rectangle
Same Interpoint Distance longer Second Background Rectangle
Same Background Rectangle shorter Second Interpoint Distance
Same Background Rectangle longer Second Interpoint Distance
C
a) Short Context Stimulation
b) Long Context Stimulation
Short Context - 12 cm X 5 cm - Box
Long Context - 18 cm X 5 cm - Box
TIME
Start Reference Body Part Stimulation
0 ms
Context Stimulation
2000 ms
Target Body Part Stimulation
4000 ms
End of Trial
5000 ms
Is the distance between the two posts longer on the Reference Body part or on the Target Body Part?
D
*
P-SECOND
80 %
70 %
60 %
50 %
40 %
30 %
20 %
10 %
0 %
Same Interpoint Distance Short Context Box
Same Interpoint Distance Long Context Box
Shorter second Interpoint Distance No Context Box
Longer second Interpoint Distance No Context Box

Figure 5.3. Visual-analogue and tactile-analogue of the tactile distance perception task.
A. Schematic representation of stimuli (on the left) and trial structure (on the right) in the visual analogue of the tactile distance perception task.
a) Example of a trial with same inter-point distance and different background rectangle length between the first and the second visual stimulus.
b) Example of a trial with same background rectangle length and different inter-point distance between the first and the second visual stimulus.
B. Results of the visual analogue of the tactile distance perception task.
A 3 by 3 combination of inter-point distances (4, 5.5 and 7 cm) and rectangle length (16, 17 and 18 cm) was used. In 36 trials, the size of the background rectangle was different between the first and the second visual stimulus (case a) – being longer for the first visual stimulus in half trials and longer for the second visual stimulus in the remaining trials - while keeping constant the inter-point distance. In 36 trials the distance between the two points was different between the first and the second visual stimulus (case b) - being longer for the first visual stimulus in half trials and longer for the second visual stimulus in the remaining trials - while keeping constant the background rectangle. In the remaining 8 trials, the background rectangle and the inter-point distance were the same for the first and the second visual stimulus. Each participant performed two blocks of 80 trials each.
The graph shows the Probability of reporting longer the distance between the two dots in the second stimulus (P-Second; Error bars denote S.E.M.), when the size of the background rectangle (on the left) or the inter-point distance (on the right) was manipulated.
C. Schematic representation of stimuli (on the left) and trial structure (on the right) in the control tactile distance perception task.
a) Examples of a trial with Short context stimulation on the Target arm
b) Example of a trial with Long context stimulation on the Target arm.
D. Results of the control tactile distance perception task.
For 12 trials, the inter-point distance for the pair of posts on the reference and on the target arm was the same (i.e., at 4 cm); for 8 trials, the inter-point distance was longer for the pair of posts on the reference (5 cm) than for those on the target arm (3 cm); vice-versa for the remaining trials (i.e., 3 cm on the reference and 5 cm on the target arm). A total of 84 trials (3 difference distance by 3 context stimulation) were administered in random order, within a single experimental block.
The graph shows the Probability of reporting longer the distance between two posts on the Target arm (P-Second, error bars denote S.E.M), when the size of the background rectangle (on the left) or the inter-point distance (on the right) was manipulated.

If we translate these effects to the results of the tactile distance perception task run before and after tool-use, these findings support the view that after tool-use subjects more frequently perceived the distance between two points longitudinally applied on their forearm as shorter because they perceived their forearm as longer than compared to before tool-use. A reversed effect was found for the distance between stimuli applied transversally: subjects more frequently perceived the distance between the two points on the forearm as wider after tool-use, because the forearm was perceived as narrower in comparison to before tool-use.

In summary, results from the first experiment demonstrated that tool-use induces plastic change in not only in PPS representation, but also in the BR, compatibly with an internal representation of a longer arm after tool-use.

5.3 Experiment 5.2

In order to give further support to data from the tactile distance perception task and actually demonstrate that tool-use resulted in an increase of the perceived length of the forearm, in Experiment 5.2 we evaluated the perceived dimension of the forearm before and after a training with a tool by using both the *tactile distance perception task* and a *body-landmarks localisation task*, explicitly assessing the perceived location of the forearm extremities, the wrist and the elbow. The distance between the two locations was computed to quantify the perceived length of the forearm.

5.3.1 Methods

Participants

Nine healthy subjects (4 females, mean age 28 years) participated in the study. All subjects were right-handed and had normal vision and touch. All subjects gave their informed consent to participate in the study, which was performed in accordance with the Declaration of Helsinki.

Materials and procedures

Tactile distance perception task

The task was the same as for Experiment 5.1, except that participants performed the task only for longitudinal orientation, in order to assess the perceived arm length.

Body-landmarks localisation task

Subjects were instructed to verbally indicate when a moving marker reached the felt position of two occluded body parts, i.e., the wrist (specifically, the ulnar styloid) and the tip of the elbow joint (i.e. the olecranon). Before the task, the experimenter explicitly showed these anatomical landmarks on her body. Subjects sat down with their right arm passively placed by the experimenter on a table in a prone position. The forearm was aligned with the shoulder joint. In order to avoid movement, for all the task duration, the arm was fixated on the table with tape. To prevent participants from viewing the forearm during the task, a rectangular black box (90 cm long X 50 cm wide) was placed over the arm. The box covered the entire width of the table. On each trial, the experimenter verbally cued the participant as to which landmark to judge. Then, the experimenter manually moved a retro-reflective marker over the surface of the box, along the longitudinal axis of the forearm. The retro-reflective marker (1.5 cm in diameter) was stuck on the tip of a black cane 50 cm long (See Figure 5.1C). On different trials, run in randomized order, the marker was moved in two different directions, either approaching to (moving in a distal to proximal direction) or receding (moving in a distal to proximal direction) from subjects' body. Participants were instructed to say "Stop" when the retro-reflective marker was perceived just above the felt position of the target anatomical landmark. At that verbal signal the experimenter ended the movement leaving the marker where indicated by the participant. The participant was allowed to further adjust the final position of the marker, by verbally asking the experimenter to move it backward or forward. When the participant confirmed the final position, the marker's location was recorded through an optical motion capture system (Vicon).

After the last trial, to record the actual positions of the elbow and the wrist, the box was removed, participants were blindfolded and two retro-reflective markers (1 cm in diameter) were placed on the anatomical landmarks. The task comprised 20 trials, 10 for each body landmark, with an equal number of trials moving in the IN and OUT directions.

The distance between the mean estimated positions of the wrist and the elbow was considered a measure of the perceived forearm length. Additionally, we checked the position error between the mean estimated location of each target landmark and its actual position. A custom MATLAB (Mathworks, Natick, MA) script was employed to analyze data.

Design

The *tactile distance perception task* and the *body landmarks localisation task* were run before and after a training session, consisting in using a tool with the right arm to retrieve objects placed in different positions in far space for 20 minutes. The structure of the Experiment was the same as for Experiment 5.1.

5.3.2 Results

Tactile distance perception task

In order to test whether the implicitly perceived arm length changed before and after tool-use, mean P-Forearm from the two sessions was compared with a paired sample t-test. P-forearm significantly decreased after tool-use (49% ±3) as compared to before tool-use (53% ±2; $t(8)=2.47$, $p<0.05$), in line with results from Experiment 5.1. According to a context-dependent bias, these results confirm that after tool-use the distance between points of contact on the forearm surface is systematically underestimated, suggesting an increased in the perceived length of the forearm.

Body-landmarks localisation task

To compare the perceived arm length before and after tool-use, we calculated the perceived arm length as the difference between the perceived position of the elbow and the wrist (E-W Distance). A repeated measure ANOVA was performed on E-W Distance, with Condition (Before tool-use, After tool-use) and Movement Direction (Distal-to-Proximal, Proximal-to-Distal) as within-subject factors. The main effect of Condition was significant [F(1,8)=5.80, p<0.05], showing that E–W distance significantly increased after the training with the tool (Before tool-use=23.57±1.8 cm; After tool-use=24.70± 1.7 cm). This effect was independent from movement direction as the two-way interaction Condition X Movements Direction was not significant (p=0.7). These results suggest that after tool-use the forearm was perceived as longer than before tool-use.

A repeated measure ANOVA was also run on wrist and elbow position error (i.e. the difference between the mean estimated location of each landmark and its actual position) with Condition (Before tool-use, After tool-use), Movements Direction (Distal-to-Proximal, Proximal-to-Distal) and Landmarks (Elbow, Wrist) as within-subject factors. Results showed a significant Condition X Landmarks interaction [F(1,8)=5.53, p<0.05]. This effect was due to a change in the perceived location of the wrist, rather then the elbow. Indeed, after tool-use the wrist was perceived farther from the body farther from the body than before (Before tool-use=-2.25±1.5, After tool-use=-.72±1.5), while the elbow position did not significantly change (Before tool-use=-1.39±0.9, After tool-use=1.05±1; p=0.38, Newman-Keuls corrected). This effect was again independent from the direction of the movement, as the three-way interaction was not significant (p=0.69).

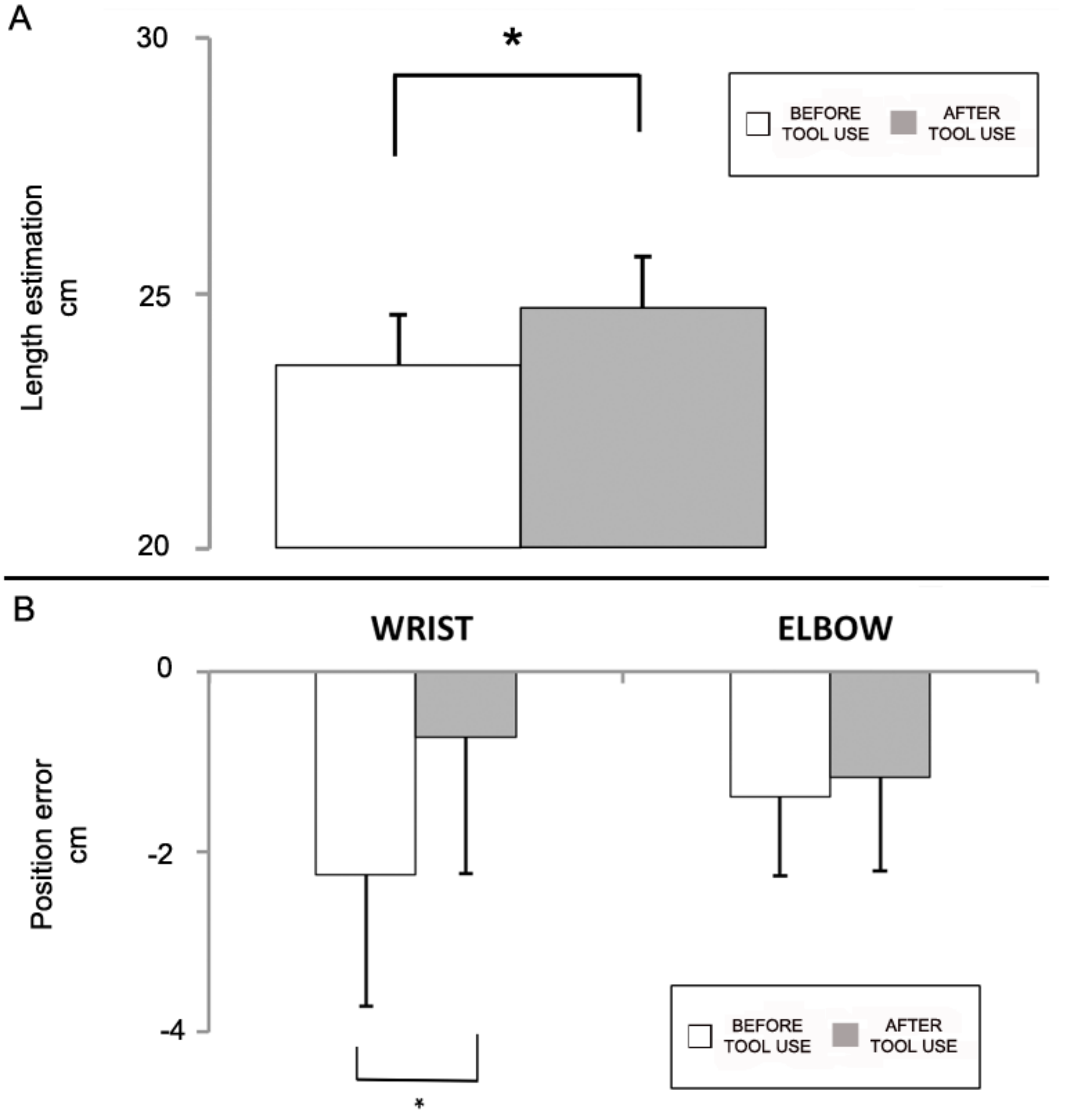

Figure 5.4 Experiment 5.2 results, body landmarks localisation task. Tool-use affects the perceived length of the forearm

A. The graph shows mean length estimation Before tool-use (white columns) and After tool-use (grey columns).

B. The graph shows mean wrist (on the left) and elbow (on the right) position errors Before tool-use (white columns) and After tool-use (grey columns).

In order to verify whether and to what extent the measures obtained from these experiments are related, we calculated an index of change for both the tactile distance perception task and the body landmark localisation task, by normalizing the scores from the two tasks and subtracting the Before Tool-use scores from the After tool-use data for each participant, in order to allow a more direct comparison between the two Experiments. We then performed a correlation analysis between these two indexes. Results did not indicate any significant correlation (r=.33, p=.38).

Results from the tactile distance perception in Experiment 5.2 were in line with results from the same task in Experiment 5.1, showing that after tool-use participants underestimated the tactile distance between two taps administered on the trained forearm. At the same time, results from the localisation task showed an increase in the distance between the perceived location of the wrist and the elbow after tool-use, compatible with an increase in the perceived forearm length after the training. Numerically, the increase was around 1.1 cm. Considering that subjects used a 100cm tool during the training, one might suggest that 1% of the tool length was "embodied" into the arm representation after tool use. However, at the moment we cannot establish whether that value has a perceptual valence, or it simply depends on the sensitivity of the task used to measure the effect of tool-use. One way to answer this question would be testing the effects of using tools of different lengths: for instance, using a 200cm tools should lead to a ~2cm of elongation. At the best of our knowledge, nobody tested whether plastic effects of tool use on BR actually depend on the physical size of the tool. Only Sposito and colleagues (2012) compared the effect of using a long vs. a short (20 cm), functionally useless, stick, and found that only the former, but not the latter, tool affected the perceived length of the forearm. But, no data are available on whether a longer tool, which would allow acting on further portions of space, would actually make the subjects feeling their arm even longer.

The present findings are in line with results of Cardinali and colleagues after a training with a long mechanical grabber (Cardinali et al., 2009a; but see also Cardinali et al., 2011). Moreover, findings from the present experiment demonstrated that the change in the perceived length of the forearm was not due to a subjective proprioceptive shift of the whole arm towards the far space, since only the wrist, but not the elbow, was perceived farther from the body (see also Sposito et al., 2012). In summary, these findings confirm the results from the Experiment 5.1, and provide strong evidence for an actual extension of the perceived length of the arm after tool-use.

5.4 Experiment 5.3

In order to demonstrate that any change in PPS representation and BR was actually due to tool-use, and not to a generic effect of movement, attention, or simply to repetition of the tasks, in Experiment 5.3 we evaluated both PPS representation with the *audio-tactile interaction task* and BR with the *tactile distance perception task* before and after a control training, consisting in pointing to objects placed in different positions in far space (Pointing task). Subjects were asked to point with their right hand towards objects placed in the same location, just as in the tool-use experiments, however no tool was used. We predicted that the pointing task, that drives subjects' attention towards the far space during the training, but does not involve any tool-mediated interaction between the subject's body and objects in far space, affects neither PPS representation nor BR.

5.4.1 Methods

Participants

Twelve healthy subjects (all females, mean age 25 years) participated in the study. All subjects were right-handed and had normal hearing and touch. All subjects, students at the University of Bologna, gave their informed consent to participate in the study, which was performed in accordance with the Declaration of Helsinki.

Materials and procedures

The audio-tactile interaction task and the tactile distance task were the same as used for Experiment 5.1.

Design

The structure of the experiment was the same as for Experiment 5.1, except for the training session, which consisted in a 20 minute pointing task: blindfolded subjects sit on chair with their left arm relaxed, while they held in the right hand a 15 cm long handle, of the same weight as the tool. In this way, fatigue effects due to holding the handle or the tool were similar between Experiment 5.3 and Experiment 5.1. During the training session, in each trial the experimenter touched an object placed on the floor, at a random location in far space, with the tip of the stick used for the previous experiments. In this way a sound was generated, comparable to that made by the subjects in Experiment 5.1 when they touched the object with the tool. Subjects were asked to point the handle towards the perceived location of the sound.

5.4.2 Results

Audio tactile interaction task

False alarm and omission rates were extremely low, i.e. 0.76% and 1.57% respectively. We analysed mean RTs to tactile targets (after outliers removal, see Experiment 5.1 for procedure) administered when sounds were perceived at different distances from the body. The ANOVA conducted on tactile RTs with Condition (Before pointing, After pointing) and Distance (from D1 to D5) showed a significant main effect of Distance [F(4,44)=25.79, p<0.01]. The pattern of results, shown in Figure 5.5, mirrors the same effect found in Experiment 5.1 before tool-use: as sound distance from the body decreased, RTs progressively shortened. Newman-Keuls post-hoc comparisons confirmed this effect, since RTs at D1 (Mean RTs ±S.E.M, 429 ms ±26) and D2 (414 ms ±27), when the sound was perceived far from the body, were slower compared to RTs at D3 (397 ms ±25), D4 (398 ms ±26) and D5 (390 ms ±25, all p_s <0.01), when the sound was perceived close to the body. Importantly, the space dependent modulation of RTs due to sound position was not different before and after the training session, as the two-way interaction was not significant [F(4,44)=1.87, p=0.13)], as well as the main effect of Condition [F(1,11)=.99, p=0.34)]. Thus, no extension effect of the boundaries of PPS representation was found after the pointing training session.

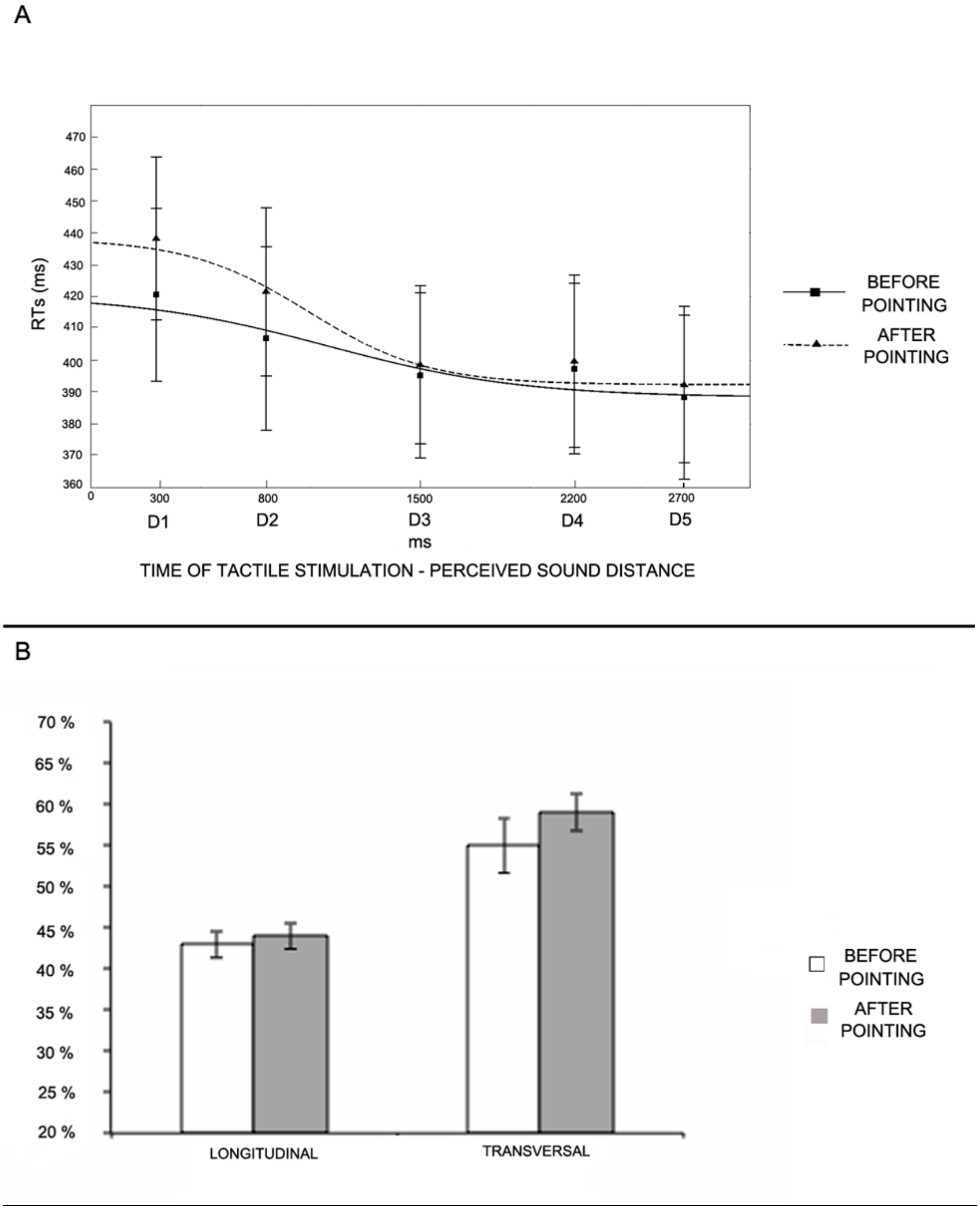

Figure 5.5 Experiment 5.3 results.
A. Pointing task does not affect PPS representation.
Audio tactile interaction task results. Mean (and S.E.M.) RTs at different perceived sound distances (from D1 - farthest - to D5 - closest), corresponding to different time of tactile stimulus delivery and best fitting sigmoidal functions describing the relationship between RTs and sound distance, Before pointing (filled line) and After pointing (dotted line). The central point of the sigmoidal function can be taken as a measure of the critical distance where sounds affect tactile RTs on the forearm, and therefore can be considered an index of the boundary of PPS. As shown in the Figure, there is no shift of the central point of the sigmoidal function After pointing (989 ms) as compared to Before pointing (1082 ms).
B. Pointing task does not affect the internal representation of arm shape.

Tactile distance perception task results. The graph shows mean (and S.E.M.) P-Forearm both for longitudinal and transversal orientations, Before pointing (white columns) and After pointing (grey columns).

Tactile distance perception task

A Repeated Measure ANOVA was conducted on the mean P-Forearm with Condition (Before pointing and After pointing) and Orientation (Transversal and Longitudinal) as within-subjects factors. The main effect of Orientation was significant [F(1,11)=29.58, p<0.01], mirroring the same trend found in Experiment 5.1 (P-forearm for Transversal orientation=57%±1; P-forearm for Longitudinal orientation=44%±1) and again in line with the results obtained by Longo and Haggard (2011). Importantly, the interaction Condition X Orientation was not significant [F(1,11)=.91, p=0.36], suggesting that the pointing task did not affect subjects' performance in the tactile distance perception task, and therefore subjects' perception of length or width of their arm.

5.5 General Discussion

In the present study we investigated whether PPS and BR changed in parallel after using a tool, extending action-space from the space immediately surrounding the body to the far space. In order to dynamically assess PPS representation we used a new audio-tactile interaction task developed by our group (Canzoneri et al., 2012; see Chapter 4): we have recently shown that tactile RTs coupled to moving sounds progressively speeded up to the extent that the sound source was perceived close to the body. The function describing the relationship between tactile RTs and the position of sounds in space can be used to localize the boundaries of PPS representation, and in this study has been used to measure plasticity of PPS representation after a short-term tool-use experience. Results from Experiment 5.1 show that after tool-use, the boundaries of PPS representation shifted to include farther locations, so that an auditory stimulus presented in a far position, where the tool has been used, was recoded as it were closer to the body, and therefore interacted with a tactile stimulus delivered on the arm. This effect was associated with a change in the representation of the arm shape: after tool-use, subjects perceived the distance between the two stimuli delivered on the forearm longitudinally to the arm axis as significantly shorter and perceived the distance between two stimuli delivered transversally on the forearm as significantly longer. Moreover, when asked to localize the position of their wrist and elbow, they localized those body landmarks farther apart between each other after tool-use. Taken together, these findings are compatible with an extension of perceived arm length after tool-use, assessed by means of two independent tasks. As the body changes continuously in position and dimensions throughout life, its brain representations need to be updated in order to correctly interact with the external world. The concept of body representations nowadays encompasses different concepts, with rather specific plastic properties. In line with a "dyadic view" of body representations, most authors usually make a distinction between Body Image and Body Schema (see de Vignemont, 2010; Dijkerman & de Haan, 2007; Gallagher, 2005; Cardinali et al., 2011). Body Schema is an implicit, on-line adapted representation of body parts size and position for action, whereas Body Image is a more explicit, off-line updated, representation of body appearance for perception (see Dijkerman & de Haan, 2007; De Vignemont, 2010; Carruthers, 2008; Gallagher, 1986). Accordingly, it has been proposed that these two representations can also be updated selectively depending on different types of experiences (de Vignemont & Farnè, 2010; Kammers, de Vignemont, Verhagen, & Dijkerman, 2009).

For instance, recent works on the effect of tool-use tried to disentangle the effects of tool-use on the body schema and the body image (see Cardinali et al., 2012; Sposito et al., 2012).

Some authors proposed instead a triadic taxonomy of body representations, whereby, maintaining the classic concept of Body Schema, the concept of Body Image is further divided into a Body Structural Description, more related to perception, and Body Semantics, interfacing with Language (see e.g., Schwoebel & Coslett, 2005; Sirigu et al., 1991). Reminiscing of the concept of Body Structural Description, Longo and Haggard (2010; 2011) recently proposed that there is a specific model of the body in the brain (which they call “body-model”), containing information about the size and shape of body parts.

At the moment, the exact number and functions of different body representations is matter of debate (see Kammers et al., 2010). For this reason, in the present study, we deliberately decide to not enter into this debate, but to adopt the more neutral and generic term of Body Representations, being well aware of potentially including in this way rather different levels of body-related information processing in the brain. Having said that, we used both the tactile distance perception task (Experiment 5.1 and 5.2) and the body landmark localisation task (Experiment 5.2) to assess a multisensory, high-level, mental representation of the body, processing several sensory cues to represent the size and shape of different parts of the body. We believe that the modification of BR after tool-use is strictly dependent on the sensory consequences of action: because, thanks to tool-use, we act on a portion of space exceeding the normal limits of our physical body, our brain start processing multisensory inputs related to one’s own body, but arising from a distal portion of space. For instance, tactile and proprioceptive cues processed at the upper limb via the tool handle, refers to objects contacting the tip of the tool. Such contacts also generate sensory feedback in other modalities, e.g. auditory feedback, as in the present experiments, when subjects were blindfolded, but also visual feedback in everyday life tool-use activities. We believe that this action-dependent extension of the space, where body-related sensory information arises from, is the trigger for the changes in body representation and PPS representation documented by the present experiments. This proposal has been recently introduced by our group in the context of a neural network model designed to account for plasticity in PPS representation (Magosso et al., 2010; see also Chapter 6).

In sum, the present study demonstrates a plastic modification of both body and space representations, suggesting that a tool, extending the action-space of the body (Gallese & Sinigaglia 2010), is incorporated into BR and affects both the spatial perception of the body itself and of objects presented in space.

A control experiment confirmed that these effects were actually due to tool-use, and were not due to the simple repetitions of the tasks or to a general attentional effect (see Holmes, 2012). Subjects performed a pointing training task, involving the same shift of attention towards far space as in the tool-use training task, but not involving any interaction between the body and far space. No changes in the audio-tactile interaction tasks and in the tactile distance perception task were found after the pointing task, indicating that both PPS representation and the BR were unaffected.

The correspondence between the extension effect for PPS and the perceived arm length suggest that body and PPS representations strongly overlap. This is not surprising considering that the receptive fields of bimodal neurons representing PPS around different body parts are anchored to specific body parts (Graziano & Cooke, 2006). Moreover, brain systems involved in PPS representation and BR are localized within the same fronto-parietal areas, encompassing the ventral premotor cortex and the posterior parietal cortex, both in monkeys (Duhamel et al., 1998; Graziano et al., 2000; Graziano et al., 1997a) and in humans (Bremmer et al., 2001; Filimon, Nelson, Huang, & Sereno, 2009; Makin et al., 2007; Sereno & Huang, 2006; Serino et al., 2011; Blanke, 2012). Thus, a similar fronto-parietal network might represent both the body surface and the visual and/or auditory space surrounding the body. PPS and BR also have a closely related role in action execution (Brozzoli et al., 2009; Gallese & Sinigaglia, 2010; Graziano & Cooke, 2006): in order to reach and manipulate an object, or in order to avoid contact with a harm, the brain needs to compute information about the position, shape, and movement of the object in space, and concurrently about the position, shape and dimensions of the body part potentially interacting with it. Moreover it has been demonstrated that the physical dimensions of the body (the arm length, in this case) determines the location of the boundary between near and far space (Longo & Lourenco, 2007). Our study provides experimental evidence of a further level of overlap between PPS and BR, i.e. their plastic properties.

Such overlap can be interpreted in three ways: it might be the case that the extension of PPS representation directly depends on the plastic change of BR, such that the elongation of the perceived size of the forearm extends the representation of the space around it (Maravita & Iriki, 2004). Alternatively, the two plastic phenomena might be simply associated, without any causal relationship between them. A third interpretation is possible, i.e., that the concept of PPS overlap with those levels of BR oriented to action, so that PPS and BR both define a unique representation of the body in space (for comments see Cardinali, Brozzoli, & Farnè, 2009b; Gallese & Sinigaglia, 2010). The present study, by providing evidence for an overlap of plastic properties of PPS and BR might support this third view, although it cannot causally confirm it.

CHAPTER SIX: A NEURAL NETWORK UNDERLYING EXTENSION OF PERIPERSONAL SPACE

6.1 Introduction

In the previous chapter we provided further evidence of plasticity of PPS representation induced by tool-use. Nevertheless, the underlying neural mechanisms of these plasticity processes are still largely unknown. The pioneering work of Iriki and colleagues (1996) specifically demonstrated that after tool use, visual receptive field (RFs) of bimodal neurons at the level of the intraparietal sulcus elongated and became responsive to stimuli presented at the tip of the tool.

Few neurophysiological studies in recent years suggest that these effects of tool-use training on the extension of the visual RFs could be explained by morphological changes at the level of synapses connection within the parietal lobe. More specifically, Ishibashi and colleagues (Ishibashi, Hihara, Takahashi, Heike, Yokota, & Iriki, 2002) suggested that the mechanism underlying this phenomenon could be the creation of new synaptic connections from the visual related areas cortex in the parietal cortex with the somatosensory neurons in the intraparietal sulcus (Ishibashi et al., 2002; Hihara, Notoya, Tanaka, Ichinose, Ojima, Obayashi, Fujii, & Iriki, 2006). Recently, a tentative has been made in order to create a theoretical model describing these neural mechanisms, taking advantages of computation neural network modelling.

Neural network models are information elaboration systems aimed at simulating neuron behaviour in a realistic way. Neural network models and computer simulation techniques represent a useful tool to investigate the mechanisms underlying PPS representation plasticity. Magosso and colleagues (Magosso et al., 2010c) presented a neural network model that simulates visuo-tactile integrative properties of multimodal neurons underling PPS representation around the hand. As a novelty, this model can be also used to simulate dynamic proprieties of PPS representation. The model originally proposed is composed of two networks (one per hemisphere), and it described visuo-tactile interaction around right and left hands. Each network is composed of three areas of neurons: two unimodal areas (visual and tactile) projecting to a third multimodal visuo-tactile area. In the model the two hemispheres are interconnected by inhibitory synapses. Thanks to the shape of the receptive fields and the arrangement of synaptic connections between unimodal and multimodal areas, neurons from the latter areas mimic neural responses of biological neurons in the primate brain, that is they respond more strongly to stimuli coming from a limited region of space around the hand. Each neuron has its own receptive field, reproduced in the model by means of a Gaussian function. The unimodal tactile area contains a matrix of neurons whose RF cover the whole hand. The visual unimodal area contains a matrix of neurons whose RF fields cover a space of approximately 1 mt around the hand. In both unimodal areas, the RFs are in hand-centred coordinates. In terms of brain structures, the tactile unimodal area might roughly correspond to high-order unisensory somatosensory (e.g., SI-SII) cortices, while the visual unimodal areas might correspond to high-order visual areas (e.g., areas MT and MST) in the parietal lobe (Boussaoud, Ungerleider, & Desimone, 1990; Cavada & Goldman-Rakic, 1989; Lewis & Van Essen, 2000; Maunsell & van Essen, 1983). According to the model, the multimodal area receives feed-forward projections from the two unimodal areas. The multimodal area corresponds to multisensory regions in the premotor or parietal cortex (Duhamel et al., 1998; Graziano et al., 1997a; Rizzolatti et al., 1981), deputed in coding PPS representation both in monkeys and in humans. In order to simulate PPS representation, projections from unimodal visual areas to multimodal areas are weighted so that neurons with visual RFs on and just immediately around the hand have stronger connections to the multisensory areas than neurons with RFs placed far from the hand. The strength of synaptic connections from the visual to the multisensory area decades as a function of distance of the visual RF from the hand. As a consequence, both a tactile stimulus at the hand and a visual stimulus close to the hand can activate the multisensory area, whereas a visual stimulus from the far space cannot. As a consequence, normally, responses from multisensory neurons are limited to stimulation arising from the space around the hand.

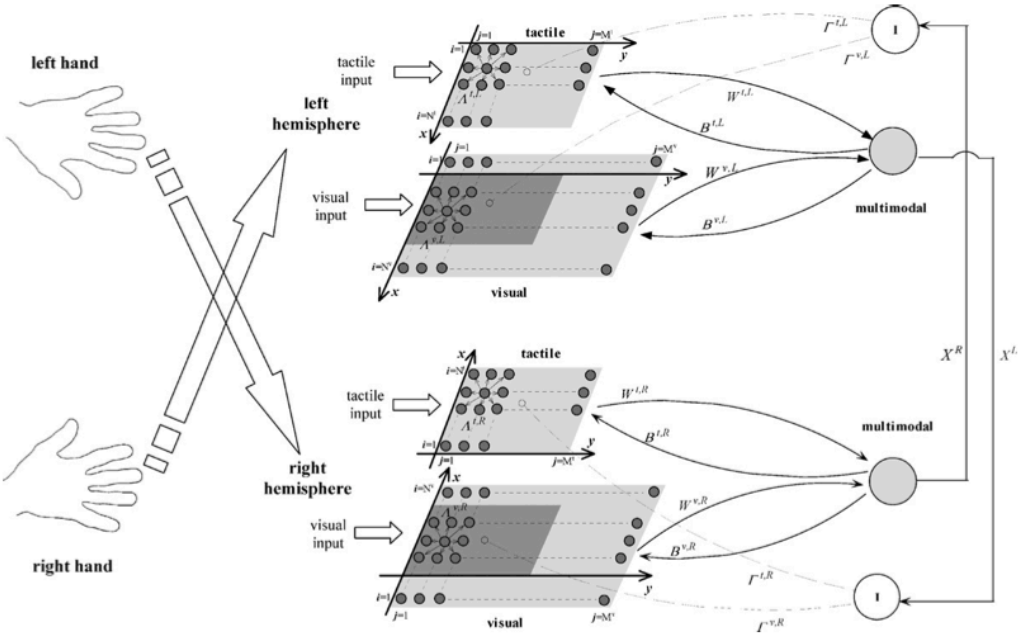

Figure 6.1 Schematic diagram describing the general structure of the model presented by Magosso and: colleagues: it represents the network for each hemisphere and the synaptic connections among regions of neurons within each hemisphere and between them. Meaning of the symbols: superscript L, R=left and right hemisphere; superscript t, v=tactile and visual; I=inhibitory interneuron; Λ=lateral synapses within the unimodal areas; W=feedforward synapses from unimodal neurons to the multimodal neuron; B=feedback synapses from the multimodal neuron to unimodal neurons; Γ= inhibitory synapses from the inhibitory interneuron to unimodal areas; X=cross-connections between the hemispheres, linking the multimodal neuron within one hemisphere to the inhibitory interneuron in the other hemisphere. **Adapted from Magosso et al., Neuropsychologia, 2010.**

This model has been used to simulate the effect of tool use on PPS representation. From a sensory point of view, a training with a tool consists in getting tactile information on the hand transmitted by the tool handle, and simultaneously visual and/or auditory information from the space were the tool is actively used. In keeping with this line of reasoning, tool-use training has been mimicked by applying both a tactile and a visual input to the network. The tactile input represents the portion of the hand stimulated while a subject holds the tool during the training. The visual input during tool-use represents the region of the visual space functionally relevant for the tool-use, that is the area where the tool was used. As activity with a 1mt tool is simulated, visual input activate neurons from the unisensory visual areas with RF allocated far from the hand. Both tactile and visual inputs project to the multisensory area. During the training, the simultaneous activation of synapses from tactile-to-multisensory and from visual-to-multisensory neurons, thanks to a Hebbian-like mechanism, makes that synapses between tactile and multisensory neurons centred on the hand and visual and multisensory neurons centred on the far space reinforces. Operationally, the weight of synaptic projections from the visual area responding to far stimuli to the multisensory areas is strengthened and therefore the visual RF of multisensory neurons enlarges to cover the far space. Indeed, computer simulations of the effects of tool-use show that, after the training, differently than before the training, multisensory neurons also respond to a visual stimulus administered in the far space (Magosso et al., 2010c). Therefore, according to this neural network model, the extension effect on PPS due to tool-use does not depend on the tool itself, but it raises because of a pairing of a tactile stimuli at the hand (via the tool handle) with synchronized visual stimuli from the far space (via the tip of the tool). Thus, it is possible to predict that simple pairing tactile near stimuli and visual far stimuli, independently from any tool-use, would be sufficient to extend PPS representation.

To test this prediction, in this experiment we assessed PPS representation before and after an audio-tactile stimulation training: subjects received a tactile stimulus at the hand while a concurrent auditory stimulus was synchronously presented in the far space for 15 minutes. As a control condition, participants PPS representation was also measured before and after an asynchronous training consisting in tactile stimuli delivered at the hand and auditory far stimuli, with a randomized temporal delay between the two. In order to measure the extension of PPS before and after auditory-tactile stimulation, we took advantage from the new audio-tactile interaction task described in the previous chapters. We decided to use an auditory training, instead of a visual training, as that simulated in the neural network model by Magosso and colleagues, because the method developed to measure PPS representation was based on audio-tactile stimulation.

6.2 Experiment 6.1

6.2.1 Methods

Participants

Sixteen healthy subjects (12 females, age ranging between 23 and 26 years) participated in the study. All subjects were right-handed and had normal hearing and touch. All subjects, students at the University of Bologna, gave their informed consent to participate in the study, which was performed in accordance with the Declaration of Helsinki.

Materials and procedures

Audio-tactile interaction task

The audio tactile-interaction task was the same as Experiment 4.1, Chapter 4. In this experiment the tactile stimulation was administered on the ventral part of the right index finger. Participants comfortably placed their right hand on he table beside them. The two loudspeakers were placed on the table beside participants, one close to the tactilely stimulated hand, the other one at ≈ 100 cm, i.e. in the far space.

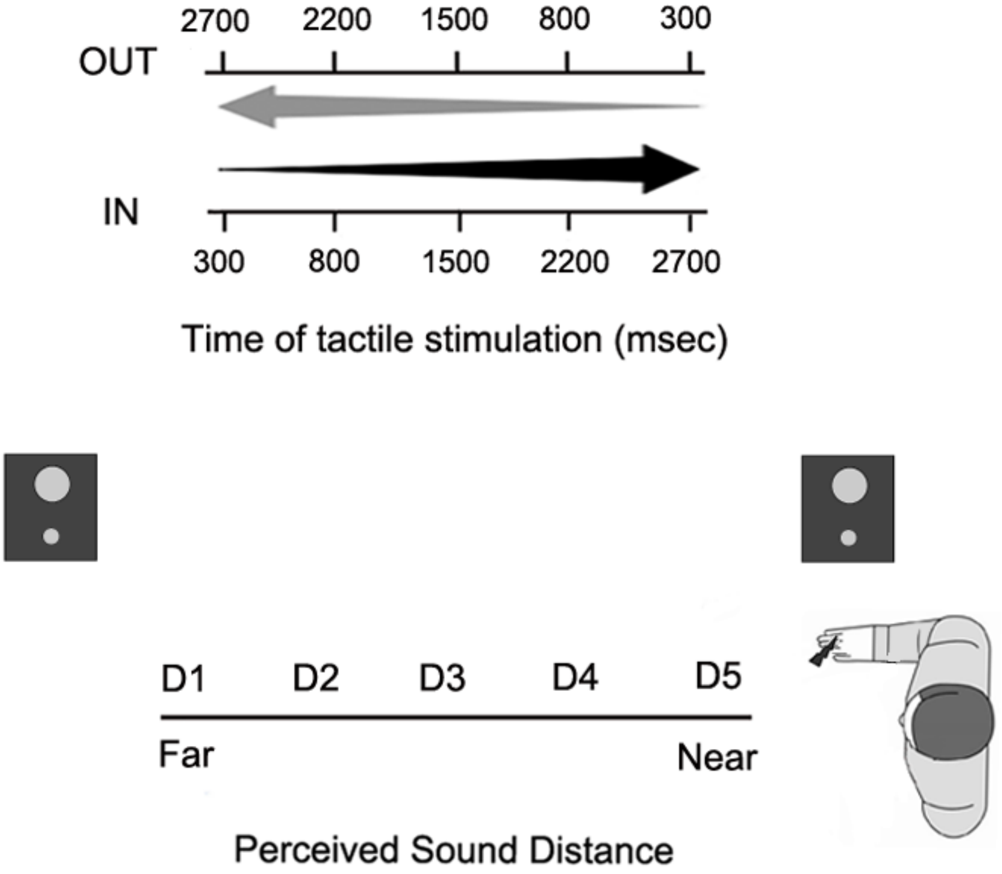

Figure 6.1 Experimental paradigm for the audio-tactile interaction task.

Synchronous Audio-tactile Training

During the training participants were blindfolded and sat down with their right arm resting palm down on a table beside them. Participants received different trains of audio-tactile stimuli. Each train consisted of ten tactile stimuli and ten auditory stimuli, synchronously presented. Tactile stimulation was administered through two solenoids applied at the tip of the right index finger (M & E Solve, Rochester, UK; http://www.me-solve.co.uk). The auditory stimulation consisted in an ecologic sound (the tapping of a pencil on a table) previously recorded. In this way, audio and tactile stimulation used for the training (i.e. ecological sounds and vibro-tactile stimulation) was different from that used for measuring PPS representation (i.e. white noise and electrocutaneous stimulation).

Sound was presented through two loudspeakers, placed on the table at a distance of ≈ 100 cm from participants' hand. A PC running C.I.R.O. software (www.cnc.unibo.psice.unibo/ciro) was used to control the presentation of the stimuli. During the training participants received 23 trains of stimuli, interleaved with 22 interstimulus intervals. Each train lasted 5000 ms. The inter stimuli interval randomly varied between 4000 and 6000 ms. In order to control for participants' attention during the training, 5 auditory stimuli (a "beep") were randomly presented during the inter stimuli intervals. Participants were asked to respond to the" beep" stimuli by tapping their foot on the floor. Before the training, participants were presented to the different tactile and auditory stimuli used, so they could easily recognize them during the task. Each training session lasted around 5 minutes.

Asynchronous Auditory Training

The same auditory and tactile stimuli used for the synchronous training were used. Each train consisted of ten tactile stimuli, ten auditory stimuli and two pauses, for a total duration of 6000 ms each. The training was the same as for the synchronous condition, but in the asynchronous condition auditory and tactile stimuli were presented asynchronously, with a randomized temporal delay between the two. This way, neither a spatial (tactile stimulus at the hand and auditory stimulus in the far space) nor a temporal coincidence was present between auditory and tactile events. Subjects were blindfolded during both the experiment and the training.

Design

Participants performed both the Synchronous and the Asynchronous auditory training in two different days. In each day of testing, we measured PPS representation before and after the training sessions. In Day 1, before tool-use participants performed the audio-tactile interaction task to assess PPS representation in a baseline condition. Then, they performed two sessions of the synchronous auditory training. Each session was intermingled with an assessment session, consisting of one block of the audio-tactile interaction task. On a different day, participants underwent the same procedure with the asynchronous training. The order of synchronous or asynchronous training was counterbalanced between subjects.

6.2.2 Results

Participants were extremely accurate in responding to the “beep” stimuli during both the synchronous and asynchronous training, meaning that they paid attention during the training (mean accuracy 97% and 98% respectively). In order to study the relationship between RTs and the different perceived position of sound in space as a proxy of PPS representation, we calculated tactile RTs both for IN and OUT sounds at the different temporal delays at which tactile stimulation was administered. RTs exceeding more than 2 standard deviations from the mean RT were considered outliers and trimmed from the analyses. At every temporal delay, from T1 to T5, sound is perceived in a different position of space with respect to the stimulated body part. Given the equivalent segmentation of the different temporal delays from T1 to T5, there was a spatial correspondence between the perceived position of IN and OUT sounds at T1 IN and T5 OUT (farthest distance from the body) and at T2 IN and T4 OUT (far distance), T3 IN and T3 OUT (intermediate distance), T4 IN and T2 OUT (close distance), T5 IN and T1 OUT (closest distance). We analysed RTs as a function of the five possible perceived distances, from D1, the farthest distance (corresponding to T1 for the IN sound and T5 for the OUT sound), to D5, closest distance (T5 for the IN sound and T1 for the OUT sound) both for IN and OUT sound. We entered tactile RTs in a repeated measures ANOVA with Training (Synchronous, Asynchronous), Condition (Before Training, After Training), Sound (IN, OUT) and Distance (from D1 to D5) as within subjects factors, and Order (Synchronous-Asynchronous; Asynchronous-Synchronous) as between subject-factor.

Results show a significant interaction Training X Condition X Order [$F(1,14)=5.73$, $p<0.05$] and a trend in the Training x Condition interaction [$F(1,14)=3.91$, $p=0.06$]. In order to explore how the different training (Synchronous, Asynchronous) affected participants' responses in the audio-tactile interaction task, we then conducted two separate ANOVAs for the two trainings.

Synchronous Auditory Training

The ANOVA conducted on RTs with Condition (Before Training, After Training), Sound (IN, OUT) and Distance (from D1 to D5) as within subjects factors showed a significant three-way interaction [$F(4,60)=2.57$, $p<0.05$]. As the present task is especially sensitive to approaching as compared to receding sounds (see Chapter 4), here we focused on results concerned IN sounds. OUT sounds data are presented in Table 6.1. Before Training, for the IN sound the function describing the relationship between tactile RTs and the perceived position of sound in space showed that tactile RTs progressively sped up as the perceived sounds' distance from the body decreased (See Figure 6.3). In particular, RTs at D1 (mean RTs ±S.E.M; 517 ms ±23) and D2 (497 ms ±24) - when sounds were perceived far from the body - were significantly slower as compared to D3 (464 ms ±22), D4 (459 ±23 ms) and D5 (455 ms ±26, all $p_s<0.01$, Newman-Keuls corrected) - when sounds were perceived close to the body. The spatial modulation of tactile perception due to sound position indicates that the boundaries of PPS representation before the training could be localized between D2 and D3, in line with previous results with the same paradigm (see Experiment 5.1, Chapter 5). Interestingly those boundaries were extended after the Synchronous training, as shown by a change in the shape of the function describing the relationship between the perceived sound position and tactile RTs. After the training, indeed, RTs at D2 (470 ms ±23), previously associated with a perceived far position in space, were no more significantly different as compared to RTs in D3 (450 ms ±22), D4 (439 ms ±22) and D5 (439 ms ±22). Thus, the critical spatial range where sounds became effective in modulating tactile RTs shifted to include positions more distant from the hand, i.e. between D2 and D1, whereas it was located between D3 and D2 before the training. Indeed, RTs at D2, and not at any other distance, were significantly faster after training as compared to before training (p<0.02).

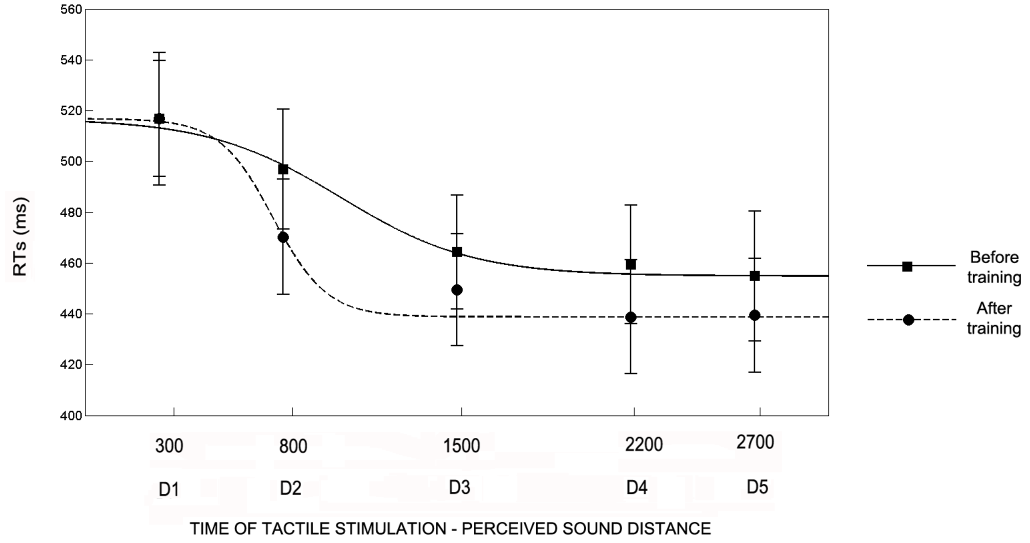

Figure 6.3 Audio tactile interaction task results for the IN sound, **Synchronous condition**. Mean (and S.E.M.) RTs at different perceived sound distances from D1- farthest - to D5- closest - (corresponding to different times of tactile stimulus delivery), Before training (filled line) and After training (dotted line).

OUT sound	**D1**	**D2**	**D3**	**D4**	**D5**
Before Training	505 ms ±27	474 ms ±24	460 ms ±25	476 ms ±25	477 ms ±26
After Training	466 ms ± 26	451 ± 23	447 ± 23	457 ± 23	445 ± 23

Table 6.1 Audio tactile interaction task results for the OUT sound, **Synchronous condition**. Mean (and S.E.M.) RTs at different perceived sound distances from D1- farthest - to D5- closest - (corresponding to different times of tactile stimulus delivery). For the OUT sound the pattern of results was similar to that for the IN sound, with a critical difference. As for the IN sound, results showed a speeding up effect of tactile RTs as soon as the sound approached the body. However, the spatial distance where sounds became effective in modulating tactile RTs was different as compared to the IN sound. Before Training tactile RTs at D1 were significantly slower as compared to RTs at D2, D3, D4, and D5. After the training, however, RTs at D1 was no longer different from RTs at every others perceived distance (all p_s>0.59), confirming a shift in the spatial range where sounds are effective in

modulating tactile RTs towards the far space, i.e. around D1, when it was located around D2 before the training. Indeed, RTs at D1 and not at any other distance were significantly faster after training as compared to before training ($p<0.01$). The different modulation of tactile RTs due to sound processing between IN and OUT sound can be explained with a stronger effect of approaching sounds in modulating tactile processing as compared to receding sound (see Chapter 4 of this dissertation). These results are in keeping with several studies both in primates and in humans, showing that approaching stimuli have been shown to be particularly relevant at different levels of information processing as compared to receding stimuli (Hall & Moore, 2003).

Asynchronous Auditory Training

We analysed RTs as a function of the five possible perceived distances, from D1, farthest distance, to D5, closest distance both for IN and OUT sound, as for the synchronous training. The ANOVA conducted on RTs with Condition (Before Training, After Training), Sound (IN, OUT) and Distance (from D1 to D5) as within subjects factors showed a significant Sound X Distance interaction [$F(4,60)=6.85$, $p<0.05$]. The pattern of results both for IN and OUT sounds mirrors the same effect found for the Synchronous training before training: as sound distance from the body decreased, RTs progressively shortened. Newman-Keuls post-hoc comparisons confirmed this effect: for the IN sound tactile RTs at D1 (Mean RTs ± S.E.M, 484 ms ±24) and D2 (481 ms ±26), when the sound was perceived far from the body, were slower compared to RTs at D3 (444 ms ±25), D4 (440 ms ±28) and D5 (433 ms, ±25, all ps <0.01), when the sound was perceived close to the body. For the OUT sound, the pattern of results was similar (see Table 6.2 caption). Importantly, the space dependent modulation of RTs due to sound position was not different before and after the training session, as the three-way interaction Condition X Time X Distance was not significant [$F(4,60)=0.39$, $p=0.82$], as well as the main effect of Condition [$F(1,15)=1.98$, $p=0.18$].

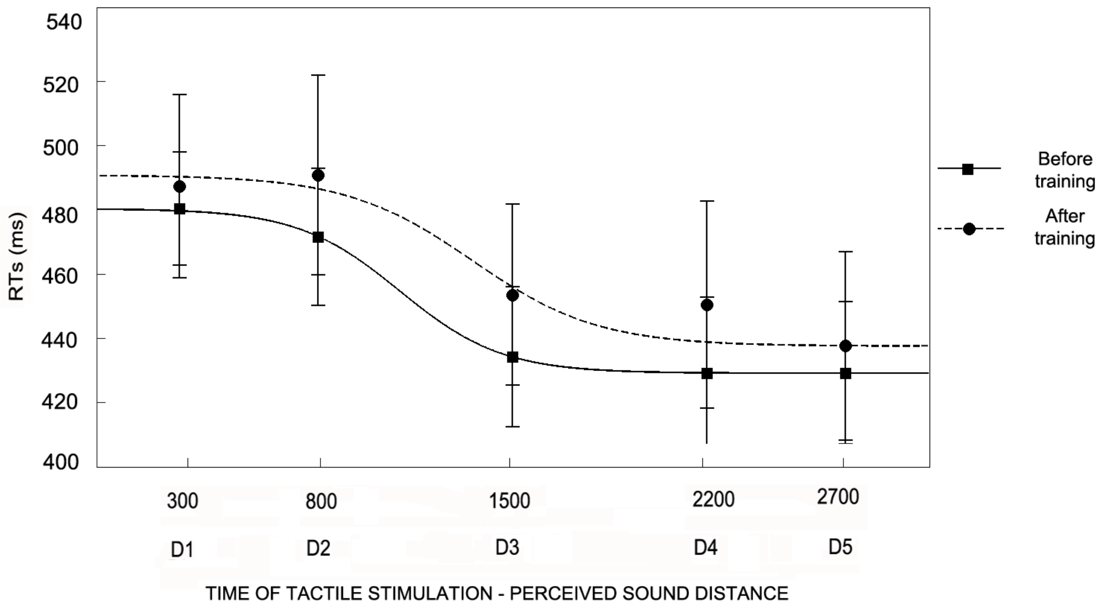

Figure 6.4 Audio tactile interaction task results for the IN sound, **Asynchronous** condition. Mean (and S.E.M.) RTs at different perceived sound distances from D1 - farthest - to D5 - closest - (corresponding to different times of tactile stimulus delivery), Before Training (filled line) and After Training (hatched line). Results for the IN sound clearly showed that the pattern of responses did not change Before and After Training: indeed, both Before and After Training tactile RTs at D1 and D2 when the sound was perceived far from the body, were slower compared to RTs at D3, D4 and D5.

OUT sound	**D1**	**D2**	**D3**	**D4**	**D5**
Before Training	466 ms ±22	443 ms ±22	426 ms ±21	447 ms ±20	449 ms ±23
After Training	485 ms ± 27	471 ± 31	457 ± 32	474 ms ± 30	451± 29

Table 6.2 Audio tactile interaction task results for the OUT sound, **Asynchronous** condition. Mean (and S.E.M.) RTs at different perceived sound distances from D1- farthest - to D5- closest - (corresponding to different times of tactile stimulus delivery), Before and After Training. Results showed that for the OUT sound, the pattern of results was similar: RTs at D1 (476 ms ±25) were significantly lower as compared to RTs at D2 (457 ms ±26), D3 (441 ms ±27), D4 (460 ms ±25) and D5 (450 ms ±26).

6.3 Discussion

Results from the present study demonstrated that a training consisting in a synchronous presentation of tactile stimuli at the hand and auditory stimuli in the far space was able to modify the boundaries of the PPS representation around the hand. In order to measure the extension of PPS, we used the task previously developed by our group and presented in Chapter 4 of this dissertation. By means of this task we measured multisensory interaction around the body along a continuum between far and near space in order to identify the boundary of PPS representation. We demonstrated that the boundary of PPS was pushed farther in space after a synchronous audio-tactile training, suggesting an extension of PPS representation after such training (see also Chapter 5). The temporal coincidence between the tactile stimulus at the hand and the auditory stimulus from the far space during the training is necessary to promote an extension of PPS representation, since the asynchronous training did not affect PPS representation.

In the last decade neurophysiological, neuropsychological and behavioural studies have investigated the dynamic changes in multisensory representation of peripersonal space due to tool-use. These studies data demonstrate that our perception of the peripersonal space is not static, but it can be modified by experience and specifically by a training with a tool that projects the possibility of acting farther in space. However, the mechanism underlying the extension of PPS after tool-use is largely unknown. In the present study we tested the prediction generated by a neural network model developed by Magosso and colleagues (2010) to explain this mechanism. The model predicts that the modification of peri-hand space arises from a strengthening of synapses between visual neurons centred on the far space and multisensory neurons, due to the coupling of tactile signals from the hand and visual signals from the far space, by means of Hebbian-like mechanism. As a consequence, visual receptive field of multisensory neurons extends towards the far space. Results from the present study after an auditory tactile training are in line with the results predicted by this neural network model. Moreover, these results are in line with results from Iriki and colleagues (1996) in monkeys, showing that hand-centred visual RFs of neurons located in the intraparietal sulcus elongated after a training period of using a rake to retrieve pieces of food placed in the far space. This effect has been attributed to the formation of new functional synapses from high-order visual areas to the intraparietal cortex (Hihara et al., 2006; Ishibashi et al., 2002).

Interestingly, the current results, as predicted by the neural network model, demonstrated that a change in peri-hand space mimicking that obtained after tool-use (see Chapter 5 of this dissertation) can be evoked also when a tool is not actually used or even present in the subject's hand. A key factor, instead, is feeding the neural network with the same sensory stimulation produced by tool-use activity, i.e. the auditory stimulation due to the sound produced by the tool when hitting an object placed in the far space and the concurrent tactile stimulation at the hand due to handling the tool: tactile unimodal stimuli at the hand and auditory unimodal stimuli in the far space send feed forward synapses to bimodal neurons. The synapses linking unimodal to bimodal neurons are reinforced following a Hebbian rule during such training. The reinforcement of these synapses, that were latent before the experiment, is compatible with an extension of audio-tactile peri hand space, with a far auditory stimulus re-codified as being closer to the body.

In the literature it has been suggested that an *active* experience with the tool is critical in promoting an extension effect on PPS, since a prolonged but passive exposure to the tool failed to elongate the peri-hand space (Maravita et al., 2001). Then, the extension of the possibility of acting in the far space has been considered a key factor in promoting PPS extension. This interpretation fits well with the original definition of tool given from Benjamin Beck (see Chapter 2) and adapted from Holmes and colleagues (see Holmes et al., 2006; 2007a), saying that only objects that physically act upon another object can be considered tools. Results from several studies supported the idea that only a tool that physically and functionally connects near and far space, allocating processes of multisensory stimuli where the goal of the action is, can extend PPS space. This idea was partially disconfirmed by a recent study of Bassolino and colleagues (2010), in which authors demonstrated that using a mouse, a technological device which establishes a virtual – but not physical - connection between near and far space (Goldenberg & Iriki, 2007), could extend PPS. However, the study of Bassolino and colleagues still supported the idea that the that the functional attributes of a tool are critical in promoting a remapping of far space as near: a mouse promoted an extension effect on PPS in the portion of space where the effect of action was realized, that is the monitor of the computer in this study, thus pointing out the critical role of the motor aspect of the tool in the plasticity of the PPS.

Results from the present study instead are new in suggesting that the motor aspect of tool-use is not so critical in promoting plastic reorganization of spatial representations: neither a functional, nor a physical interaction between near and far space is necessarily required to determine an extension of PPS. According to the results of the present study, supported by the neural network model, tool-use extends PPS representation because it provides the brain with a tactile stimulation at the hand and a synchronous multisensory stimulation in the far space. Due to neuronal plasticity based on Hebbian mechanism, multisensory areas associate two stimuli as they occur from the same space.

A similar multisensory mechanism might underlie the Rubber Hand Illusion (RHI). In RHI experiments, a realistic fake hand can be perceived as a part of one's own body if concurrent visuo-tactile stimulation is seen on the fake hand and felt on one's own hand, hidden from view (see also Chapter 1). Makin and colleagues (2008) suggested that the illusory body parts ownership that people experience during the RHI might involve bimodal and/or trimodal neurons at the level of the premotor and parietal cortices that normally respond only to stimuli presented within one's own PPS. It has been proposed that during the RHI just seeing the rubber hand being stimulated and experiencing a synchronous tactile stimulation on one's own hand triggers a shift of the receptive field of bimodal neurons towards the fake body part (see also Blanke, 2012, for a review). This effect might generate a change in body perception that is the rubber hand is perceived as the real hand.

This interpretation of the RHI is in line with a recent fMRI study of Brozzoli and colleagues (Brozzoli, Gentile, & Ehrsson, 2012). In this study the authors tested how activity of premotor and parietal cortices in humans coding the PPS varies in response to visual stimuli presented close to the subject's real hand or to a rubber hand, placed several cm away from it. They found that only after that subjects experienced ownership for the rubber hand, through induction of the RHI, PPS areas responded also to stimuli presented close to the rubber hand. These findings suggest that visual RF of multisensory neurons extended to incorporate the rubber hand into PPS representation. Findings from the present study suggest that ownership for the rubber is not a necessary condition to trigger PPS expansion; rather, synchronicity between tactile stimulation at the hand and auditory or visual stimulation from a space location other than that of the hand seems the critical factor.

A final remark it that in the present experiment we demonstrated a change in the auditory PPS around the hand after a synchronized auditory-tactile training. A still open question is whether a visuo-tactile training would be able to dynamically modify the representation of the auditory space around the hand, or whether instead these mechanisms operate only within the same modality (auditory-auditory; or visual-visual). Indeed, the model proposed by Magosso and colleagues (Magosso et al., 2010c) simulated the activity of two unimodal (visual and tactile) areas, connected to a third multimodal area. Several pieces of evidence both in primates and in humans (see Chapter 1) demonstrated that also auditory information are coded within the PPS. Moreover results from the present study supported the idea that this neural network model could be updated with a third unimodal auditory area. However, it is still unclear whether a visual training, promoting the strengthening of the synaptic connections between visual neurons centred on the far space and multisensory neurons, by means of Hebbian-like mechanism, could extend an auditory representation of PPS. If this is the case, we could suppose the existence in the model of trimodal neurons that, during the training, receive information from visual neurons and send feedback synapses to unimodal auditory neurons. This interesting hypothesis deserves to be investigated in future studies.

CHAPTER SEVEN: PLASTIC MODIFICATION OF BODY AND PERIPERSONAL SPACE REPRESENTATION AFTER AMPUTATION

[Canzoneri, E., Marzolla, M., Amoresano, A., Verni, G., & Serino, A. Amputation and prosthesis implantation shape body and peripersonal space representations. Under revision.]

7.1 Introduction

Result from the studies of the present work, as presented in Chapter 5, as well as several studies reviewed in the Introduction of this dissertation (see Chapter 2), demonstrated that both multisensory BR and PPS representations functionally changed and adapted after a training with a tool that extended the possibility of interacting with external stimuli *beyond* the limits of the physical body. Given the plasticity of these two forms of representation, we asked whether and how BR and PPS modify when the possibility of acting changes in the opposite direction, i.e. towards limitation, as it happens after upper limb amputation that, by modifying the physical structure of the body, dramatically limited the possibility of acting in the body space. From this point of view amputation represents a unique possibility to study brain plasticity due to the sudden lost of a part of the body.

Unimodal somatosensory and motor body representations directly depend on the structure of the physical body. Indeed, a large body of evidence shows that when a sudden change in the physical body occurs, such as in the case of traumatic amputation, extensive changes in unimodal body representations in MI and SI also occur (Buonomano & Merzenich, 1998; Chen, Classen, Yaseen, Hallett, & Cohen, 1998; Reilly & Sirigu, 2008; Borsook et al., 1998). Little is known however about the extent to which multimodal body and space representations are dependent on the structure of the physical body, and how plastic these representations are following changes in body structure. Indeed, much less information is available about the effects of amputation on BR (see e.g. Nico, Daprati, Rigal, Parsons, & Sirigu, 2004 or Ehrsson, Rosen, Stockselius, Ragno, Kohler, & Lundborg, 2008) or on PPS representation (see e.g. Makin, Wilf, Schwartz, & Zohary, 2010). Therefore, the first aim of the present study is to investigate the effects of a sudden change in the structure of the physical body, such as after amputation of an upper limb, on a critical feature of BR, i.e., the perceived dimension of the residual body part, and on the extension of PPS around the affected body part.

In amputee patients, the consequences of amputation are partially palliated by means of prosthesis implantation. Prostheses are artificial devices that on the one hand have the same role as a tool in expanding the functional potential of the physical body. On the other hand, in addition to tools, upper limb prostheses can also visually and aesthetically replace the amputated body part. Little is known on whether and how partially restoring the function and structure of the physical body by means of prosthesis implantation affects BRs and PPS representations. Thus, the second aim of the present study is to assess changes on the perceived dimensions of the stump and on the extension of the PPS around the upper limb, in individuals who use a prosthesis to compensate for upper limb loss.

To these aims, we recruited a group of 10 patients who underwent traumatic amputation of one upper limb at least 24 months before testing, and were implanted with and normally used a functional prosthesis. Patients performed a tactile distance perception task in order to assess the perceived length of the stump and of the healthy arm (see Experiment 7.1) and an audio-tactile interaction task in order to measure the extent of PPS representation around the stump and the healthy limb (see Experiment 7.2). The comparison between the results for the two hemisomata provided evidence about the effects of amputation. The same experiments were also run while patients were or were not wearing their prosthesis during testing, and the results from these two conditions were compared in order to study the effect of prosthesis implantation on body and PPS representations.

7.2 Methods

Amputee participants

Ten volunteers participated in the study (8 males and 2 females, mean age 45 years, range 21-66 years), recruited at the INAIL Prostheses Centre, Budrio, Bologna (http://www.inail-ricerca.it/index.aspx). They were healthy with the sole exception being that they had all one upper limb amputated either below or above the elbow, following a traumatic accident. Eight patients had their right arm amputated and the other two had their left arm amputated. Before the accident all patients were right-handed. The inclusion criterion was that they must have been using a functional prosthesis at least 4–8 h daily for 5–7 days per week for at least 1 year. At the moment of testing, five patients had been using kinematic prostheses and the other five had been using myoelectric prostheses, from a variable period of time ranging from 2 to 42 years (mean=15.5; S.E.M.=±4.16). Functional prostheses were cosmetically designed, so they resembled arm appearance. Patients' demographic and clinical data are reported in Table 7.1.

Control participants

Twenty-nine healthy volunteers (22 females and 7 males, mean age 26.4 years, range 19-62 years) participated in the study in three different experiments as a control group.

Patient	Age	Gender	Handiness	Amputation side, level	Prosthesis type	Years since amputation	Phantom limb symptoms
P1	41	F	Dx	Right, above elbow	Kinematic	2	Yes
P2	56	M	Dx	Left, above elbow	Myoelectric	21	Yes
P3	50	M	Dx	Right, above elbow	Myoelectric	18	No
P4	30	M	Dx	Right, below elbow	Kinematic	1.5	No
P5	21	F	Dx	Right, below elbow	Kinematic	2.5	Yes
P6	38	M	Dx	Right, below elbow	Myoelectric	18	No
P7	66	M	Dx	Right, below elbow	Myoelectric	16	Yes
P8	62	M	Dx	Right, below elbow	Myoelectric	42	No
P9	41	M	Dx	Right, below elbow	Kinematic	4	No
P10	43	M	Dx	Left, above elbow	Kinematic	3	Yes

Table 7.1 Patients' demographic and clinical data

All subjects gave their informed consent to participate in the study, which was performed in accordance with the Declaration of Helsinki.

Experimental procedure: overall structure

Amputee patients participated in two experiments, assessing BRs (Experiment 7.1) and PPS representations (Experiment 7.2A), performed in a single 2-hour and a half session. Between the first and the second experiment participants had a 15 min break. Seven out of ten patients participated in Experiment 7.1: two patients were excluded because of the very high level of the amputation (above the elbow), thus not allowing administering tactile stimuli of sufficient dimensions (see Experiment 7.1 methods), because the prosthesis covered most of the stump surface. One patient could not perform the experiment for matter of time. All patients participated in Experiment 7.2A.

Patients performed Experiment 7.1 and Experiment 7.2A in three different experimental conditions: stimuli were administered on the healthy limb (Healthy limb condition), on the amputated limb without prosthesis (Without-prosthesis condition) and on the amputated limb with prosthesis (With-prosthesis condition). In the healthy limb condition, tactile stimulation was administered on the upper part of the non-affected limb, corresponding to the stump. In the with- and without-prosthesis conditions, tactile stimulation was administered on the stump on the more distal skin region reachable when the prosthesis was on. Tactile stimulation was never administered to scar tissue of the stump, to avoid any confounding effect due to loss of tactile sensitivity caused by peripheral deficits. The different experimental conditions were run in a counter-balanced between-subjects order for each experiment.

Seven healthy subjects (five males and two females, mean age 33.7 years, range 25-62 years) were recruited as a control group for Experiment 7.1 and other ten healthy subjects (all females, mean age 22.1 years, range 19-24 years) for Experiment 7.2. Twelve naïve healthy subjects (two males and ten females, mean age 23.4 years, range 20-26 years) participated in Experiment 7.2B on PPS representation (see below). All healthy subjects from the control group performed the tasks on their right upper arm, on a skin region matching the site of stump stimulation used for amputee patients.

Materials and procedure

Experiment 7.1: Tactile distance perception task

In order to assess the perceived length of the arm, we used the tactile distance perception task previously described in Chapter 5. Subjects received two pairs of tactile stimuli, one pair on the forehead (serving as a reference body part) and one pair on the upper arm (target body part), and they were asked to judge whether the distance between the two stimuli was longer on the forehead or on the arm. The perceived size of tactile stimuli touching the body depends on the perceived dimension of the body part tactilely stimulated (see de Vignemont, Majid, Jola, & Haggard, 2009; Longo et al., 2010; Medina & Coslett, 2010; Spitoni, Galati, Antonucci, Haggard, & Pizzamiglio, 2010: Longo & Haggard, 2011), and is influenced by visual (Taylor-Clarke et al., 2004) or proprioceptive (de Vignemont et al., 2005) information about the stimulated body part. Thus, the tactile distance perception task can be used as an indirect measure of the internal representation of body part size. In particular, we posit that perception of the distance between two tactile stimuli is rescaled on the basis of the context in which they are presented, according to a context-dependent bias: the same distance is perceived as longer when presented in a smaller context as compared to when presented in a bigger context. This context-dependent effect is well documented in the field of visual perception, (e.g., the Ebbinghaus illusion, 1897), and haptic perception (e.g., Linkenauger et al., 2010; Linkenauger et al., 2011) and we have recently confirmed this effect for a visual and a tactile distance perception task (Canzoneri, Ubaldi, Rastelli, Finisguerra, Bassolino & Serino, under revision; see Chapter 5).

In the present experiment, we administered the tactile distance perception task, with tactile stimuli longitudinally delivered on the upper arm, along the arm axis, in order to measure the perceived length of the arm. In amputees, the task was performed in 3 blocked conditions, run in counterbalanced between-subjects order, on the healthy limb and on the stump, with or without the prosthesis.

Experiment 7.2: Audio-tactile interaction task

In order to assess PPS representation, we used here the audio-tactile interaction task previously presented in Chapter 4. We measured vocal reaction time (RTs) to a tactile stimulus administered either on the upper arm in the healthy arm condition or on the stump in the with and without prosthesis condition, while task-irrelevant dynamic sounds were presented, giving the impression of a sound source either approaching, or receding, from the subject's limb. On different trials, tactile stimulation was delivered at different temporal delays from the onset of the sound, such that it occurred when the sound source was perceived at varying distance from the body. Subjects were asked to respond as rapidly as possible to the tactile stimulation, trying to ignore the sound.

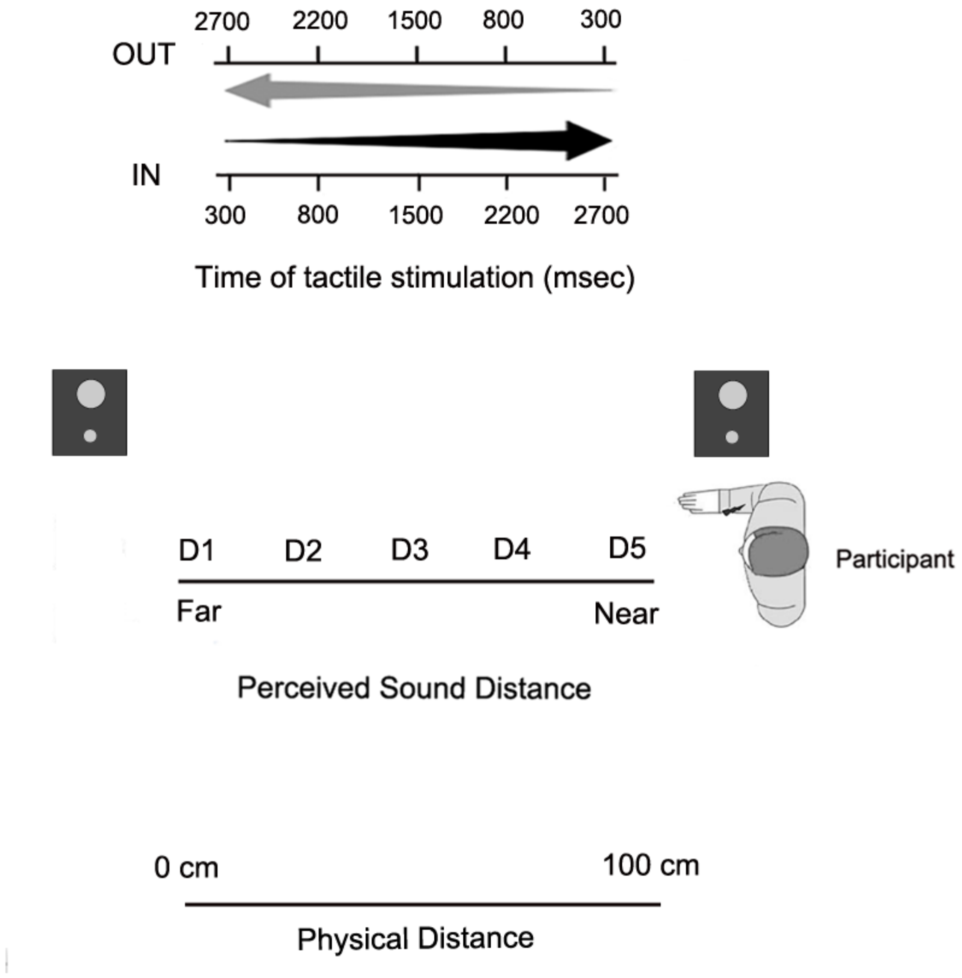

Figure 7.1 Experimental set up for Experiment 2 and Experiment 2B.

We have repeatedly demonstrated that sounds boost tactile RTs when presented close to the body and not at a distance (Serino et al., 2007; Bassolino et al., 2010; Serino et al., 2011) and we have recently found that tactile RTs coupled to moving sounds progressively speeded up, to the extent that the sound source was perceived as approaching the body, and conversely slowed down, to the extent that the sound source was perceived as receding from the body (Canzoneri et al., 2012; See Chapter 4). According to these effects, the function describing the relationship between tactile RTs and the perceived position of sounds in space at the occurrence of the tactile stimulation can be used to measure the extension of PPS along a continuum between near and far space.

7.3 Results

Experiment 7.1: tactile distance perception task

For each subject, we calculated the mean probability of reporting the distance on the upper arm as longer for all combinations of inter-point distances (P-Arm). A priori P-Arm is 50%, given the same number of longer stimuli administered of the forehead or on the arm. Recent findings indicate that subjects normally underestimate tactile distance along the arm axis, because of the distribution of tactile receptive fields on the arm surface (Longo & Haggard, 2011; Cody, Garside, Lloyd, & Poliakoff, 2008). Critically, based on probabilistic or physiological considerations, P-Arm should be constant for the different experimental conditions of stimulation on the healthy limb and on the amputated limb, both with and without prosthesis. We predicted that P-Arm would vary depending on the perceived size of the stimulated arm. Specifically, in line with the context-dependent bias hypothesis (see Methods), the same tactile distance would be perceived as longer when presented on a body part perceived as shorter, as compared to when presented on body part perceived as longer. In other words, higher or lower P-Arm would indicate, respectively, that the upper arm is perceived as shorter or as longer.

First of all, we compared mean P-Arm between the amputees' healthy arm and the right arm of healthy controls, by means of an independent samples t-test. Results showed that scores did not differ significantly between the two groups [t(12)=1.42, p=0.18]. Scores were below 50%, as expected according to Longo and Haggard (2011), for both the amputees' healthy arm (Mean P-Arm, ±S.E.M., 45%, ±4%) and for healthy controls (37%, ±3%). These results suggest that amputation of one upper limb did not affect the implicitly perceived length of the healthy arm.

In order to study the effect of amputation and prosthesis implantation on perceived arm length, we compared mean P-Arm between the healthy and the amputated limbs of patients, by means of a repeated measure ANOVA with Condition (Healthy Arm, With-prosthesis and Without-prosthesis) as within-subjects factor. The main factor of Condition was significant [$F(2,12)=11.77$; $p<0.01$]. In order to study the effect of amputation, we compared P-Arm for the healthy arm and the Without-prosthesis conditions: P-Arm was significantly higher when patients performed the task on the affected limb, while not wearing the prosthesis (61%, ±5%), as compared to the healthy arm (45%, ±4%; $p<0.01$; Newman-Keuls corrected). In line with the context-dependent hypothesis (see Chapter 5), this result suggests that amputation reduces the perceived length of the remaining part of the affected limb. Critically, when patients performed the task with the stump, but while wearing their prosthesis, P-Arm is significantly lower (52%, ±6%) compared to the Without Prosthesis condition (61%, ±5%; $p<0.05$ - Newman-Keuls corrected). These results suggest that wearing the prosthesis increased the perceived length of the stump, making it more similar to the perception of the healthy arm, such that the prosthesis partially replaced the missing limb. P-Arm was not statistically different between the healthy arm and the stump while patients wore the prosthesis ($p=0.07$).

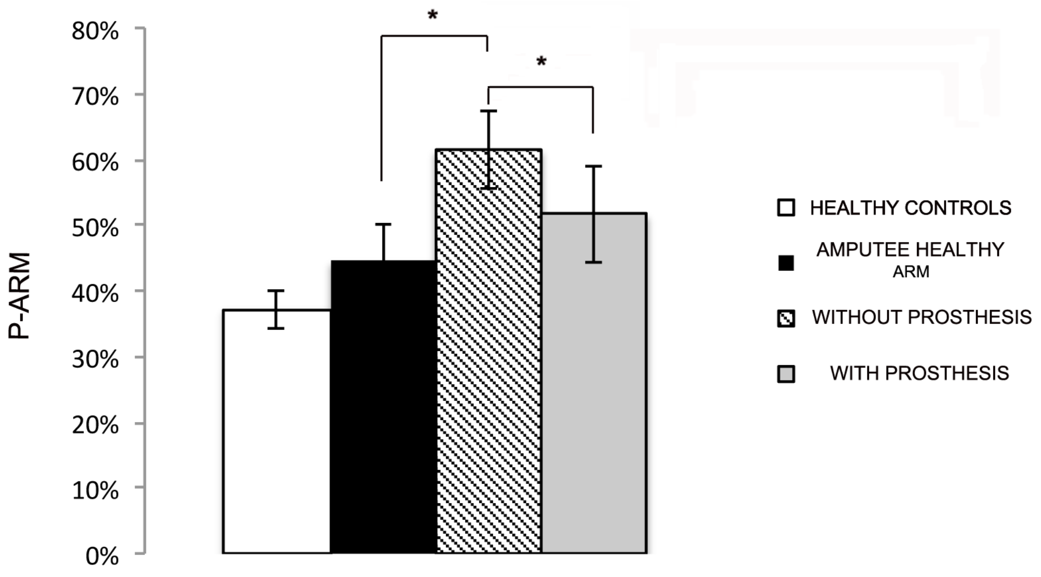

Figure 7.2. Experiment 7.1 results. The graph shows mean P-Arm for healthy controls (white column), amputee healthy arm (black column), amputated arm without prosthesis (hatched column) and amputated arm with prosthesis (grey column). Error bars denote S.E.M.

As this was a relatively unselected group of amputees, some patients verbally reported variable phantom limb pain and phantom limb sensations, whereas other patients did not refer any phantom limb phenomena at the time of the testing. Thus, in order to consider any possible effect of phantom limb sensations on the perceived length of the stump, we divided patients in two groups, one comprising four patients, who had experienced variable phantom limb sensations from the moment of the amputation until the moment of the test, and the other one, comprising three patients, who had not experienced any phantom limb sensations for at least 1 year previous to the time of testing. Due to the small sample size of the group, we used non-parametric tests. Mann-Whitney U analyses showed that P-Arm was not different between the two groups both in the With prosthesis condition (U=4, p=0.48) and in the Without prosthesis Condition (U=6, p=1), thus not showing any effect of phantom limb sensations of the perceived size of stump.

Experiment 7.2A: audio-tactile interaction task

As tactile stimulation was set clearly above threshold, false alarms and omissions were rare (on average: 0.86% and 2.87%, per subject, per condition, respectively). Thus, performance was studies in terms of RTs only. In order to study the relationship between RTs and perceived sound position as a proxy of PPS extension, we calculated mean RTs to tactile target both for IN and OUT sounds at the various temporal delays at which tactile stimulation was administered. RTs exceeding more than 2 standard deviations from the mean RTs were considered outliers and trimmed from the analyses (on average: .81% of trials per subject per condition). At every temporal delay, from T1 to T5, sounds are perceived as being at a different position in space with respect to the stimulated body part (see Canzoneri et al., 2012). Given the symmetric shape of the two waveforms for the IN and OUT sounds, and the equivalent segmentation of the different temporal delays from T1 to T5, there was a spatial correspondence between the perceived position of IN and OUT sounds at T1 IN and T5 OUT (farthest distance from the body), at T2 IN and T4 OUT (far distance), T3 IN and T3 OUT (intermediate distance), T4 IN and T2 OUT (close distance), and T5 IN and T1 OUT (closest distance). We averaged tactile RTs for these couples of delays and analysed RTs as a function of the five possible perceived distances, from D1, farthest distance, to D5, closest distance, in a unique function.

First of all, in order to study PPS representation around the healthy limb, we compared tactile RTs at each distance, from D1 to D5, when stimulation was administered to the amputees' healthy arm and to the arm of healthy controls. A repeated measures ANOVA with Distance (D1, D2, D3, D4, D5) as the within subject factor and Group (Amputees Healthy Arm - Controls) as the between subject factor revealed a significant main effect of Distance [$F(4,72)=17.31$, $p<0.001$], showing that tactile RTs progressively speeded up as the perceived sound approached the body (see Figure 7.3). Newman-Keuls post-hoc tests confirmed that RTs at D1 (Mean RTs ±S.E.M., D1=440 ms ±16) and D2 (430 ms ±17) – when the sound was perceived as being far from the body – were significantly slower as compared to RTs at D3 (414 ms ±16), D4 (402 ms ±16) and D5 (404 ms ±16; all $p_s<0.01$) – when the sound was perceived as being close to the body. This pattern of results was equivalent between patients and healthy controls. Indeed, neither the main effect of Group [F(1,18)=0.81, p=0.38] nor the Distance X Group interaction [F(4,72)=0.32, p=0.86] were significant. Taken together these results suggest that there is a critical spatial range (in this case between D2 and D3) within which auditory stimuli begin interacting with tactile stimuli administered on the body surface, resulting in quicker tactile RTs. This spatial range could be considered as the boundaries of the PPS. Certainly, the present results suggest that the boundaries of PPS representation around the upper limb do not differ between healthy controls and amputees, for what concerned the non-affected side of the body.

In order to study the effect of amputation and prosthesis implantation on PPS representation, we compared the results between patients' healthy and amputated arm, while wearing or not wearing their prosthesis. We entered tactile RTs in a repeated measure ANOVA with Condition (Healthy Arm, With-prosthesis and Without-prosthesis) and Distance (D1, D2, D3, D4, D5) as the within subject factors. The main effect of Distance was significant [F(4,36)=19.92, p<0.001], resembling the pattern of responses found for the healthy arm and for controls: RTs became faster when the sound was perceived as being closer to the body (see Figure 7.4). Critically, the main effect of Condition was also significant [F(2,18)=3.64, p<0.05].

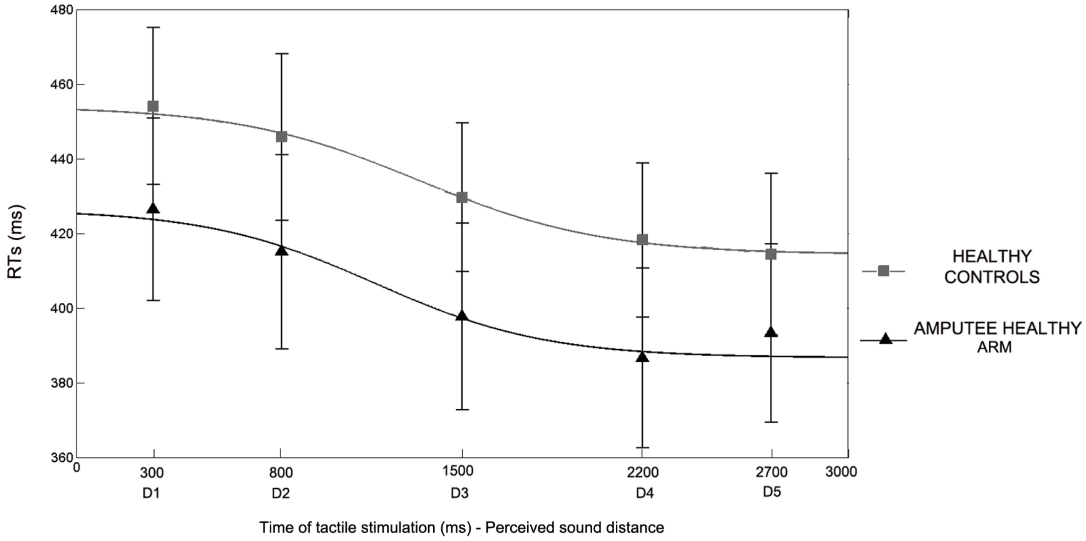

Figure 7.3. Experiment 7.2A results for healthy controls and amputee healthy arm. Mean RTs at different perceived sound distances (from D1 - farthest - to D5 - closest), corresponding to different time of tactile stimulus delivery and best fitting sigmoidal functions describing the relationship between RTs and sound distance, for healthy controls (grey line) and for amputee healthy arm (black line). Error bars denote S.E.M.

A Newman-Keuls post-hoc test showed that when patients performed the task without the prosthesis, RTs were slower (418 ms, ±29) as compared to when they performed the task with the healthy arm (404 ms, ±29; $p<0.05$; one-tailed). When patients performed the task with the amputated arm, RTs were faster when they wore the prosthesis (398 ms ±26) as compared to when they did not wear the prosthesis ($p<0.05$). RTs were not significantly different between the Healthy Arm and the With-prosthesis conditions ($p=0.45$). Taken together these results suggest that amputation affected PPS representation around the stump, as compared to the non-affected limb, but wearing a prosthesis compensated this effect, making PPS representation around the stump more similar to PPS representation around the healthy arm. The two-way Distance X Condition interaction was not significant [$F(8,72)=1.13$, $p=0.35$], suggesting that the modulation of RTs depending on the perceived position of sound in space did not differ between the different conditions.

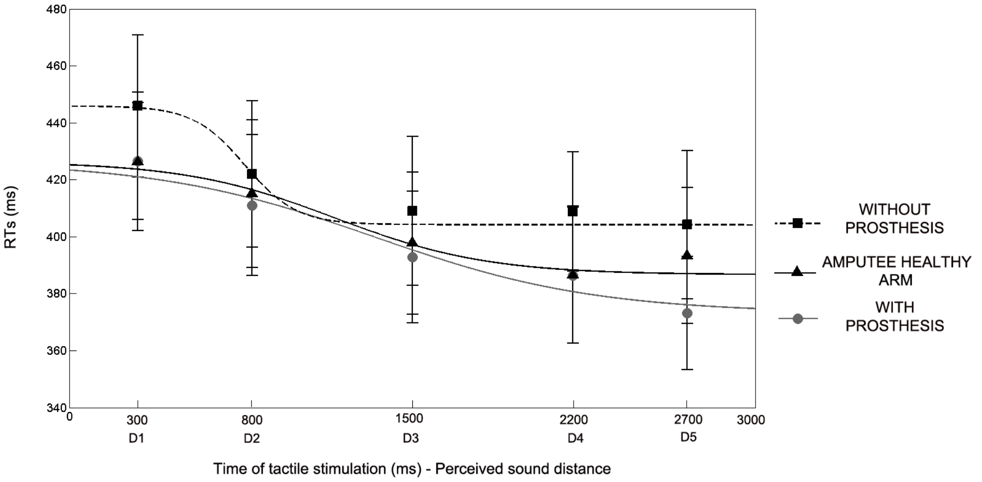

Figure 7.4. Experiment 7.2A results. Mean RTs at different perceived sound distances (from D1 - farthest - to D5 - closest), corresponding to different time of tactile stimulus delivery and best fitting sigmoidal functions describing the relationship between RTs and sound distance, for amputee healthy arm (black line), amputated arm without-prosthesis (dotted line) and amputated arm with-prosthesis (grey line). Error bars denote S.E.M.

As for Experiment 7.1, in order to consider any possible effect of phantom limb syndrome on PPS representation, we compared results in the PPS task between patients with (5 patients) or without (5 patients) phantom limb sensations. Mann-Whitney U analyses showed that mean RTs to tactile stimuli did not differ between the two groups in the With-prosthesis (U=8, p=0.35) and in the Without-prosthesis (U=9, p=0.46) conditions.

Experiment 7.2B

In order to interpret the differential effect on RTs found between the with- and without prosthesis conditions in the entire patient sample, we hypothesized that, when patients did not wear the prosthesis, sound position was codified with respect to the stump, which represented the boundaries of the physical body; instead, when patients wore the prosthesis, the perceived position of sound in space was re-calibrated with respect to the prosthetic hand, such that the prosthetic hand itself represented the new body boundary. In this way, a sound perceived as being distant with respect to the stump without the prosthesis, was represented as closer to the body when the prosthesis was on, because it was closer to the prosthetic hand. In other words, tactile stimulation was coded with respect to the stump in the without-prosthesis condition and with respect to the prosthetic hand in the with-prosthesis condition. This recalibration resulted in a general reduction of RTs in every temporal delay, i.e., at each sound distance from the body. In order to test this hypothesis, we ran a further experiment in a group of twelve naïve, healthy subjects (Experiment 7.2B). The task was the same as for the previous experiment, but while sound positions were kept in a constant relationship to the upper arm (i.e. the near loudspeaker was close to the upper arm and the far loudspeaker was at 100 cm), tactile targets were administered in two different experimental conditions: either to the arm (Upper Arm condition), or to the hand (Hand condition). Thus we simulated, respectively, the stump stimulation in the without-prosthesis condition and the recoding of tactile stimulation to the prosthetic hand in the with-prosthesis condition in amputee patients.

Subjects performed two blocks for each experimental condition (Upper Arm and Hand condition), ran in a counterbalanced order. False alarms and omissions were rare (on average: 0.45 and 1.89%, per subject, per condition, respectively). Mean RTs (after trimming outliers, .54% of trails per subject per condition) to tactile stimulation were entered in a repeated measures ANOVA with Condition (Upper Arm – Hand) and Distance (from D1 to D5), as within subject factors, and Order of administration (Upper Arm – Hand; Hand – Upper Arm) as between subject factor. As in the previous experiment, the main effect of Distance was significant [$F(4,40)=11.63$, $p<0.0001$], replicating the modulation of tactile RTs depending on the position of sound in space (see Figure 7.5), while the Condition X Distance interaction was not significant F(4,40)=1.56, p=0.20]. Critically, the main effect of Condition was significant [F(1,10)=5.34, p<0.05]. Newman-Keuls post-hoc tests showed that when subjects performed the task while receiving the tactile stimulation on the hand they were generally faster (Mean RTs ± S.E.M, 353 ms ±15) in every temporal delay as compared to when they received the tactile stimulation on the upper arm (370 ms, ±21).

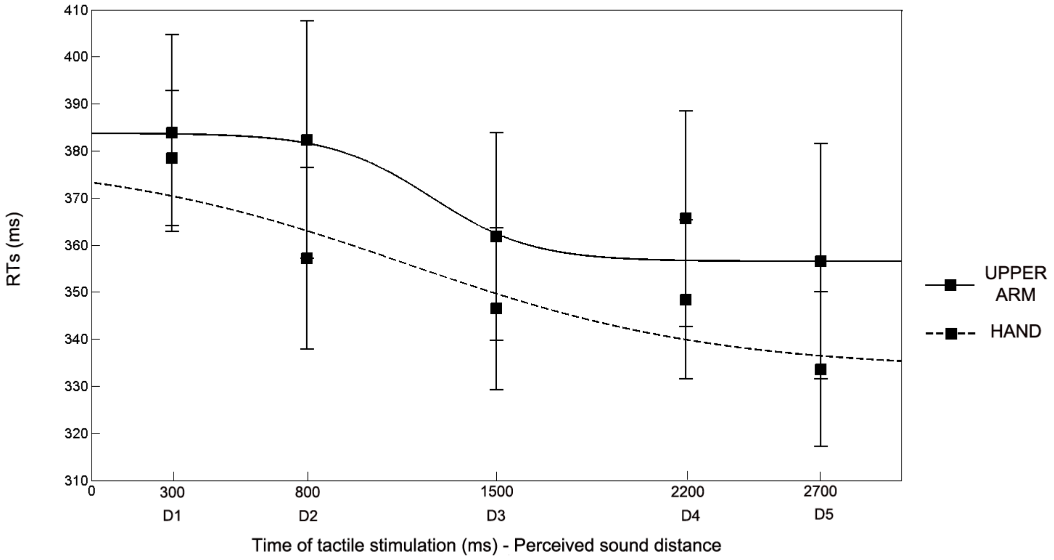

Figure 7.5. Experiment 7.2B results. Mean RTs at different perceived sound distances (from D1 - farthest - to D5 - closest), corresponding to different time of tactile stimulus delivery and best fitting sigmoidal functions describing the relationship between RTs and sound distance, for Upper Arm condition (black line) and Hand condition (dotted line). Error bars denote S.E.M.

These results suggest that when the tactile stimulation was administered at the hand, while the near sound source was placed close to the upper arm, sounds were processed as if they were closer to the boundaries of the stimulated limb, i.e., the hand, resulting in a general reduction of tactile RTs in every temporal delay as compared to when tactile stimuli were administered at the upper arm. This effect suggests that the perceived position of sound was computed with respect to the part of the limb tactilely stimulated, thus being salient to the task, and clearly resembles the effect found in amputee patients when task was performed while wearing, as compared to not wearing, the prosthesis.

7.4 Discussion

Two main results have been obtained by the present study. First, a modification in the physical structure of the body, such as limb loss due to traumatic amputation, affects high-order multisensory representations of the body and of the space around the body. Second, such effects are, at least partially, compensated by prosthesis implantation substituting the lost body part. Results from Experiment 7.1 show that, following amputation, the implicitly perceived length of the residual part of the upper arm decreased, such that patients perceived their stump as shorter as compared to the healthy arm. Wearing a prosthesis increased the perceived length of the arm, making the perception of the stump length more similar to that of the healthy arm. Results from Experiment 7.2 show that amputation and prosthesis implantation also affected the representation of PPS around the stump. We showed that task-irrelevant sounds boosted tactile RTs in so far as they were perceived as being closer to the stimulated body part, both in healthy controls and in amputees tested on their healthy arm. This multisensory effect was reduced when amputated patients were tested on their amputated arm (without-prosthesis); in this condition patients showed slower RTs as compared to conditions involving healthy arm assessment or healthy controls, suggesting that after amputation, the boundaries of PPS shifted towards the stump. However, when the task was administered on the stump while patients wore their prosthesis, there was again the same speeding effect on tactile RTs depending on the position of sounds in space, as for the healthy limb and in controls, suggesting that prosthesis implantation restored the boundaries of PPS so that they included the prosthetic hand.

Until now, an extensive body of evidence has demonstrated that amputation leads to a modification in unimodal motor and somatosensory representations of the body in the brain, both in monkeys (Wu & Kaas, 1999; Merzenich, Nelson, Stryker, Cynader, Schoppmann, & Zook, 1984; Buonomano & Merzenich, 1998) and in humans (Chen et al., 1998; Reilly & Sirigu, 2008; Borsook et al., 1998; Ramachandran & Hirstein, 1998; Serino & Haggard, 2010) suggesting a strong dependency of unimodal body representations on the structure of the physical body. Phantom limb phenomena, such as tactile sensations arising from the missing limb or feeling of moving the amputated limb, occur at one point in almost every individual suffering amputation and offer a striking example of the link between plasticity in primary cortical body representations and body experience (Karl, Birbaumer, Lutzenberger, Cohen, & Flor, 2001; see Ramachandran, 1993 and Serino & Haggard, 2010 for reviews). Interestingly, phantom limb phenomena are not limited to a sensory or motor percepts originating from the missing body part (Hunter et al., 2003; Kooijman et al., 2000), but are often referred by patients as conscious awareness of the presence - implying position, shape and size - of the missing limb (Flor et al., 2006; Hunter et al., 2003). The complexity and richness of these phantom limb phenomena is hardly explainable as resulting only from cortical reorganization in unimodal primary cortices. Rather, they suggest an involvement of multisensory body representations, which integrate the continuous flow of information from different sensory modalities in order to give raise to the experience of the body and its parts (Blanke & Metzinger, 2009; Petkova et al., 2011a; Ionta et al., 2011). Yet surprisingly little is known about the extent to which multisensory body and space representations are dependent on the structure of the physical body and are affected by limb loss. By showing that upper limb amputation changes the perceived dimension of the residual limb and alters multisensory integration in the space surrounding the limb, the present study offers evidence of plasticity in multisensory body representations following a change in the physical structure of the body.

The present results also provide new insights about the direction of these effects: shrinkage of a part of the physical body following amputation resulted in contraction of multisensory body and space representations; when they did not wear their prosthesis, amputee patients perceived their stump as shorter and PPS representation around the stump shrunk. Previous studies provided evidence of plastic modifications of both body and PPS representations in the direction of extension. It is well known that PPS representation, normally limited around the body, extends toward far space after using a tool in order to reach for distant objects (Farnè et al., 2005b; Farnè & Làdavas, 2000; Maravita et al., 2001 Holmes et al., 2004; Maravita et al., 2002). More recently, it has been shown that tool-use also affects the perception of the body itself, as it changes arm motor kinematics and increases the perceived dimension of the limb operating the tool (Cardinali et al., 2009a; Canzoneri, Ubaldi, Rastelli, Finisguerra, Bassolino, & Serino, Tool use shapes the boundaries of both body and peripersonal space representations, under revision; see Chapter 5). Interestingly, there is much less evidence of contraction of body and PPS representation (e.g., see Di Russo et al., 2006; Longo, Kammers, Gomi, Tsakiris, & Haggard, 2009). Since development tends in the direction of growing and cannot normally be reversed, it makes sense that extension phenomena are more common and more easily demonstrated than contraction phenomena. Limb loss represents a rare mean to study plasticity in body representations in the direction of shrinkage. Wearing a prosthesis, however, partially replaces the physical presence of the amputated limb and partially re-establishes its function of acting in space.

The second main finding of the present study is that while wearing a functional prosthesis, long-term prosthesis-users, such as the patients of the present sample, perceive their stump as longer and the boundaries of PPS representation shifted to include the region around their prosthetic hand. In order to interpret these plasticity effects in multimodal body and space representations after amputation (in the direction of contraction) and prosthesis implantation (in the direction of extension) we refer to the well-documented sensory-to-motor functions of BRs and PPS representations. The body is the medium through which we interact with external stimuli, and such interactions normally occur in the space immediately surrounding the body. It is well known that both in monkeys (Graziano & Cooke, 2006) and in humans (Serino et al., 2009; Makin et al., 2009) multisensory fronto-parietal areas responding selectively to stimuli within PPS are directly linked to the motor system in order to trigger fast and appropriate motor reactions to stimuli potentially interacting with body. In the same way, information related to the size and position of different body parts is critical for action upon external objects. Consistent with this view, we show that when the possibility of acting with a limb is limited, due to amputation, BR and PPS representations contract, whereas when such possibility is, at least partially, restored by using a functional prosthesis, BRs and PPS representations extend, such that they incorporate the prosthesis into the representation of the upper limb.

The prosthesis' function of restoring the possibility of the body to act in its space in amputees resembles that of a tool in extending the reachable space of healthy subjects.

However a prosthesis is more than a tool, in that the majority of the prosthetic limbs, differentially from tools, also mimic the visual appearance of a limb. The prostheses used by the present sample of patients were artificial devices that faithfully reproduced the exterior appearance of a real arm and hand; they were also controlled mioelectrically or kinematically by residual muscles in order to allow quite complex limb movements, such as precision grip through thumb opposition and wrist rotation. Since prosthetic limbs share more features with an anatomical limb as compared to tools, prosthesis-use and tool-use could have differential effects on the plasticity of body representations. In particular, distinction has been proposed between the effects of body extension (e.g., in the case of tool-use) and body incorporation (e.g., in the case of prosthesis-use) (De Preester & Tsakiris, 2009; see also Giummarra et al., 2008). It is still not clear, however, whether and to what extent a prosthetic limb can be embodied such that it becomes in some sense indistinguishable from a real body part. We did not directly test the subjective experience of prosthesis embodiment, but the present results suggest that although the effect of prosthesis implantation might overcome that of tool-use, prosthetic limbs cannot be totally conceived as a real part the body, at least because they are known to be attachments that can be taken off. Accordingly, our data show that in amputee patients, two different body representations coexisted and were differentially activated when patients did or did not wear their prosthesis. Indeed, the perceived length of the stump and the extension of PPS immediately shrunk or elongated, depending on whether the prosthesis was respectively on or off. The coexistence of multiple body representations depending on different body states (with or without a tool) resembles other forms of plasticity shown after long-term tool-use experiences (Serino et al., 2007; Bassolino et al., 2010; see Longo & Serino, 2012).

A final critical feature in which most commonly used prostheses and a real part of the body differ is in providing afferent sensory information from the limb to the brain. Although the vast majority of current prosthetic limbs (including those used by the present sample of patients) allow a rather sophisticated level of motor control, they do not normally include any means of providing somatosensory feedback. Incoming afferent information from the body surface is a fundamental cue for the sense of body ownership (see Serino & Haggard, 2010; Tsakiris, 2010). Recent findings suggest that providing amputees with somatosensory feedback from prosthetic limbs might induce a stronger sense of body ownership (Ehrsson et al., 2008) and contribute to better acceptance and incorporation of the prosthesis into their body representation (Marasco, Kim, Colgate, Peshkin, & Kuiken, 2011; Mulvey, Fawkner, Radford, & Johnson, 2009). Understanding the mechanisms of prostheses embodiment and identifying key features of prosthetic devices favouring prosthesis-use and acceptance are key issues for rehabilitation of limb loss and the new field of neuroprosthetics. The present study might contribute to research in this field: on the one hand, it demonstrates striking effects of amputation and prosthesis implantation on the perception of body part size and on multisensory integration in the space around the body; and, on the other hand, it proposes sensitive and easy-to-apply tasks to measure the effects of using prosthetic devices on BRs and PPS representation.

CHAPTER EIGHT: SOCIAL MODULATION OF PERIPERSONAL SPACE BOUNDARIES

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"My body appears to me as an attitude directed towards a certain existing or possible task… its spatiality is not, like that of external objects or like that of "spatial sensations", a spatiality of position, but a spatiality of situation."

(Merleau-Ponty, The Phenomenology of Perception, 1962; pp. 114–115)

8.1 Introduction

In Chapter 1 and Chapter 2 several studies were reviewed showing how, in a variety of species including humans, multisensory stimuli are integrated in a limited space surrounding the body, i.e. within the Peripersonal Space representation. Critically, evidence from neurophysiology, neuropsychology and behavioral studies demonstrated that this representation is plastic, since it extends after using a tool to reach objects placed in the far space (see Chapter 2). Most of the previous cited studies investigated how PPS representation is shaped as a consequence of using a tool to interact with external objects. Although within the PPS other human beings represent the most "salient" and important stimuli we can interact with, less is known about how other people could affect PPS representation. In order to investigate this issue, in the present study we tested how PPS changes as a function of the presence of (Experiment 8.1), and the interaction with (Experiment 8.2 and 8.3), others. In order to measure the extent of peripersonal space representation we used the audio-tactile interaction task presented in previous chapter of this thesis (see Chapter 4, 5, 6 and 7). Participants performed a tactile detection task on their face while concurrent task-irrelevant sounds approached toward or receded from their face. Because a sound affects touch when occurring within PPS, by using this task we measured the critical distance from the subjects' bodies, where sounds affected tactile RTs, along a continuum between near and far space: this point can be considered as the boundary of PPS representation.

In Experiment 8.1A, participants performed the audio-tactile interaction task in two experimental conditions, facing either a mannequin (Mannequin condition), or another person (Other condition). The other person and the mannequin were placed at a distance of 100 cm from the participant, i.e. close to a far loudspeaker where approaching sounds originated from and receding sound terminated. If PPS representation is sensitive to social factors, a change in the extent of PPS boundaries is expected when participants face the other person as compared to when they face a mannequin. We anticipated that this was our actual finding. Then, in order to support the above conclusion, we run a series of control experiments to exclude confounding factors. First, in order to demonstrate that the paradigm used in the present study specifically measured a body-centred representation of PPS, in Experiment 8.1B a new group of participants performed the same audio-tactile interaction task facing either a mannequin or another person, as for Experiment 8.1A, with a critical manipulation: participants were placed at an intermediate position between the near and far loudspeaker (at 50 cm from both), so that the distance between their body and the source of far sounds was halved, while the other (or the mannequin) occupied the same position close to the far loudspeaker. If the present task specifically assesses a body centred representation of PPS, in Experiment 8.1B the speeding effect on tactile RTs due to sounds occurrence should be less dependent on the positions of sounds in space, in comparison to Experiment 8.1A.

Second, in order to demonstrate that that the social modulation of audio tactile interaction shown in Experiment 8.1A and 8.1B was specifically related to PPS representation, and was not a general crossmodal effect, in Experiment 8.1C a new group of participants performed an audio-visual interaction task while facing either another person, or a mannequin. We postulated that if the spatial modulation of multisensory interaction due to the presence of the other is a distinctive hallmark of a change in the representation of the space around the body, no spatially-dependent modulation of sensory processing should be found when participants process sensory stimuli not related to their body - “disembodied” –, e.g., visual stimuli.

In Experiment 8.2 participants performed the audio-tactile task before and after playing a modified version of the Mutual Advantage Game (McCabe, Rassenti, & Smith, 1996; see Procedures below). Subjects were confronted either with a fair and cooperatively acting confederate or with a confederate who was unfair and acted not cooperatively, in order to verify whether the perceived feelings about the other person affected PPS representation.

8.2 Experiment 8.1

8.2.1 Methods

Participants

Fifty students, all females, to avoid effects due to gender differences, participated in Experiment 8.1A (N=18, mean age=25.7 ±1 years, mean years of schooling=16 ±.43), Experiment 8.1B (N=18, mean age=26) and Experiment 8.1C (N=14; mean age=24). All participants were healthy and reported no history of psychiatric illness or neurologic disorder, and no problem of hearing, vision and touch. Participants were all blind regarding the nature of the experiments. All subjects gave their informed consent to participate in the study, which was approved by the local ethics committee in accordance with the Declaration of Helsinki.

Materials

Audio-tactile interaction task

The audio-tactile interaction task was the same as previously described for Chapter 4 (see Figure 8.1). During the task subjects were comfortably seated during the experiment beside a table, which the audio-tactile apparatus was mounted on. A black paperboard box (100 cm high, 120 cm long) was positioned on the table beside them, in order to cover two loudspeakers, one placed close to the participants' right cheek (at ~5 cm), the other one placed at a distance of ~100 cm from the near loudspeaker (at the same elevation), thus far from the participant's head. The two loudspeakers were hidden from view in order to prevent subjects from visually locating the origin of the sounds presented during the experiment. Tactile stimulus was administered on participants' right cheek.

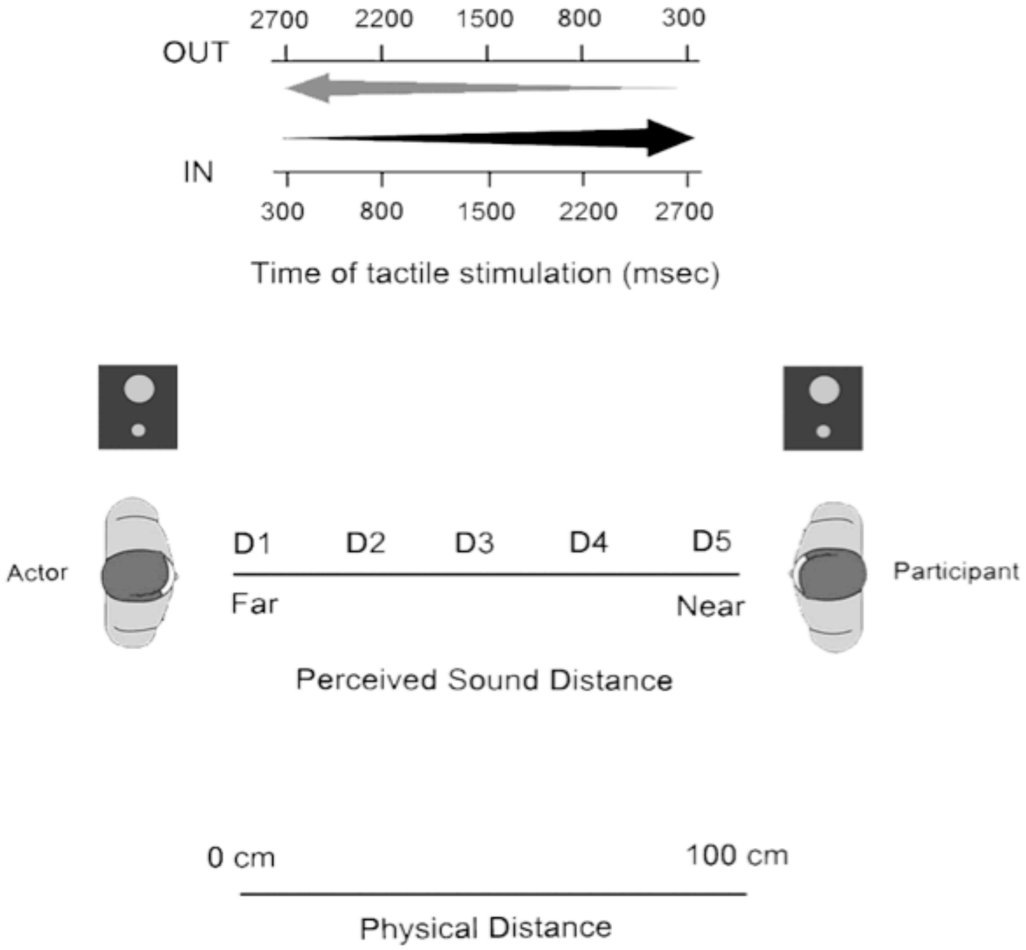


Figure 8.1 Experimental paradigm

Each experimental condition consisted in a random combination of 8 target stimuli for each temporal delay from T1 to T5, for the IN and OUT sounds, resulting in a total of 80 trials with a tactile target, randomly intermingled with 24 catch trials. Trials were equally divided in two blocks, lasting about 5 minutes each.

In order to demonstrate subjects actually perceived the sound source at different locations according to different temporal delays (from T1 to T5) for the IN and the OUT sound, we ran a sound localisation experiment on 18 naïve subjects. Subjects were blindfolded and received a tactile stimulation on their right cheek at one of the different temporal delays in a series of 80 trials, randomly presented. At the end of each trial, they were asked to verbally indicate the perceived position of the sound in space when they had felt the tactile stimulus, on a scale from 1 (very close) to 100 (very far). Participants were explicitly invited to use the entire range between 1 and 100, taking in account also for small differences in the perceived position of sound. A repeated measure ANOVA with the factors Sound (IN, OUT) and Temporal Delay (from T1 to T5) showed a significant two-way interaction [$F(4,68)=256$, $p<0.0001$]. Figure 8.2 clearly shows that, for the IN sound, subjects progressively perceived the sound closer to their body when the tactile stimulus was administered at successive temporal delays from T1 to T5. The pattern of responses was completely reversed for the OUT sound, when the sound was perceived in spatial positions progressively farther from the body from T1 to T5. Post-hoc comparisons (Newman-Keuls corrected) confirmed that localisation judgments for each temporal delay were significantly different from both the immediately successive and the immediately preceding one (all $p_s<0.01$). Localisation judgments were also compared between IN and OUT sounds at spatially corresponding temporal delays: i.e. T1 IN ≈ T5 OUT; T2 IN ≈ T4 OUT; T3 IN ≈ T3 OUT; T4 IN ≈ T2 OUT; T5 IN ≈ T1 OUT. There was a significant difference in perceptual judgments only for the comparison between T5 IN and T1 OUT ($p<0.05$): at the temporal intervals corresponding to the closest distance from the body, subjects perceived the OUT sound more proximal than the IN sound. No other significant differences between perceptual judgments for IN and OUT at corresponding temporal delays were found (all $p_s>0.12$).

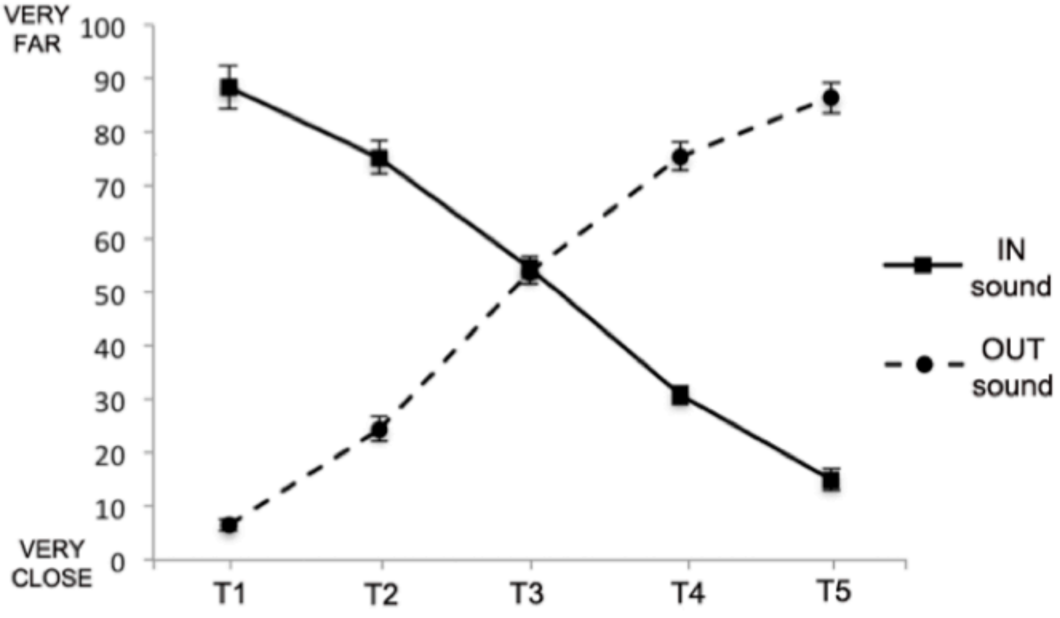


Figure 8.2. Sound localisation experiment results.

Audio-visual interaction task

The experimental set up was the same as for Experiment 8.1A, except that here participants were requested to respond as fast as possible to a visual stimulus (i.e., the illumination of an LED; diameter 40 mm; onset duration 100 ms), while ignoring dynamic sounds. No tactile stimulation was delivered. The visual target was placed between the participant and the mannequin/other, at a distance of 60 cm from the participant, aligned along the direction of gaze of the participant, who was instructed to look at the face of the mannequin/other during the task. The 60 cm distance was chosen in order to present the visual target clearly outside the participant's visual PPS (which in monkeys has been shown to extend for ~30 cm; (Rizzolatti et al., 1981b), as well as outside the other's PPS, while being clearly visible to the participant.

As in Experiment 8.1A, the near and the far loudspeakers, placed respectively at the participant's and the mannequin/other locations, generated illusory dynamic sounds, giving the impression of a sound source either approaching to or receding from the participant. Visual targets were administered at 5 different temporal delays from sound onset, implying that they were processed when sounds were perceived at 5 possible different distances from the subject (ranging from D1, very far, to D5, very close). Given the location of the LED, sounds were perceived at approximately the same location of the visual target when this was delivered at D3 (see Sound Localisation experiment, Figure 8.2).

Procedure

In Experiment 8.1A, participants performed the audio-tactile interaction task assessing PPS representation in two within-subjects conditions, facing either a mannequin (Mannequin condition), or another person (Other condition). The other person was an actor, a female, of approximately the same age as the participants, unknown to the participants. Subjects were told the actor was another student involved in another experiment. Two different actors were used, one for each half of participants, in order to avoid any idiosyncratic effects due to the actor's appearance. The mannequin was a human-like torso (with head), made of white expanded polystyrene (length: 93 cm; shoulder-to-shoulder width: 43 cm), seated on a chair in front of the subjects. Schematic eyes and mouth were drawn on the mannequin head, to identify its face. In Experiment 8.1A, the other person and the mannequin were placed at a distance of 100 cm from the participant, i.e., close to a far loudspeaker from where approaching sounds originated and receding sounds terminated. During the task subjects were instructed to gaze at the mannequin's or the other's face. The order of administration of the Mannequin and the Other condition was counterbalanced between subjects. After the experiment participants also completed an Italian (Bonino, Lo Coco, & Tani, 1998) version of the Interpersonal Reactivity Index (IRI) (Davis, 1966), in order to exclude that results were contaminated by inter-group differences in empathy. IRI is a 28-item self-report survey that consists of four subscales, namely Perspective Taking (PT, that assess the tendency to spontaneously imagine and assume the cognitive perspective of another person), Fantasy scale (FS, that assess the tendency to project oneself into the place of fictional characters in books and movies), Empathic Concern (EC, that assess the tendency to feel sympathy and compassion for others in need) and Personal Distress (PD, that assess the extent to which an individual feels distress as a result of witnessing another's emotional distress). PT and FS assess cognitive components of empathy, while EC and PD correspond to the notions of other-oriented and self- oriented empathy-related emotional reactions.

In Experiment 8.1B, the procedure for similar to that of Experiment 8.1A, except that participants were placed at an intermediate position between the near and far loudspeaker (at 50 cm from both), so that the distance between their body and the source of far sounds was halved, while the Other (or the Mannequin) occupied the same position close to the far loudspeaker. As for Experiment 8.1A, the other person was an actor, a female, of approximately the same age as the participants, unknown to the participants. Subjects were told the actor was another student involved in another experiment. At the end of the experiment, as for Experiment 8.1A, subjects performed a sound localisation task, in which were asked to indicate on a scale from 1 (at the position of the near loudspeaker) to 100 (at the position of the far loudspeaker) where they perceived the moving sound at the time of tactile stimulation. Subjects occupied a position corresponding to 50 in this scale. Results from this task are shown in Table 8.2, revealing that, accordingly to the experimental manipulation of this experiment, sounds were perceived closer to the subjects’ body, as compared to Experiment 8.1A.

Data analysis and sigmoid fitting

Vocal responses to tactile (Experiment 8.1A and 8.1B) and visual (Experiment 8.1C) stimuli were recorded by means of a voice-activated relay, and stored for off line analyses. RTs for trials from the same condition were then averaged for statistical analyses. For Experiment 8.1A, mean RTs to the tactile target at the different time intervals (for IN sounds only) were also fitted to a sigmoidal function described by the following equation: $y(x) = \frac{y_{min} + y_{max} \cdot e^{(x-x_c)/b}}{1 + e^{(x-x_c)/b}}$, where x represents the independent variable (i.e., the timing of touch delivery in ms), y the dependent variable (i.e., the reaction time), *ymin* and *ymax* the lower and upper saturation levels of the sigmoid, *xc* the value of the abscissa at the central point of the sigmoid (i.e., the value of x at which y = (ymin+ ymax)/2) and *b* establishes the slope of the sigmoid at the central point.

8.2.2 Results

Experiment 8.1A. PPS Representation as a Function of the Presence of Others

Because of the titration of tactile stimuli, error rates were extremely low (Other condition: mean omissions=3%, ±.1; mean false alarms=.4%, ±.001; Mannequin condition: mean omissions=2%, ±.008; mean false alarms=.4%, ±.004.) and therefore the performance was analysed in terms of RTs only.

Mean RTs to the tactile stimulus administered at the different perceived sound distances were calculated for IN and OUT sounds and compared between the two conditions of facing the other or the mannequin, by means of an ANOVA with factors Distance (D1–D5, with D1 = farthest Distance and D5 = closest Distance), Sound (IN, OUT), and Condition (Other, Mannequin). The critical three-way interaction was significant [F(4, 44)=2.70; p<0.05]. Thus, two separated ANOVAs were conducted for IN and OUT sounds, with the factors Distance and Condition. For the IN sound, the interaction Distance by Condition was significant [F(4,44)=4.54; p<0.01], suggesting that RTs were differently modulated depending on the perceived position of sound in space, as a function of whether subjects faced the mannequin or the other person. As Figure 8.3 shows, in the Mannequin condition RTs were significantly faster when concurrent sounds were perceived at D2, D3, D4, and D5, as compared to when sounds were perceived at D1 (p<0.001 in all cases, Newman-Keuls corrected; effect present in 14 out of 18 subjects). Thus, the estimated PPS boundaries were located between D1 and D2. In contrast, in the Other condition, RTs were faster when sounds were perceived at D3, D4, and D5, as compared to when sounds were perceived at D2 and D1 (p<0.05 in all cases, Newman-Keuls corrected; effect present in 15 out of 18 subjects), thus indicating that PPS boundaries were located between D2 and D3, that is, in a spatial position closer to the subject as compared to in the Mannequin condition. Indeed, RTs at D2 and D3 were faster in the Mannequin than in the Other condition (p<0.05 in all cases). No change in RTs was instead found for the farthest (D1, p=0.68) or the closest (D4 and D5, p>0.18 in all cases) distances. No significant effects were found in the case of OUT sounds, indicating that RTs in this condition were less affected by the position of sounds in space (see Table 8.1).

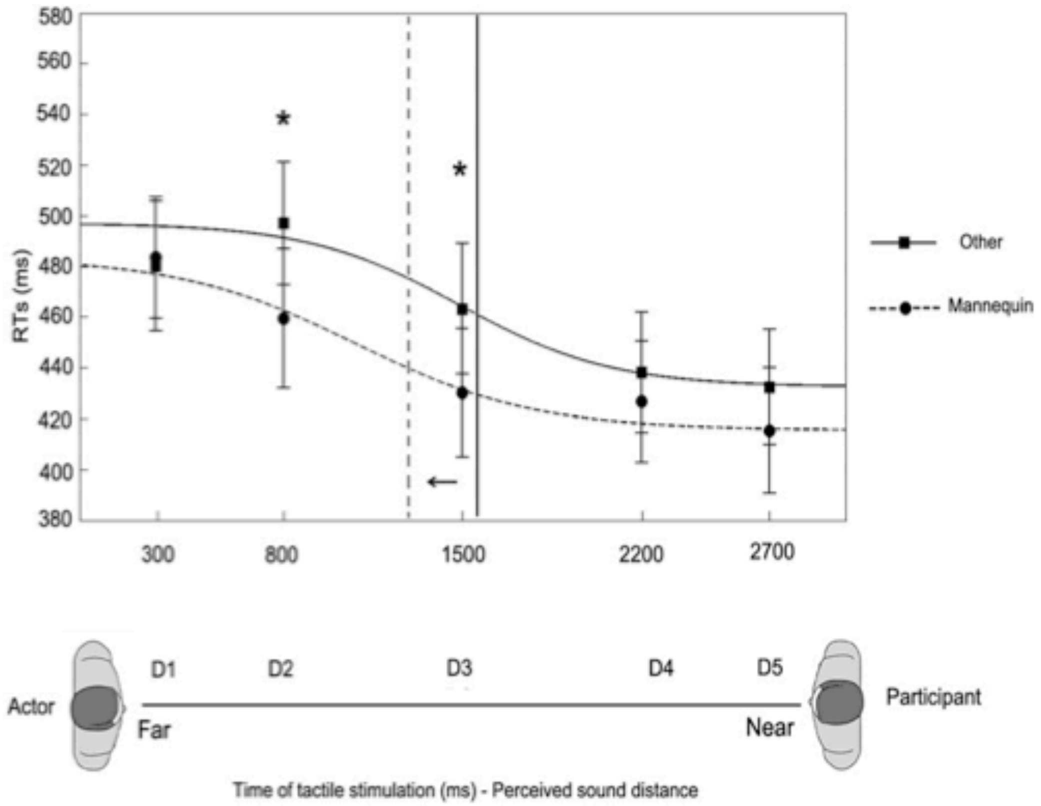


Figure 8.3. The figure shows mean RTs at different perceived sound distances (for the IN sound; see Table 8.1 for the OUT sound), corresponding to different times of tactile stimulus delivery, when participants faced the other person or the mannequin (error bars represent S.E.M.). RTs at the different temporal delays have been fit with a sigmoid function. The sigmoid central point curve was computed as a measure of the temporal delay, i.e., the distance, at which sounds start affecting RTs and was analyzed in order to quantify PPS boundaries. The sigmoid central point was higher in the Other (1.566 ms) as compared to the Mannequin (1.384 ms) condition (t[15]=21.6; p<0.05, one-tailed; two subjects were not included in the analysis due to bad fitting), meaning that PPS boundaries were closer to the participants when they faced the other person than when they faced the mannequin.

Results from the sound localisation experiment (see Methods) excluded that that the differential effect found for IN and OUT sounds was due to differences in the way subjects localized the two sound sources at corresponding temporal delays.

Rather, the stronger spatially dependent effect shown for the IN sound is coherent with previous findings showing higher relevance of looming stimuli for PPS neurons (Canzoneri et al., 2012; Tajadura-Jimenez, Väljamäe, Asutay, &Vastfjall, 2010; Hall & Moore, 2003; Fogassi et al., 1996). In sum, these findings show that PPS representation shrank when the far space was occupied by another person, as compared to when it was occupied by an artificial body-like object, suggesting that one's own PPS accommodates in the presence of others.

We also investigated whether the extent of PPS representation correlated with traits of personality assessed by means of the IRI questionnaire. By using partial correlation analyses analysis, we investigated the relation between the score of participants' at the different four subscales of IRI and an esteem of PPS boundaries in the Other condition. In order to quantify PPS boundaries, the sigmoid central point curve was computed as a measure of the temporal delay, i.e. the distance, at which sounds start affecting RTs. Results showed that score of the PD subscale correlated positively with the boundaries of PPS in the Other condition (r=0.59, p<0.03, two-tailed; see Figure 8.4): the higher the score in the PD subscale, the closer to the body the PPS boundaries. No other significant correlation was found with the other IRI subscales (FS: r=0.06, p=0.82; PT: r=-0.13, p=.65; EC: r=-0.18, p=0.52).

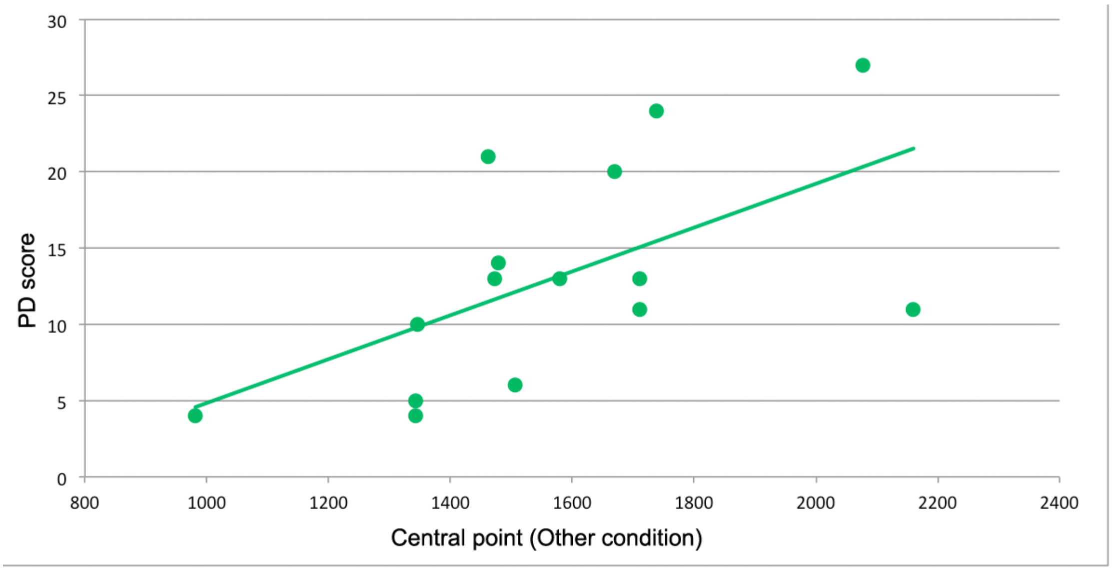
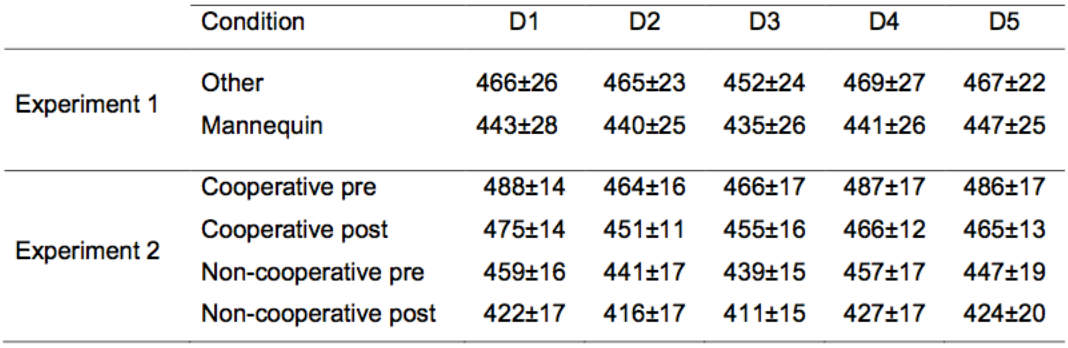


Figure 8.4 The graph shows the relationship between the participants' score at the IRI's PD subscale and the Central point of the sigmoid function. Two subjects were not included in the analysis due to bad fitting, while another subject was excluded because she did not complete the questionnaire at the end of the experiment.



	Condition	D1	D2	D3	D4	D5
Experiment 1	Other	466±26	465±23	452±24	469±27	467±22
	Mannequin	443±28	440±25	435±26	441±26	447±25
Experiment 2	Cooperative pre	488±14	464±16	466±17	487±17	486±17
	Cooperative post	475±14	451±11	455±16	466±12	465±13
	Non-cooperative pre	459±16	441±17	439±15	457±17	447±19
	Non-cooperative post	422±17	416±17	411±15	427±17	424±20

Table 8.1 RTs (±S.E.M.) in ms to tactile targets associated with receding sound (OUT), perceived at different distance from the body (from D1, very far to D5, very close), for Experiment 8.1A and Experiment 8.2.

Experiment 8.1B

If the present audio-tactile interaction task specifically assesses a body centred representation of PPS, in Experiment 8.1B, the speeding effect on tactile RTs due to sounds occurrence should be less dependent on the positions of sounds in space, in comparison to Experiment 8.1A. To test this prediction, mean RTs to the tactile stimulus administered at the different perceived sound distances were calculated for IN sounds, and compared between Experiment 8.1B and Experiment 8.1A. RTs were entered in an ANOVA with factors Distance (D1-D5), and Condition (Other, Mannequin) as within subject factors and Experiment (Experiment 8.1A, Experiment 8.1B) as between subject factors. The critical three-way interaction was significant [$F(4,136)=2.4$, $p<0.05$], suggesting that RTs were differently modulated in the two Experiments, depending on the perceived position of sounds in space, as a function of whether subjects faced the mannequin or the other person. In Experiment 8.1A in the Mannequin condition, RTs were significantly faster when concurrent sounds were perceived at D2, D3, D4 and D5, as compared to when sounds were perceived at D1 (all $p_s<0.05$, Newman-Keuls corrected), far from the subject's body, thus the PPS boundary was localized between D1 and D2. Instead, in Experiment 8.1B, when the participant was closer to the origin of far sounds, RTs to tactile stimuli administered together with sounds at D1 were not slower than RTs coupled with sounds at D2, D3 and D4 (all $p_s>0.10$) suggesting that all sound distances were now included within PPS. In contrast, a modulation of tactile RTs due to sounds position in space was instead found in Experiment 8.1B in the Other condition: RTs at D4 and D5 were significantly faster than RTs at D1, D2 and D3 (all $p_s<0.05$). Thus, a PPS boundary could be identified in the Other condition and this was located between D3 and D4, confirming the main finding from Experiment 8.1A that the presence of other induced a shrinkage in PPS representation.

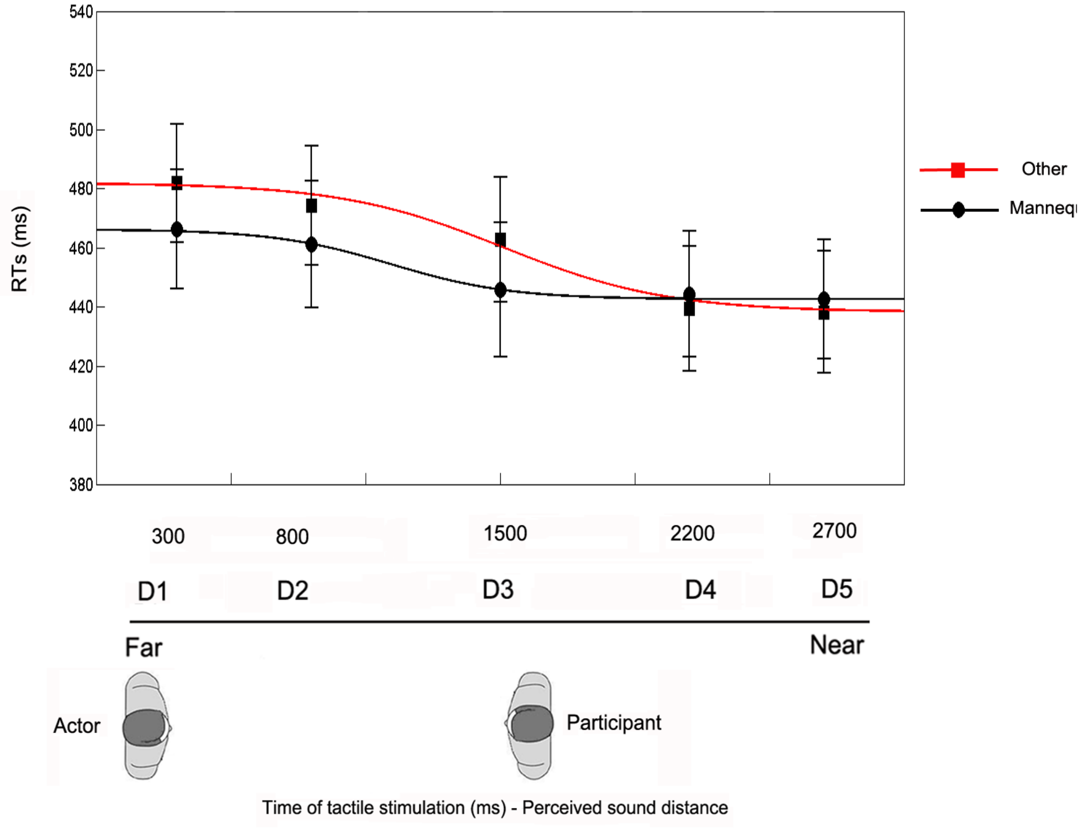


Figure 8.5 Experiment 8.1B results. The figure shows mean RTs at different perceived sound distances (for the IN sound; for the OUT sound results see Table 8.2), corresponding to different times of tactile stimulus delivery, when participants faced the other person or the mannequin (error bars represent S.E.M.).

	Condition	D1	D2	D3	D4	D5
a) Experiment 8.1B	Other	552±25	556±21	542±22	550±19	553±19
	Mannequin	534±21	546±22	526±23	530±18	538±20
b) Sound localisation experiment		67±6	67±5	59±4	44±3	36±3

Table 8.2. Experiment 8.1B. OUT sound and Sound Localisation Experiment results
a) RTs (±S.E.M.) in ms to tactile targets associated with receding sounds (**OUT**), at the different sounds distances, when the participant was placed at 50 cm (instead that a 100 cm) from the origin of far sounds.
b) Responses from the sound localisation task. At the end of the experiment, subjects were asked to indicate on a scale from 1 (at the position of the near loudspeaker) to 100 (at the position of the far loudspeaker) when they perceived the moving sound at the time of tactile stimulation. Subjects occupied a position corresponding to 50 in this scale.

Interestingly, however, PPS boundaries were located at a different location in Experiment 8.1B as compared to Experiment 8.1A, when tactile RTs were faster for sounds at D3, D4 and D5, as compared to sounds at D2 and D1 (all ps<0.05, Newman-Keuls corrected), indicating that PPS boundaries were located between D2 and D3. Taken together results from Experiment 8.1B confirm that the modulation of tactile processing due to the position of sounds depends on the location of the subject's in space. The effect vanishes if subjects are placed closer to the origin of far sounds in presence of a mannequin. However, in presence of the other, PPS further contract as to accommodate in relationship to the space of the other, and a new PPS boundary emerges.

Experiment 8.1C

If the spatial modulation of multisensory interaction due to the presence of the other is a distinctive hallmark of a change in the representation of the space around the body, no spatially-dependent modulation of sensory processing should be found here when participants process sensory stimuli not related to their body - "disembodied" –, e.g., visual stimuli. Accuracy was extremely high (average=98%, S.E.M.=±0.004), meaning that subjects could see and paid attention to the visual stimulus during the task. Mean RTs to the visual stimulus administered at the different perceived sound distances were calculated for IN and OUT sounds, in the Mannequin and in the Other conditions, and entered in a repeated measure ANOVA with factors Sound (IN, OUT), Distance (D1-D5) and Condition (Other, Mannequin). The main effect of Distance was significant [F(4,48)=5.63, p<0.01]. Newman-Keuls post-hoc comparisons showed that RTs to the visual target were significantly faster when the sound was perceived at D3 (486 ms ±17) than when the sound was perceived at D1 (504 ms ±17), D2 (501 ms ±17), D5 (501 ms ±21; all ps<0.01) and marginally faster than when the sound was perceived at D4 (495 ms ±18, p=0.06).

	Condition	D1	D2	D3	D4	D5
a) Experiment 1C IN sound	Other	522±20	536±20	492±16	497±21	504±21
	Mannequin	504±16	510±18	475±19	469±18	485±21
a) Experiment 1C OUT sound	Other	503±18	498±21	496±19	518±22	521±21
	Mannequin	484±19	481±15	482±19	494±18	496±21
b) Sound localization task						
IN sound		90±3	76±7	58±3	37±2	19±4
OUT sound		86±5	78±2	56±3	33±2	15±8

Table 8.3 The table shows a) RTs (±S.E.M.) in ms to visual stimulus associated with approaching sounds (IN) and receding sounds (OUT), at the different sounds distances for Experiment 8.1C; b) Responses from a sound localisation task conducted as those described for Experiment 8.1A.

Given the spatial location of the LED, sounds were perceived at approximately the same location of the visual target when this was delivered at D3 (see Sound

Localisation experiment, Table 8.3, panel b). The present finding reflects a well-known principle of multisensory integration, that is auditory and visual stimuli are more effectively integrated when stimuli from both modalities are spatio-temporally coincident. The main effect of Condition was also significant [F(1,12)=11.12, p<0.01], showing that RTs were generally faster when participants faced the mannequin (488 ms ±17) than when they faced another person (509 ms ±19). The same main effect of Condition was present also in Experiment 8.1A, with faster RTs in the Mannequin (442 ms ±25) than in the Other (463 ±24) condition [F(1,17)=7.61, p<0.05]. An inhibitory effect on RTs due to the presence of others has been already reported in Social cognition literature. Critically, however, in Experiment 8.1C, when target visual stimuli were unrelated to participant's body, the inhibitory effect due to the presence of the other on visual RTs was totally independent from the perceived position of sounds in space, and it did not affect the position in space where sounds affected visual processing as compared to the Mannequin condition. Indeed, neither the two-way Condition X Distance interaction nor the three-way Condition X Sound X Distance interactions were significant (p=0.60 and 0.86 respectively). In contrast, the key finding of Experiment 8.1A was that the presence of the other, as compared to the mannequin condition, changed the position in space where sounds affected tactile processing at the participant's body that is the boundaries of PPS.

8.3 Experiment 8.2

8.3.1 Methods

Participants

Thirty-two students, all females, to avoid effects due to gender differences, participated in Experiment 8.2 (Cooperative game condition: N=16, mean age=20.69 ±.41, mean years of schooling=14.81, ±.39; Non-cooperative condition: N=16, mean age=20.87 ±.44, mean years of schooling=15, ±.39). All participants were healthy and reported no history of psychiatric illness or neurologic disorder, and no problem of hearing, and touch. Participants were all blind regarding the nature of the experiments, and none had experienced an economic game previously. All subjects gave their informed consent to participate in the study, which was approved by the local ethics committee in accordance with the Declaration of Helsinki.

Materials

Audio-tactile interaction task

The same audio-tactile interaction task as described for Experiment 8.1A was used.

Procedure

In Experiment 8.2, participants performed the audio-tactile task before and after playing a one-shot bargaining game with a human partner (i.e., an actor previously unknown to the participant) via a computer interface. There were two treatment conditions of the game: Cooperative and Non-cooperative condition. Half of the participants were randomly assigned to the Cooperative condition and the other half to the Non-cooperative condition. Two female subjects acted as confederate (player B). The two confederates were used equally often across the experiment, counterbalancing the role (Cooperative or Non-cooperative) across subjects. The experiment was run in individual sessions. On entering the laboratory, participants were greeted by an experimenter who informed them that they would participate in two separate and unrelated studies: one designed to evaluate tactile perception and the other to study economic decision-making. In the ostensible first study, participants were told that they would be asked to respond to tactile stimuli delivered on their face. In the supposedly second study, participants were told they would be paired with another participant to decide how to divide a sum of money. The experimenter also informed that, because the tactile task required two sessions separated by a brief interval (i.e., the first experiment), they would be asked to complete the second experiment in between these two sessions.

Subjects participated in a modified version of a behavioural Mutual Advantage Game (McCabe et al., 1996), in which two human players, A and B, interact with each other to earn real stakes. Participants were informed that they would be playing with the partner (i.e., one of the two actors) they faced during the tactile perception task. They received written instructions about the nature and rules of the bargaining game, and the experimenter verbalized the instructions to ensure that participants understood them. In the instructions, it was emphasized that participants would play the game only once with their opponent player, and that they were randomly assigned the role of player A and B, respectively. In fact, participants were always assigned to the role of player A, while the confederates were always assigned to the role of player B. Participants were also informed that monetary sum earned during the game would be used to purchase different commercial products (i.e., USB keys, mobile phones credit, drinks, clocks, pens, books) at the end of the experiment, of monetary value corresponding to the outcome earned during the game.

The game took place in a quiet room in which an opaque, removable partition wall was used to create two separate settings. On either side of the wall, we placed a desk with a computer. Participants sat at one desk in front of the computer, while at the other sat the confederate. In the game, player A (the participant) moved always first by choosing either “left” or “right”. For half participants, if she chose “left” (defect), she earned €7 for herself, giving €3 to player B, and the game was over. Alternatively, player A could chose "right" (cooperate), putting player B (the confederate actor) on the move. Player B could either reciprocate cooperation, taking an option paying €10 to both players, or defect, earning €7 for herself and giving €3 to player A. For the other half of participants, the correspondence between sides and choices was reversed. If players defected, they could purchase with their income whatever product they wanted. If players cooperated, they had to agree with their partner on which product to purchase. Half of the participants were confronted with a fair and cooperatively acting confederate (player B), and the other half were confronted with a confederate who was unfair and acted not cooperatively. Two out of 32 participants (players A) decided to defect (earning €7 for themselves and giving €3 to their partners) in the first decision of the game. These two subjects were excluded from the experiment, and replaced with two other participants. Thus, all 32 subjects included in Experiment 8.2 chose to cooperate with their partner.

Before participants left the laboratory, they purchased a different product accordingly to the monetary outcome earned during the game. They were then questioned for suspicion during stepwise debriefing. Accordingly to their report, no participant guessed the actual purpose of the study. Participants also expressed no suspicion regarding the cooperative or not cooperative behaviour of player B during the bargaining game. At the end of their experimental session, subjects involved in the economic game were invited to fill in a questionnaire, aimed at verifying that the 2 different game conditions (Cooperative and Non-cooperative) induced different subjective feelings about the confederate. Participants were asked to answer, on a scale ranging from 1 (not at all) to 7 (very much), to the questions reported in the first column of Table 8.4.

8.3.2 Results

As for Experiment 8.1, error rates were extremely low (Cooperative game condition: mean omissions=3.75%, ±.75; mean false alarms=.5%, ±.52; Non- cooperative game condition: mean omissions=3.59%, ±.83; mean false alarms=.8%, ±.42), so the performance was analysed in term of tactile RTs only.

In order to test how PPS representation varied before and after the game, as a function of the partner's game behaviour, we ran an ANOVA on mean tactile RTs with the within-subjects factors of Distance (D1-D5), Sound (IN, OUT), Session (before and after the game), and the between-subjects factor Condition (Cooperative and Non cooperative). The four-way interaction was significant (F[4,120]=2.45; $p<0.05$). Thus, we conducted separate ANOVAs, one for each Condition.

In the Non-cooperative game group, for the IN Sound, the main effects of Distance (F[4,60]=21.63, $p<0.00001$) and Session (F[1,15]=13.12; $p<0.01$) were significant, but not the two-way interaction ($p=0.10$). Both before and after the game, RTs recorded when sounds were perceived at the farthest distances (i.e., D1 and D2) were significantly slower than those for sounds at the closest distances (i.e., D3, D4, and D5, $p<0.001$ in all cases, Newman-Keuls corrected), thus suggesting that PPS boundaries were located approximately at the same spatial range as in Experiment 8.1A, in the Other condition. RTs for all sound distances were speeded up after the Non-cooperative game as compared to before the game. Importantly, the critical point where sounds affected RTs did not change before and after the game (see Figure 8.6A). In the case of the OUT sounds, only a significant effect of Session (F[1,15]=7.82; $p<0.05$) was found, showing, again, a general speeding effect in RTs after the Non-cooperative game (see Table 8.1).

A different pattern of results was found in the Cooperative game condition. In case of

IN sounds, the two-way interaction Distance by Session was significant (F[4,60]=4.20; p<0.01). As Figure 8.6 shows, before the game, RTs varied as a function of the position of sounds in space, with slower RTs for the farther distances (D1 and D2), as compared to the closer distances (D3, D4, D5; p<0.001 in all cases, Newman-Keuls corrected). Thus, the estimated boundary of PPS was located between D2 and D3. On the contrary, after the game, PPS boundaries between near and far space vanished; there was no significant difference between RTs at any sound distance (p>0.12 in all cases). Such an effect was due to faster RTs associated to sounds perceived at the farthest distances (i.e., D1 and D2) after the game as compared to before the game (p<0.001 in all cases). No change in RTs was instead found for closest sound distances (D3, D4, and D5; p>0.20 in all cases). Thus, after the Cooperative interaction, audio tactile integration increased for stimuli presented at the space occupied by the Other (far distances), and not for stimuli presented within one's own PPS (close distances). As a consequence, there were no more detectable PPS boundaries between the self and the other after the game: the participant's PPS had extended as far as to include the space around the partner. No significant effect of Session (p=0.19) or Interaction (p=0.86) was found for the OUT sound (see Table 8.1).

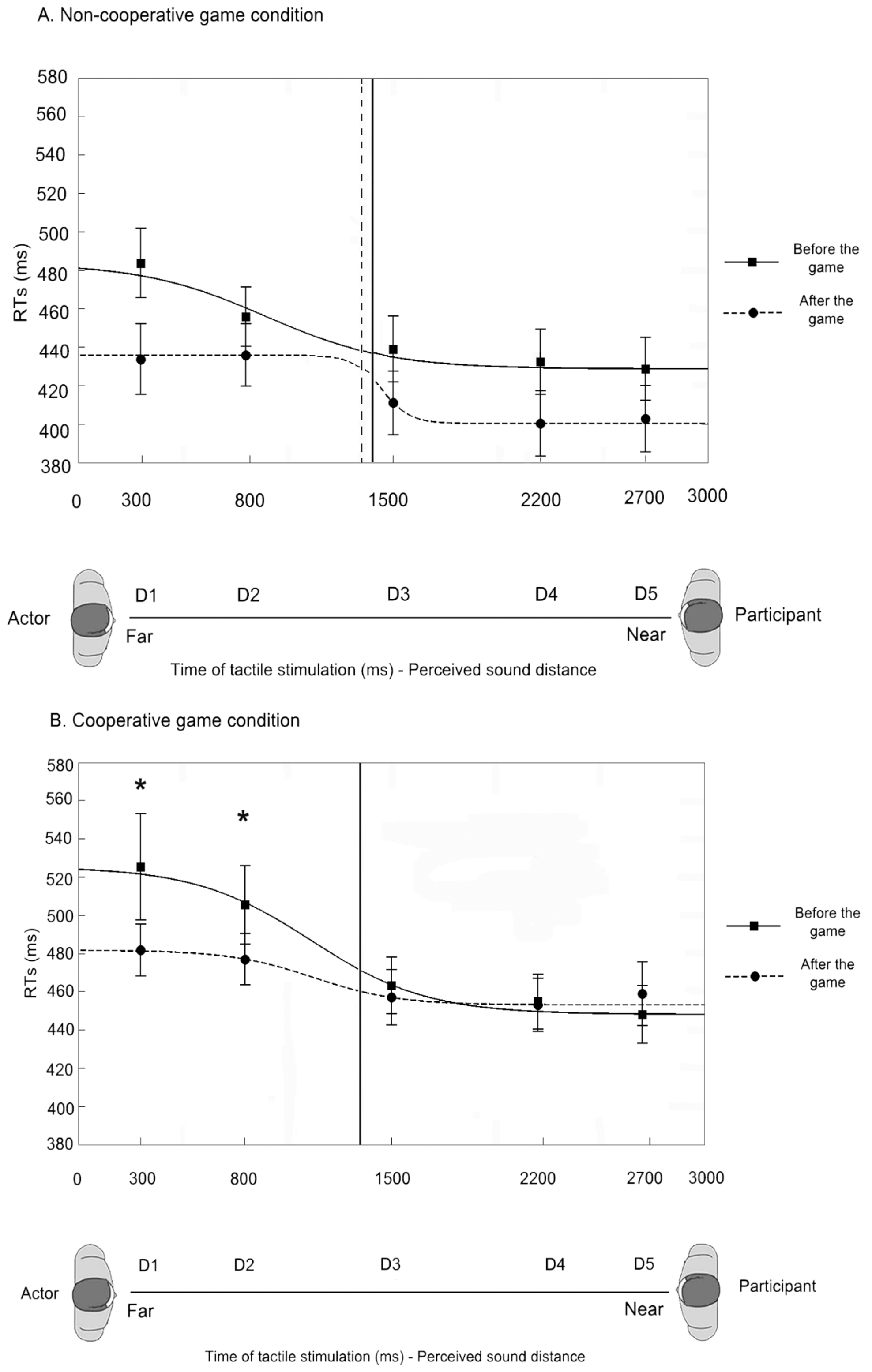


Figure 8.6 The figure shows mean RTs at different perceived sound distances (for the IN sound; see Table 8.1 for the OUT sound), corresponding to different times of tactile stimulus delivery (error bars represent S.E.M.). (A) and (B) show, respectively, the results from the Non-cooperative game condition and from the Cooperative game condition, before and after the game. RTs at the different temporal delays have been fit with a sigmoid function. In the Non-cooperative game group, RTs were generically faster at any sound distances after the game than before the game, but PPS boundaries did not shift. The central sigmoid central point did not differ between the two sessions (before the game=1.467 ms; after the game=1.443 ms; t(13)=0.32, p=0.76; two subjects were excluded due to bad fitting). In the Cooperative game group, RTs were faster after the game than before the game only at the farthest sound distances (D1 and D2), that is at the space occupied by the cooperative other.

Results from the present Experiment suggested that, after a cooperative interaction, PPS boundaries between the self and the other merged, since after the game the PPS boundaries could not longer be reliably established. In order to confirm that the cooperative game resulted in an extension of PPS space boundaries up to include the other, and not in a generic weakening of audio-tactile interaction, in Experiment 8.3 we tested audio-tactile interaction in a wider spatial range, including portion of space beyond the cooperative Other. If the effects we found in Experiment 8.2 reflected an extension in PPS representation, we did expect a change in audio-tactile interactions in the space occupied by the Other (confirming results from Experiment 8.2), but not at farther location (i.e. beyond the actor).

8.4 Experiment 8.3

8.4.1 Methods

Participants

Twenty students, all females, to avoid effects due to gender differences, participated in Experiment 8.3 (N=20, mean age=23.68 ±.63, mean years of schooling=16.21 ±.57). All participants were healthy and reported no history of psychiatric illness or neurologic disorder, and no problem of hearing, vision and touch. Participants were all blind regarding the nature of the experiments, and none had experienced an economic game previously. All subjects gave their informed consent to participate in the study, which was approved by the local ethics committee in accordance with the Declaration of Helsinki.

Audio-tactile interaction task

In Experiment 8.3 participants performed the same audio-tactile interaction task as previously described for both Experiment 8.1A and 8.2, but in this case a wider spatial range was used.

To this aim, near and far loudspeakers were separated by 2 m and 7 instead of 5 temporal delays were used, so that sounds were perceived at seven different spatial positions. The participant was placed at the location of the near loudspeaker, whereas the actor was placed at 1 m from the participant, thus midway between the two loudspeakers. Only IN sounds were used. Sound duration was 4000 ms (instead of 3000 ms, as in Experiment 8.1A and 8.2). For each trial, the sound was preceded and followed by 500 ms of silence. Temporal delays for Experiment 8.3 were set so that tactile stimulation occurred: 250 ms after the IN sound onset (corresponding to 750 ms from the beginning of the trial) at D-2; at 750 ms from sound onset at D-1; at 1300 ms from sound onset at D1; at 1800 ms from sound onset ad D2; at 2500 ms from sound onset at D3; at 3200 ms from sound onset at D4; and at 3700 ms from sound onset at D5. Temporal delays were chosen so that the last five delays (D1–D5) corresponded to time intervals used in the previous experiments, whereas D-1 and D-2 occurred earlier along in the trial. In this way, when the tactile stimulus was administered at D-2 and D-1, the sound was perceived at further locations, as compared to the other intervals, beyond the actor.

Experimental Procedure

In Experiment 8.3, participants were confronted only with a fair and cooperatively acting confederate. The procedure for the Mutual Advantage Game was the same as for Experiment 8.2.

8.4.2 Results

Error rates were extremely low (mean omissions=4.01, ±.77; mean false alarms=.6%), so the performance was analysed in terms of RTs only. An ANOVA with the factors Distance and Session (before and after the game) showed a significant two-way interaction [$F(6,114)=2.21$; $p<0.05$]: at D1, RTs after the game were faster than before the game ($p<0.05$; $p>0.10$ for all other comparisons, Newman-Keuls corrected), confirming that, after the Cooperative interaction, audio tactile interaction increased for sounds presented at the position occupied by the Other. Crucially, RTs were modulated by the spatial location of sounds both before and after the game. However, the critical point where sounds began affecting tactile RTs was located at a further distance after the game than before the game (see Figure 8.7 and legend for statistical analysis). These results, together with those from Experiment 8.2, indicate that PPS boundaries extended, after the Cooperative interaction, to include the space occupied by the Other.

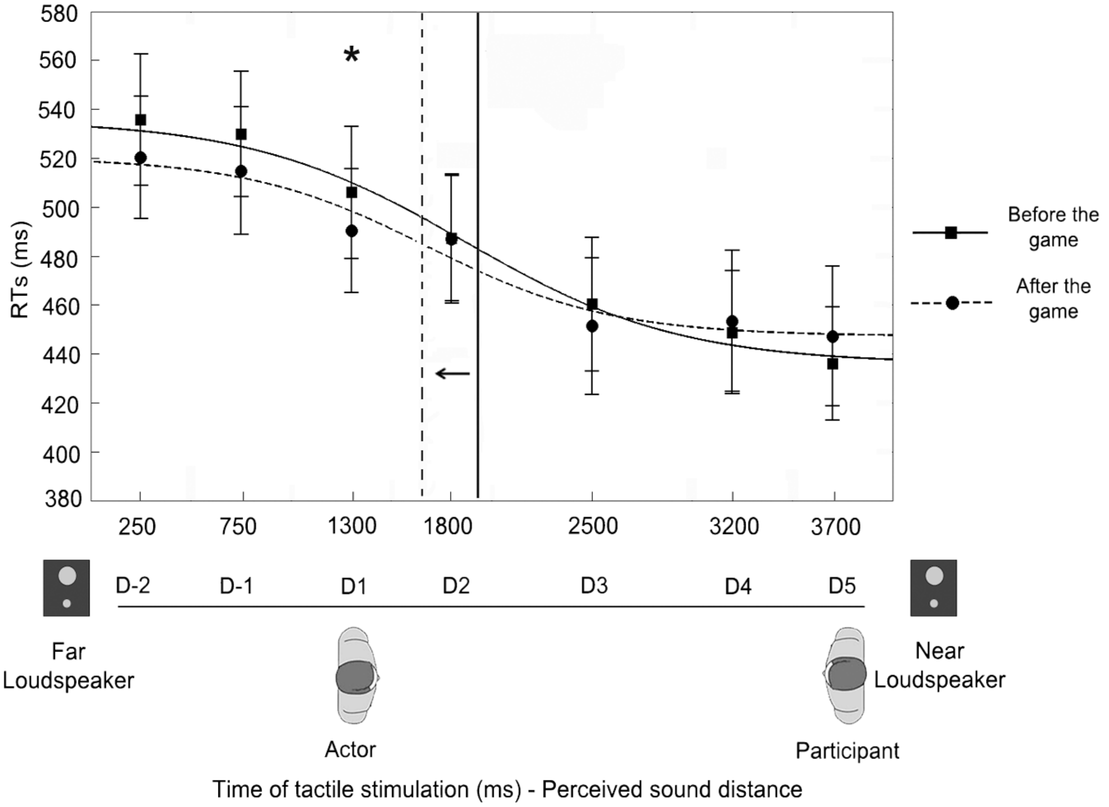


Figure 8.7 Mean RTs at the seven different perceived sound distances, before and after the game, are reported (error bars represent S.E.M.). RTs at the different temporal delays are fit with a sigmoid function. The sigmoid central point curve was computed as a measure of the temporal delay, i.e., the distance at which sounds start affecting RTs, and was analyzed in order to quantify PPS boundaries. The sigmoid central point was lower (1.731 ms) after the game than before the game (1.911 ms); (t[19]=2.10; p<0.05, one-tailed), indicating that PPS boundaries extended toward the space occupied by the cooperative other.

	Experiment 2			Experiment 3
During the game…	Cooperative condition	Non cooperative condition	Conditions comparisons	Cooperative condition
How fair did you perceive the other player's action?	6.70 (.17)	2.46 (.47)	t(30)=9.83; p<.0001	6.69 (.21)
How likable did you perceive the other player?	6.16 (.22)	1.38 (.14)	t(30)=22.62; p<.00001	6.21(.20)
How similar to you did you perceive the other player?	6.00 (.35)	1.92 (.38)	t(30)=9.42; p<.0001	5.42 (.32)
How angry were you toward the other player?	1.08 (.07)	4.38 (.48)	t(30)=7.89; p<.00001	1.05 (.05)

Table 8.4 Mean ratings ± S.E.M. at the questionnaire after the bargaining game from participants taking part to Experiment 8.2, Cooperative and Non-cooperative conditions, and Experiment 8.3 (Cooperative condition). These ratings show that the experimental manipulation (e.g., partners' playing

strategy during the economic game) affected participants' perceptions of fairness. Specifically, participants rated cooperative partners as being significantly fairer, more likeable, and more similar to them than non-cooperative partners. Moreover, they felt significantly less angry at cooperative than at non-cooperative partners. Between-groups comparisons for the Cooperative and Non-cooperative conditions of Experiment 8.2 are also reported.

8.5 General Discussion

Results from the present study shows that PPS representation not only is sensitive to the presence of others but also is shaped by interactions with others and, more specifically, by valuation of other people's behaviour during the interaction.

Previous studies highlighted the behavioral function of PPS representation, which has been conceived as a space of interaction critical for triggering defensive (Graziano & Cooke, 2006; Serino et al., 2009) or approaching (Rizzolatti et al., 1981; Brozzoli et al., 2009) behaviors. Most studies on PPS tested subjects processing artificial stimuli in neutral environments in absence of co-specifics. This is surprising, because the others often represent the most behaviorally relevant stimuli in the environment. Few previous findings suggest a "social" modulation of PPS representation. In monkey, bimodal neurons in the posterior parietal cortex respond to tactile stimuli on the animal's body and to visual stimuli presented close to the experimenter's body (Ishida, Nakajima, Inase, & Murata, 2010). Homologous areas in humans respond to tactile stimuli on one's own face and to visual stimuli approaching another person's face (Cardini, Costantini, Galati, Romani, Làdavas, & Serino, 2011). Thus, some PPS neurons process events occurring not only within one's own PPS but also within the PPS of others. Heed and colleagues (Heed, Habets, Sebanz, & Knoblich, 2010) recently showed that multisensory integration is modulated as a function of the presence and activities of others within one's own PPS. The present data extend previous findings by showing that the presence of others also in the extrapersonal space shapes PPS representation, such that the presence of others structures the representation of space around oneself. As Deleuze said: ‘‘the other is neither an object in my field of perception, nor a subject who perceives me: it is first and foremost a structure of the perceptual field, without which this field as an ensemble would not function as it does’’ (see Deleuze, 1969, pp. 356–357).

The role of others in modulating spatial representation is particularly evident if PPS is conceived as a space of interaction. Results from experiment 8.2 and 8.3 showed that not only the presence of others but also the nature of interaction with others shapes PPS representation.

Previous evidence shows a link between PPS representation and individuals' emotional states (e.g., claustrophobic fear; Lourenco, Longo, & Pathman, 2011). Results from the present study are new in showing a direct link between PPS representation and feelings generated by interaction with others. After an unfair, uncooperative interaction, subjects were generically faster to respond to tactile stimuli, independently from the position of concurrent sounds in space. Such a general speeding effect seems not directly related to spatial processing and is likely to depend on increased arousal following a socially unacceptable behaviour of the other (Anderson, 2005). Prior evidence indicates that perceived unfairness of treatment arouses negative emotions (Dawes, Fowler, Johnson, McElreath, & Smirnov, 2007; Singer, Seymour, O'Doherty, Stephan, Dolan, & Frith, 2006), increases skin conductance responses (van 't Wout, Kahn, Sanfey, & Aleman, 2006), and activates the insula (Sanfey, Rilling, Aronson, Nystrom, & Cohen, 2003) and the amygdala (Baumgartner, Heinrichs, Vonlanthen, Fischbacher, & Fehr, 2008), brain areas consistently implicated in mediating negative emotional reactions and modulating arousal. Instead, after a fair, cooperative interaction, PPS boundaries between the self and the other merged. Such effect can be interpreted in the light of the nature of the interaction experience. According to Bakan, cooperative interactions are characterized by the concept of communion: ‘‘communion arises from strivings to integrate the self in a larger social unit through caring for others’’ (Bakan, 1966). The change in PPS representation found following the cooperative interaction seems to reflect Bakan’s definition, grounded at the level of sensory-motor processes underlying spatial representations. As a consequence of cooperative, communal interaction, the boundaries of space within which external stimuli are more efficiently processed in order to implement defensive behavior (Graziano & Cooke, 2006) shifted beyond the space occupied by the cooperative other.

The present findings highlight a strong relationship between basic sensorimotor functions and complex social representations. They are consistent with approaches to cognition suggesting that mental processes are situated and embodied in our physical experiences (Barsalou, 2008; Gibbs, 2006; Niedenthal, Barsalou, Winkielman, Krauth-Gruber, & Ric, 2005; Wilson, 2002; Gallagher, 2005). In this view, high-level social and cognitive representations (e.g., cooperation) are immersed or recoded into the physical and perceptual experiences of the body, thereby providing concrete and rich feelings that facilitate prediction, evaluation, and social behaviour.

CHAPTER NINE: GENERAL DISCUSSION

A successful interaction with objects in the environment typically requires integrating information concerning the object-location with the shape, dimension and position of body parts in space. The former information is coded in a multisensory representation of the space around the body, a representation of peripersonal space (PPS), whereas the latter is enabled by an online, constantly updated, action-orientated multisensory representation of the body (BR) that is critical for action.

A general aim of this thesis was to investigate function and properties of multisensory representation of body and space in humans, by focusing on plastic properties of these two representations. We asked whether and how different kinds of experience which may change the function, structure and context of the physical body, affect body and PPS representation. We began investigating the neural correlates of a multisensory PPS representation in humans in Chapter 3. In Chapter 4, we presented a new audio-tactile paradigm (Canzoneri et al., 2012), developed to measure the extent of PPS representation. In the second part of this dissertation, we applied that and other tasks to measure changes in PPS and BR as a function of different types of the experiences, such as tool-use (Chapter 5), multisensory stimulation (Chapter 6) amputation and prosthesis implantation (Chapter 7) and social interactions (Chapter 8).

9.1 Studying multisensory PPS in humans through audio-tactile interaction.

In monkeys, PPS representation is enabled by multisensory system responding to tactile, visual and auditory information on and close to the body. In the case of audio-tactile stimulation, Graziano and colleagues (Graziano et al., 1999; Graziano & Gandhi, 2000) and Schlack and colleagues (2005) showed that some multimodal neurons in the ventral premotor cortex and in the ventral parietal sulcus respond to tactile stimuli given on the controlateral side of the moneys' head and to an auditory stimulus presented close (within 30 cm) but not far from the head. Audio-tactile responses were stronger for sounds coming from behind the monkey's head. An interaction between auditory and tactile stimuli around the head has been demonstrated in neuropsychological patients suffering from cross-modal extinction (Farnè & Làdavas, 2000), as well as in healthy subjects, both for back (Kitigawa et al., 2005) and front space (Zampini et al., 2005; see Occelli et al., 2011, for a review). In the first part of this dissertation we investigated properties and neural correlates of audio-tactile representation of PPS around the hand in healthy human by means of two behavioral paradigms that use respectively static (Chapter 3) and dynamic (Chapter 4) auditory stimuli. In Chapter 3 (Experiment 3.1A and 3.1B) participants were asked to respond to a tactile stimulus at the hand while an ecologic static sound (a burst of white noise) was presented either close to the hand or far from it. Results confirmed that sounds boosted the processing of tactile stimuli presented to the hand as compared to when tactile stimuli only were presented. Critically, the audio–tactile interaction effect was stronger when sounds were presented in the space around the hand rather than in the far space. These results are in line with previous studies of our group (Serino et al., 2007; Bassolino et al., 2010) revealing audio-tactile interaction processes around the hand. In Experiment 3.1B we also investigated whether this audio-tactile integrative effect is related to a hand-centered representation of the PPS and not to a general proximity of the sound to the body. To this aim, we manipulated the relative distance between the hand and the sound sources, while keeping constant the distance from the body, by asking participants to retract and place their hand far from the source of the near sound. Results showed that in this posture, the speeding effect associated to near sounds disappeared, thus confirming that the audio–tactile interaction effect was dependent on hand location. Hence, the sound's proximity to the hand (and the tactile stimulus), not to the subject in general, was critical for modulating tactile processing. These results are in line with several studies both in monkeys and in humans revealing how multisensory information are integrated in the PPS in a body part centred frame of reference.

In Chapter 4 we presented a new paradigm, which applies dynamic instead of static auditory stimulation, with the aim of assessing the extension of PPS in a more functionally and ecologically valid condition. We measured reaction time (RTs) to a tactile stimulus at the hand while dynamic sounds were presented, giving the impression of a sound source either approaching, or receding from the subject's hand. Tactile stimulation was delivered at different temporal delays from the onset of the sound, such that it occurred when the sound source was perceived at varying distances from the body. Results showed that RTs to tactile stimuli at the hand progressively decreased as a function of the sound source's perceived approach, and conversely they increased as a function of the sound source's perceived recession.

Similar results were obtained in Chapter 8, when audio-tactile interaction was studied in the space around the head. Tactile stimuli at the face were modulated by the perceived position of a looming sound in space, in line with the results we obtained with the same paradigm around the hand. However, differently from hand stimulation, tactile processing at the face was not modulated by the position in space of receding sounds. I will extensively discuss this important difference in Paragraph 4.

Results from Experiment 8.2B and 8.2C further demonstrated that this audio-tactile paradigm specifically assessed a body-centred representation of the PPS. Indeed, results from Experiment 8.2B showed that by manipulating the position of the body in space with respect to the perceived sound position, tactile RTs were no longer modulated by the position of sound in space. This result confirmed that the modulation of tactile processing due to the position of sounds depends on the location of the subject's in space. The effect vanishes if subjects are placed closer to the origin of far sounds in presence of a mannequin. Moreover, results from Experiment 8.2C further confirmed that the modulation of audio tactile interaction we found by using this paradigm was related to PPS representation, and was not a general crossmodal effect: when participants responded to target visual stimuli, unrelated to participant's body, in presence of a Mannequin, RTs to a visual "disembodied" stimulus were not affected by the perceived position of sound in space in the same way as tactile RTs. Critically, RTs were faster only at D3, when sounds were perceived at approximately the same location of the visual target. These findings reflect a well-known principle of multisensory integration, that is auditory and visual stimuli are more effectively integrated when stimuli from both modalities are spatio-temporally coincident.

Taken together, results both from Experiment 3.1, and Experiment 8.1 demonstrated the existence of an auditory PPS representation in humans that has been tested both around the hand and the face in two different experiments. The present results also show that 1) audio–tactile interaction is sensitive to the position of body parts (the hand) in space; 2) is sensitive to the location of the whole body in space; 3) is specific for "embodied" multisensory effects implying tactile stimulation.

The present audio-tactile interaction effects are in keeping with previous studies showing that auditory stimuli affect the perception of tactile stimuli, both in terms of detection ability (e.g., Ro et al., 2009) and RTs (e.g., Zampini et al., 2007). Notably, evidence indicates that these audio–tactile interactions require a multisensory integrative mechanism rather than a simple summation of unisensory signals (Murray et al., 2005). Moreover, Serino and colleagues (Serino et al., 2009) previously showed that task-irrelevant sounds presented near the hand transiently increased the excitability of hand representation in the motor cortex and that this effect was specific to a hand-centered, not a body-centered, reference frame. We propose that the facilitation effect due to near sounds on tactile processing arises from the summation of multisensory inputs within the same spatial representation, that is, within representation of PPS around the hand. Thus, if one interferes with activity of putative areas integrating multisensory stimuli in PPS, such facilitation effect should be abolished. This prediction has been tested in Experiment 3.2 and I will discuss it in the following Paragraph 9.2. I will conclude my presentation of the functional properties of PPS representations by extensively discussing the difference in PPS representation assessed by using static (Chapter 3) or dynamic (Chapter 4 and 8) auditory stimuli.

9.2 Neural correlates of PPS representation: a (multi) sensory-motor system to represent the space around the body.

In Experiment 3.2 we demonstrated also that virtual lesions to the ventral premotor cortex (vPMc) and the posterior parietal cortex (PPc), but not to the primary visual cortex (V1) – serving as a control site - disrupted audio-tactile interaction mechanisms around the hand. These results provide the first empirical evidence for a necessary role for vPMc and PPc in representing multisensory PPS around the hand. In a recent study Avenanti and colleagues (Avenanti, Annella, & Serino, 2012) specifically investigated the selective role of vPMc and of PPc in fronto-parietal networks representing PPS representation. In this study the authors combined the use of the transcranial direct current stimulation (tDCS) - in order to perturb the activity of those two target areas - with the TMS technique, used to measure the excitability of the motor system. Specifically, a single-pulse TMS was applied over the hand representation in the primary motor cortex in order to induce motor-evoked potentials (MEPs) from hand muscles, so to measure the excitability of the hand motor representation. MEPs were compared when a sound was presented either close to the hand or far apart, at a 1mt distance (see also Serino et al., 2009). In a control (sham tDCS condition), results showed an inhibitory effect of MEPs when an auditory stimulus is presented close to the hand rather than at a distance, suggesting that, when the peri-hand space representation is activated, a freezing-like response of the motor system was evoked. Importantly, the differential effect of near and far sounds on MEPs was abolished after inhibitory tDCS over PMc, showing that this area plays a critical role in the motor coding of sensory events occurring within the PPS. Interestingly, when tDCS was applied over the PPc, the results were similar to what happened in the shame tDCS condition. Results from this study expanded results presented in this dissertation in Chapter 3. Indeed, results from Experiment 3.2 suggested that these two regions were similarly involved in a multisensory representation of PPS. Critically, these two nodes of the fronto-parietal network representing PPS seem instead to have partially dissociable functions, with PMc being more involved in mapping sensory representations of space onto the motor system (Avenanti et al., 2012). These results supported the idea that the brain has evolved an efficient sensorimotor mechanism, mapping sensory stimuli in the space immediately surrounding the body onto potential motor responses (Graziano & Cooke, 2006; Rizzolatti et al., 1997; Serino et al., 2009; Makin et al., 2009). These results are in line with the well-known sensory-to-motor function of PPS representation (see also Paragraph 1.1.2). These findings are also consistent with the notion of the existence of a series of parieto-frontal circuits in the monkeys brain involving a series of sensory to motor transformations. In monkeys, the areas around the intraparietal sulcus (IPS; Grefkes & Fink, 2007) can be divided in several distinct cortical areas named after their topographical position (see Figure 9.1): the anterior intraparietal area (area AIP), the ventral intraparietal area (area VIP), the medial intraparietal area (area MIP), the lateral intraparietal area (LIP) and the caudal intraparietal area (area CIP). Like the posterior parietal cortex, in the macaque's brain also the motor cortex is formed by anatomically and functionally distinct areas (areas F1, F2, F3, F4, and F5) that appear to play different roles in motor control (see Figure 9.1): these areas receive their predominant cortical inputs from the previously cited areas around IPS in the parietal lobe (see Matelli & Luppino, 2001, for a review). The specificity of these parieto frontal circuits depends on the preferred type of stimulus and behavior of the neurons.

- **MIP-F2:** F2 neurons are thought to respond to somatosensory and proprioceptive stimuli, while bimodal neurons identified in the MIP area are strongly activated when the monkey reaches for a visual target. So, this circuit has an important role in planning, execution and monitoring of **reaching** movements.

- **LIP–FEF.** These neurons mainly respond to visual stimuli in an eye centred frame of reference. This circuit is thought to code for **eye movements**.
- **AIP-F5.** This circuit is involved in the creation of a representation of the object that is useful in order to select the most appropriate way to grasp it. Indeed, neurons in F5 neurons typically code goal-directed motor acts, while AIP neurons frequently discharge during the manipulation of objects both in dark and light condition.
- **VIP-F4.** Neurons in this areas share a lot of properties that have been extensively reviewed in Chapter 1 of the present dissertation. Indeed, in these areas we can find bimodal neurons with large somatosensory RFs located on the face, trunk, arms and hands and corresponding visual RFs generally limited in depth around the tactile RFs. This circuit is thought to encode for PPS in a body part-centered frame of reference and to transform the position of object in space into appropriate movements toward them.

Interestingly, the equivalent of this last circuit in humans seem to be represented by the vPMc and of PPc circuit described in Experiment 3.2 (see Chapter 3; Bremmer et al., 2001; see also Grefkes & Fink, 2005, for a review), demonstrating the existence in the human brain of a parieto-frontal circuit deputed to the special coding for stimuli presented close to the body in order to plan a proper and rapid motor reaction towards a potentially interesting stimulus or a potential aversive one.

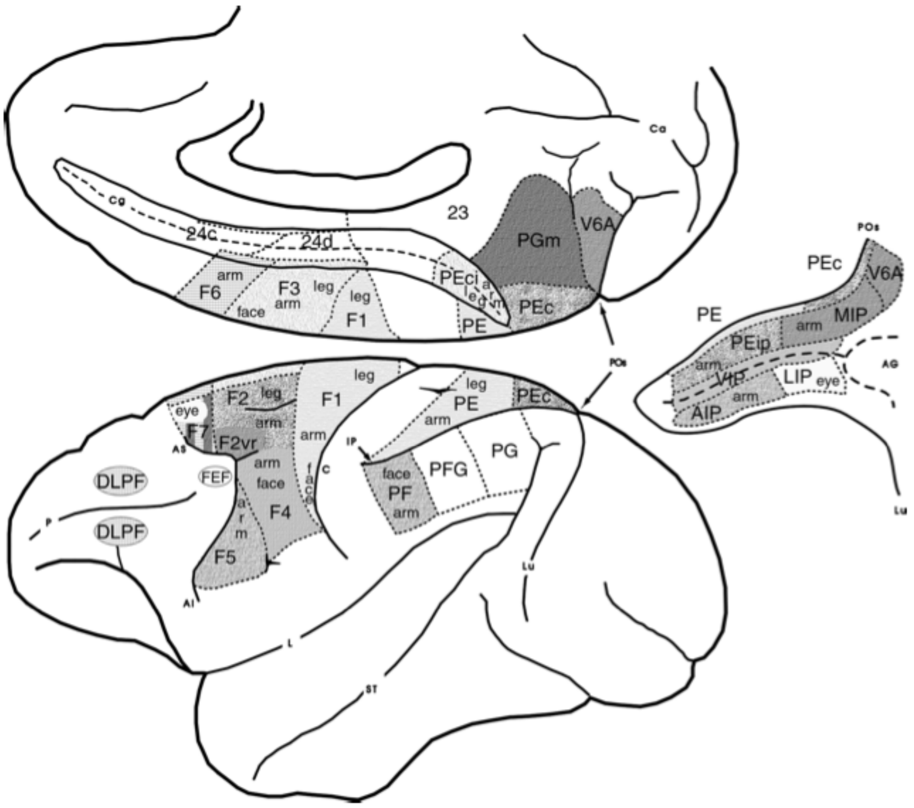


Figure 9.1 Mesial and lateral views of the macaque brain showing the parcellations of the frontal motor cortex and of the posterior parietal cortex. **Adapted from Matelli & Luppino, 2001.**

9.3 A dynamic representation of the space around the body

In Chapter 4 we investigated the properties of PPS representation by developing a new audio-tactile paradigm. Given the high relevance of moving objects to the PPS system, we propose that using dynamic, instead of static auditory stimuli could be a more powerful way to assess the extension of PPS representation in humans in a more functionally and ecologically valid condition. We had already shown that an auditory stimulus speeds up the processing of a tactile stimulus at the hand, if the sound is administered within a limited distance from the hand (see Serino et al. 2007 and Experiment 3.1). Critically, by using dynamic sounds we were able to study such critical distance along a continuous spatial range, spanning near and far space, thus estimating the boundaries of PPS representation.

Interestingly, our results also suggest that, among dynamic stimuli, approaching sounds have a stronger spatially dependent effect on tactile processing as compared with receding sounds. Indeed, when PPS representation was assessed around the hand, the function describing the relationship between tactile RTs and timing at which tactile stimuli were delivered was significantly steeper for approaching than for the receding sounds. Such difference was even stronger in the case of peri-face PPS: results from Chapter 8 showed that while looming sounds modulated tactile processing with a clear spatial pattern, receding sounds had no effect. Taken together, results on the peri-hand PPS and peri-face PPS suggest that while both approaching and receding sounds activate PPS around the hand, only the former and not the latter type of sounds activates PPS around the face. This difference can be explained considering the different motor functions of the two body parts: we normally use our hands to grab receding objects, while we hard use our face for that.

The stronger effect on PPS representation found for looming sounds is in keeping with several studies showing that primates sensory systems are particularly sensitive to approaching stimuli. Indeed, an attentional bias toward approaching stimuli was shown in monkeys, both in visual and auditory domains, as compared with receding stimuli (Maier, Neuhoff, Logothetis, & Ghazanfar, 2004; Maier & Ghazanfar, 2007; Ghazanfar, Neuhoff, & Logothetis, 2002; Schiff, 1965; Bach, Schachinger, Neuhoff, Esposito, Di Salle, et al., 2008). In addition, bimodal and/or trimodal neurons in multisensory brain areas in the ventral premotor cortex and in the posterior parietal cortex in monkeys were shown to respond preferentially to approaching visual (Duhamel et al., 1997; Colby et al., 1993; Bremmer et al., 2002) and auditory

(Graziano et al., 1999; Maier et al., 2004) stimuli as compared to receding stimuli. At a behavioural level, human subjects show a perceptual bias to detect an approaching, rather than a receding, stimulus (Cappe, Thut, Romei, & Murray, 2009; Leo, Romei, Freeman, Ladavas, & Driver, 2011; Cappe, Thelen, Romei, Thut, & Murray, 2012). Human listeners also underestimate time of contact with the body of an approaching sound as compared to a receding sound (Seifrtiz et al., 2002; Neuhoff, 1998). Moreover, audio-visual integration is stronger for approaching than for static or receding stimuli (Cappe et al., 2009; 2012; Romei, Murray, Cappe, & Thut, 2009). Thus, approaching stimuli have been shown to be particularly relevant at different levels of information processing (Hall & Moore, 2003). Our results provide a further level of evidence for this argument by showing a stronger effect of approaching sounds in modulating tactile processing.

In future studies it might be interesting to study the effect of other possible sound trajectories on PPS representation. For instance it is well know that sound localisation is more precise for side-to-side trajectories than for frontal trajectory, because in the former case, cues based on interaural differences are stronger (Middlebrooks & Green, 1991). So, it is possible that, using this paradigm, the function describing the relationship between tactile RTs and sound positions is more sensitive along side-to-side trajectories that along the frontal direction. It is also possible that the critical position in space where sounds begin affecting tactile RTs is localized at a different distance from the body for side-to-side as compared to frontal directions. Indeed, PPS could differently extend in the front space where both hands can immediately and coordinately act, as compared to the space aside the body, where bimanual actions do not occur. It is worth noting, however, that in the everyday life we are more likely to interact with stimuli presented in the frontal space. For this reason, in this study we decided to test audio-tactile interactions on a frontal plane.

To sum up, the present task provides an effective, sensitive and ecologically valid approach to measure the extent of PPS representation. The function describing the relationship between tactile processing and the position of sounds in space along a spatial continuum can be used to localize the boundaries of PPS representation. We show that such a relationship is better described by a sigmoidal (rather than linear) function, meaning that RTs sharply decreased as a sound crosses a spatial limit, over which the addition of an auditory stimulus speeds up the detection of a tactile stimulus administered on the body. Such spatial limit can be considered as the boundary of PPS representation. This paradigm has been used in this dissertation to study plasticity of PPS representation in different contexts and following different types of short term and long term experiences. In the second part of this dissertation, plastic properties of PPS and BR after different experiences have been investigated.

9.4 Plasticity in PPS and BR: tool-use

In Chapter 5 we investigated whether using a functional tool to act upon objects at a distance concurrently affects both space and body representation in the same sample of subjects, using different tasks that specifically tap into PPS representation and BR. Results from Experiment 5.1 show that after tool-use, the boundaries of PPS representation shifted to include farther locations of space. This effect was associated with a change in the representation of the arm shape: after tool-use, subjects perceived the distance between two stimuli delivered on their forearm longitudinally to the arm axis as significantly shorter and perceived the distance between two stimuli delivered transversally on the forearm as significantly longer. Moreover, when asked to localize the position of their wrist and elbow, they localized those body landmarks farther apart between each other after tool-use. Taken together, these findings are compatible with an extension of perceived arm length after tool-use, assessed by means of two independent tasks. The results confirmed evidence in the literature showing that PPS is dynamically shaped as a function of the experience (Maravita et al., 2002, Serino et al., 2007; Gallese & Sinigaglia, 2010) but critically, they are also new in showing a parallel effect on plastic properties of BR and PPS.

9.5 Mechanism of plasticity in PPS representation

The modification of BR and PPS after tool-use seems to be strictly dependent on the sensory consequences of action: thanks to tool-use, participants acted on a portion of space exceeding the normal limits of our physical body. As a consequence, their brain started processing multisensory inputs related to one's own body, but arising from a distal portion of space. For instance, tactile and proprioceptive cues processed at the upper limb via the tool handle refers to objects contacting the tip of the tool. Such contacts also generate sensory feedback in other modalities, e.g. auditory feedback, as in the present experiments, when subjects were blindfolded, but also visual feedback in everyday life tool-use activities. We believe that this action-dependent extension of the space, where body-related sensory information arises from, is the trigger for the changes in body representation and PPS representation documented by the experiments presented in Chapter 5. This proposal has been recently introduced by our group in the context of a neural network model designed to account for plasticity in PPS representation (Magosso et al., 2010c), and it was specifically tested, for what concerns the PPS, in Chapter 6 of the present dissertation. Results from Experiment

6.1 demonstrated that a training consisting in a synchronous presentation of tactile stimuli at the hand and auditory stimuli in the far space was able to modify the boundaries of the audio-tactile representation of the peri-hand space. Interestingly, the current results, as predicted by the neural network model, demonstrated that a change in peri-hand space mimicking that obtained after tool-use (see Chapter 5 of this dissertation) can be evoked also when a tool is not actually used or even present in the subject's hand. A key factor in promoting an extension on PPS representation, instead, seem to be feeding the neural network with the same sensory stimulation produced by tool-use activity, i.e. the auditory stimulation due to the sound produced by the tool when hitting an object placed in the far space and the concurrent tactile stimulation at the hand due to handling the tool. According to the neural network model proposed by Magosso and colleagues (2010c), tactile unimodal stimuli at the hand and auditory unimodal stimuli in the far space send feed forward synapses to bimodal neurons. The synapses linking unimodal to bimodal neurons are reinforced following a Hebbian rule during such training. The reinforcement of these synapses, that were just latent before the experiment, results in an extension of audio-tactile peri hand space, with a far auditory stimulus re-codified as being closer to the body. Results from the present study are new in suggesting that the motor aspect of tool-use is not so critical in promoting plastic reorganization of spatial representations: neither a functional, nor a physical interaction between near and far space are necessarily required to determine an extension of PPS.

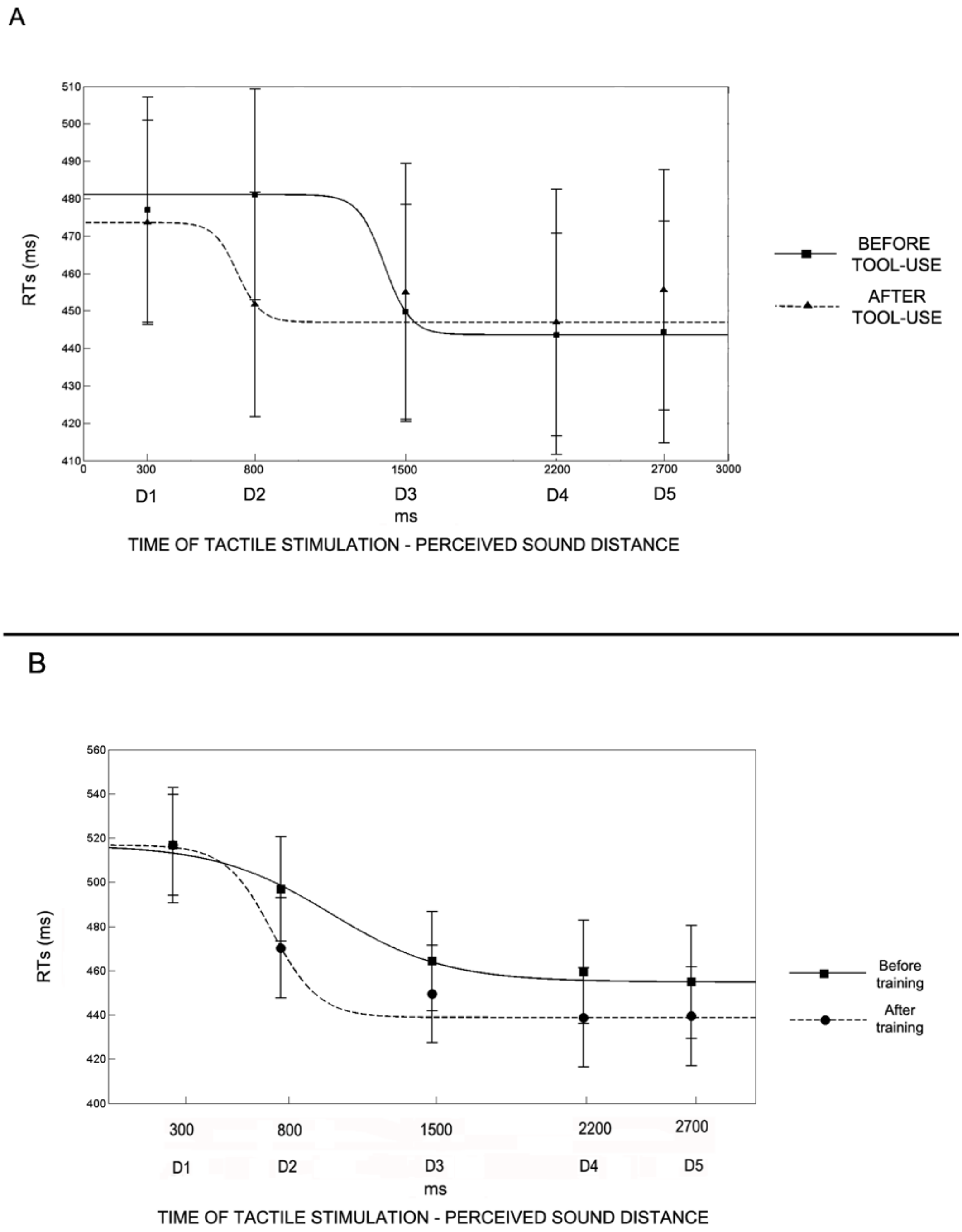


Figure 9.2 Audio-tactile interaction task. Results from Experiment 5.1 (panel A) and Experiment 6.1, synchronous condition. Graphs reveal extension effect on PPS representation both After tool-use (Experiment 5.1) and After a synchronous training (Experiment 6.1)

According to the interpretation of results from the present study, supported by the neural network model, tool-use extends PPS representation because it is an experimental condition that provides the brain with a tactile stimulation at the hand

and a synchronous multisensory stimulation in the far space. It has been proposed that a similar multisensory mechanism plays an important role in eliciting the Rubber Hand Illusion (RHI): during the RHI just seeing the rubber hand being stimulated and experiencing a synchronous tactile stimulation may lead to a shift of the receptive field towards the fake body part (see also Blanke et al., 2012 for a review), leading to a change in body perception, that is the rubber hand is perceived as the real hand.

9.6 Plasticity in PPS and BR: amputation

Most evidence of plasticity in PPS and BR following tool use (Serino et al., 2007, Cardinali et al., 2011; Sposito et al., 2012) or multisensory illusions (de Vignemont, 2005; Taylor Clarke et al., 2004; Tajadura Jimenez et al., 2012) demonstrates extension effects. Effects of contraction are, instead, rarely reported (see e.g. Longo et al., 2009). This asymmetry in extension vs. contraction effects makes sense in the view that the body normally grows, but not, or minimally (with aging), shrinks. Extension effects in PPS and BR after tool-use are strictly dependent by projecting the possibility of action *beyond* the limit of the physical body. In Chapter 7, in order to study whether PPS and BR are also plastic in the direction of contraction, we tested how BR and PPS dynamically change when the possibility of acting in space is dramatically reduced, such as after upper limb amputation. We also asked whether such effects are reversible, by means of prosthesis implantation, which partially restore the possibility of acting in space. Results showed that amputation reduces the perceived length of the remaining part of the affected limb and, accordingly, affected PPS representation around the stump. Wearing the prosthesis restored both BR and

PPS around the healthy limb, making these representations more similar as compared to the one of the healthy limb. These results are interesting for three reasons. First, they show that shrinkage of a part of the physical body following amputation resulted in contraction of multisensory BR and PPS; when they did not wear their prosthesis, amputee patients perceived their stump as shorter and PPS representation around the stump shrunk. Second, until now an extensive body of evidence has demonstrated a strong relationship between a modification of the physical body and unimodal body representations (see Chapter 2). Surprisingly, little is known about the extent to which multisensory body and space representations are dependent on the structure of the physical body and are affected by limb loss. Results from the present study demonstrated that a change in the physical body structure similarly affected high-level multisensory body and space representation. Critically, prosthesis implantation, by restoring the possibility of acting in space, partially compensated the effects of amputation on BR and PPS. Finally, results from the present study showed parallel effects on BR and PPS also after amputation and prostheses implantation, as previously demonstrated in Chapter 5 after tool-use. The correspondence between the plastic properties of these two representations under different kinds of experiences suggests that BR and PPS representations strongly overlap. This is not surprising, considering the several level of overlapping of these two representations, both at level of neural representation (see Chapter 3 of the present dissertation; Bolognini & Maravita, 2007; Azanon et al., 2010) and action execution. I will discuss extensively this point in the next section.

9.7 PPS and BR: a representation of the body in space

It is matter of debate how much PPS and BR are dissociable or rather represent a unique representation of the body in space for action. Our data from the study presented in Chapter 5 show an overlap of plastic properties of PPS and BR. Such overlap can be interpreted in three ways. First, it might be the case that the modification of PPS representation directly depends on the plastic change of BR. In other words, a "longer" arm would imply a more extended PPS around it, while a "shorter" arm would imply a reduced PPS representation. Conversely, an opposite relationship between the two effects, for instance that the arm is perceived as longer, because the PPS around it has extended (see Experiment 5.1), appears less likely. Second, the two plastic phenomena might be simply associated, sharing the properties of being body-related, without any causal relationship between them. A third interpretation is possible, i.e., that the representation of the size and position of body parts devoted to action, i.e. BR, and that of the space immediately surrounding the same body parts actually consist in a unique representation of the body in space (for comments see Cardinali et al. 2009b; Gallese & Sinigaglia, 2010). Results from the studies presented in Chapter 5 and 7, by providing evidence for similar plastic effects on PPS and BR, support this third view, in favour of a unified body and space representation. However, this evidence is not sufficient to definitively conclude that PPS and BR consist, as showing an association does not necessarily imply any causal relationship. Interestingly, our group (Bassolino, Finisguerra, Canzoneri, Serino, & Pozzo, in preparation) investigated in healthy subjects the effect of both motion deprivation of one arm (through an immobilization procedure) and the compensatory overuse of the other arm on BR (by using the same tactile distance perception task and body landmark localisation task as Chapter 5 of this dissertation) and PPS (by using the audio-tactile interaction task). Results showed dissociated effects on BR and PPS: indeed, after immobilization, the representation of PPS around the immobilized arm was reduced, while the representation of the perceived dimension of the arm was not affected. Such asymmetrical effects between PPS and the perceived length on the arms are new in suggesting a different role of action on space and body representations. Future studies are needed to theoretically and experimentally investigate possible consistency or dissociation between body and space representation.

9.8 Extension or incorporation effects?

Another interesting question is whether the effect of using a tool to extend the normal limits of the physical body and that of wearing a prosthesis to partially restore the integrity of the body result in analogous plastic phenomena or consist in different processes. Since prosthetic limbs share more features with an anatomical limb as compared to tools, prosthesis-use and tool-use could have differential effects on the plasticity of body representations. In particular in the literature a distinction has been proposed between the effects of body extension (in the case of tool-use) and those of body incorporation (in the case of prosthesis-use; De Preester & Tsakiris, 2009; see also Giummarra et al., 2008). It is still not clear, however, whether and to what extent a prosthetic limb can be embodied such that it becomes in some sense indistinguishable from a real body part. We did not directly test the subjective experience of prosthesis embodiment in our study on amputee (see Mayer, Kudar, Bretzet, & Tihanyi, 2008). However, some interesting comparisons between the effects of tools (Chapter 5) and prostheses use (Chapter 7) are possible, thanks to the fact that we used the same tasks to investigate plastic changes in BR and PPS in the two conditions. In particular, as far as PPS is concerned, we found a different modulation of tactile stimuli due to the sound processing in the case of tool-use as compared in the case of prosthesis use. In the study presented in Chapter 5, after tool-use there was a recoding of a portion of far space (where participants acted with the tool) as near. More precisely, in case of tool-use we observed a speeding up of tactile RTs only in a portion of space that was perceived as far before tool-use (i.e. at D2), corresponding to the portion of space where the tool was used. In case of prosthesis implantation in amputees, instead, results from the audio-tactile interaction task showed a speeding up effect at every perceived distance of the sound from the body (see Figure 9.3.). The first result (in case of tool-use) is more compatible with an extension effect, while the second result results is coherent with a shift of PPS representation from the stump (in the without prosthesis condition) to the prosthetic limb (in the with prosthesis condition), up to incorporate the prosthesis in its representation. This interpretation has been confirmed by a control Experiment on healthy subjects (see Experiment 7.2B), in which we tactilely stimulated either the hand or the upper arm, while dynamic sounds moved between the far space and the arm. When tactile stimulation was presented at the upper arm, the results resembled those found in the amputees in the without prosthesis condition (see Figure 9.3). Instead, when tactile stimulation was administered at the hand, we observed a speeding up effect of tactile RTs at every temporal delay, similarly to what we found in amputees when they wore their prosthesis. Taken together these results suggest that in amputee a tactile stimuli at the stump was automatically referred to the prosthetic arm, such as it becomes the new boundary of their body. It is tempting to conclude that prosthesis implantation in this study is compatible with a body incorporation process, which is different from a body extension processes triggered by tool use.

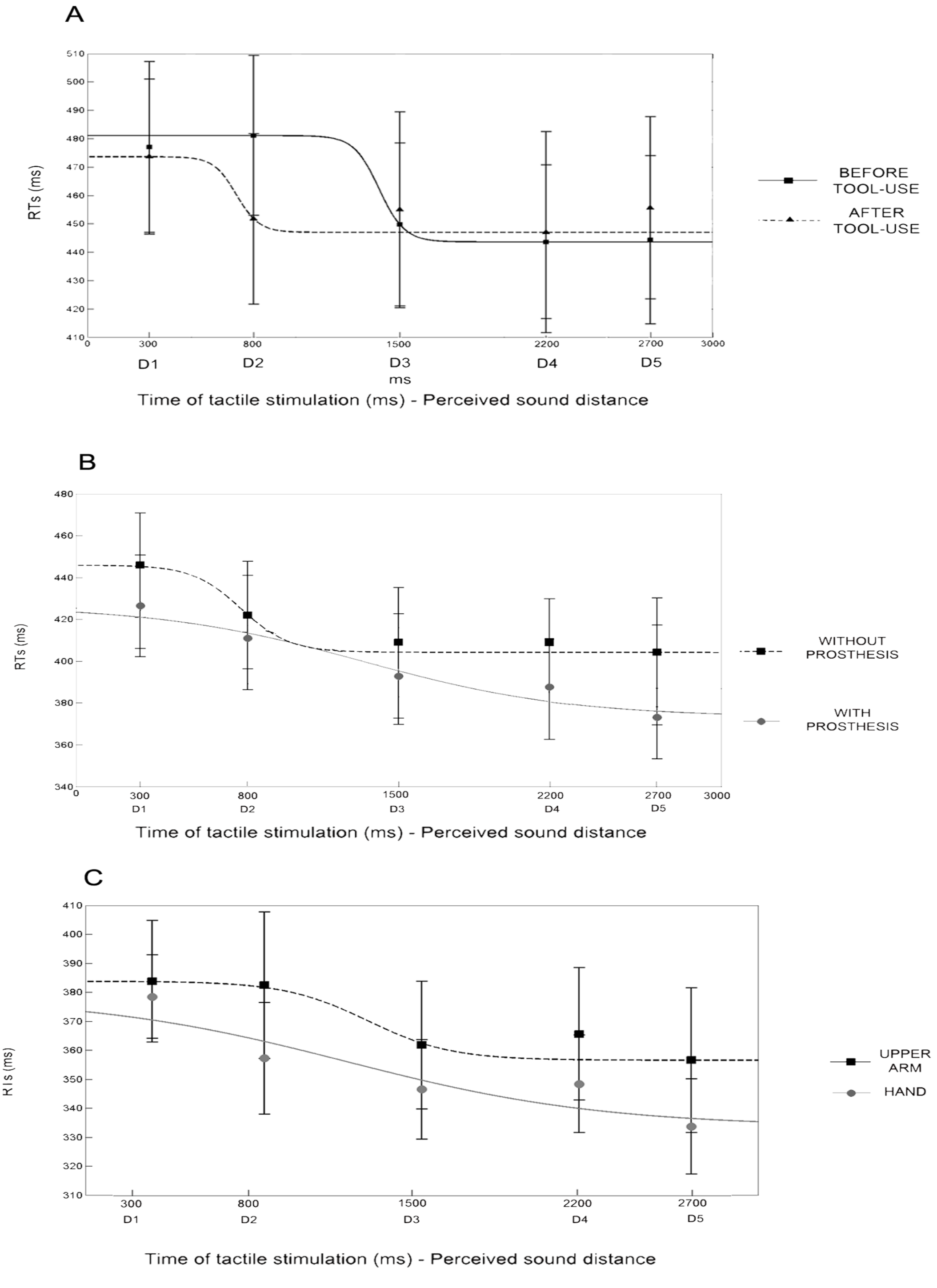


Figure 9.3
A. Chapter 5, Experiment 5.1 results. Mean RTs at different perceived sound distances (from D1 - farthest - to D5 - closest), corresponding to different time of tactile stimulus delivery and best fitting sigmoidal functions describing the relationship between RTs and sound distance, before tool-use (black line) and after tool-use (dotted line). Error bars denote S.E.M.
B. Chapter 7, Experiment 7.2A results. Mean RTs at different perceived sound distances (from D1 - farthest - to D5 - closest), corresponding to different time of tactile stimulus delivery and best fitting sigmoidal functions describing the relationship between RTs and sound distance, without prosthesis (dotted line) and with prosthesis (grey line) conditions. Error bars denote S.E.M.

C. Chapter 7, Experiment 7.2B results. Mean RTs at different perceived sound distances (from D1 - farthest - to D5 - closest), corresponding to different time of tactile stimulus delivery and best fitting sigmoidal functions describing the relationship between RTs and sound distance, Upper Arm (dotted line) and Hand (grey line) conditions. Error bars denote S.E.M.

However, it is worth reminding that the present study did not specifically tested, for instance, the feeling of body ownership when patients wore their prosthesis. Interestingly, this aspect has been investigated by Ehrsson and colleagues (2008) by using the Rubber Hand Illusion. In this study, the authors tested whether it was possible to elicit the Rubber Hand illusion in a group of upper limb amputee by providing a tactile stimulation of the stump in synchrony with a visual tactile stimulation at the prosthetic hand. Results showed that the RHI was effective also in this case, since participants perceived an illusory sensation of perceiving touch on the artificial hand, rather than on the stump, accompanied by a feeling of ownership of the rubber hand.

9.9 PPS as a social interface

Most of the studies previously presented in this dissertation investigated how the representation of the space around the body changes as a function of interaction with an artificial object. By using a tool, for instance the distinction between a near space - where I can normally act - and the far space – where I can act with the tool - is altered. Critically, in everyday life the distinction between near and far space is meaningful not only in terms of possibility of *object* interaction, but mainly in terms of *social* interaction. In Chapter 8 we investigated how PPS representation was shaped both by *presence* and *behaviours* of other individuals. We used the same audio-tactile interaction task previously described, but in this case we investigated audio-tactile interaction around the face where people were facing either a mannequin or another person. Results from Experiment 8.1 showed that PPS boundaries shrink when subjects face another individual, as compared to a mannequin, placed in far space. This effect is sensitive to the physical distance between the subject and the other individual, since if the distance between them was reduced, the PPS boundaries changed accordingly. Experiment 8.2 and 8.3 showed that after playing an economic game with another person, PPS boundaries between self and other merge, but only if the other behaved cooperatively.

Philosophical considerations as well as neurophysiology, neuropsychology, and behavioral evidence converged in showing that the PPS representation is a space of fundamental importance for the individual, being the space where every interaction with the external world take place. It worth noting, however, that the relevance of space for both animals and humans is particularly inherent in social interaction, since many of our most meaningful interactions take place with objects with an high emotional and motivational significance, such as other human beings. In cognitive psychology most of the study on PPS had focused in showing how multisensory stimuli that fell within or outside the PPS are processed. Until now, as far as we know, only few studies in the literature have investigated social modulation of PPS representation. In monkey, bimodal neurons in the posterior parietal cortex respond to tactile stimuli on the animal’s body and to visual stimuli presented close to the experimenter’s body (Ishida et al., 2010). Homologous areas in humans respond to tactile stimuli on one’s own face and to visual stimuli approaching another person’s face (Cardini et al., 2011). Thus, some PPS neurons process events occurring not only within one’s own PPS but also within the PPS of others. Heed and colleagues (2010) recently showed that multisensory integration is modulated as a function of the presence and activities of others within one’s own PPS. Data from the present study here presented in Chapter 8 are new, since they extend previous findings by showing that the presence of others also in the extrapersonal space shapes PPS representation, such that the presence of others structures the representation of space around oneself. Moreover we also demonstrated a correlation between personality traits and the extension of PPS in social interaction. Individual differences in the size of near space, where participants were facing another person in the Other condition (Experiment 8.1A) were related to individual differences in own feelings of fear, apprehension and discomfort in presence of other people as assessed by the Personal Distress subscale of the IRI questionnaire. People with a higher score at the Personal Distress subscale also perceived the boundaries of PPS as closer to the body when facing another person as compared to when facing a mannequin.

These results suggest that PPS can be conceived as a social space, in which distance has a particular meaning in terms of the kind of interaction allowed. In social psychology, the concept of a space where social interaction takes place is usually referred as “Personal Space” (Hall, 1963). An intriguing hypothesis is that the concept of Peripersonal Space, as intended in neuroscience, and the concept of Personal Space, as intended in a social psychology, do actually represent the same psychological entity. In the social psychology literature the space around the body, the Personal Space, has been defined as the “*area individuals maintain around themselves into which others cannot intrude without arousing discomfort or even withdrawal*” (Hayduk, 1978, 1983; see also Lloyd, 2008, for a review). So, the Personal Space is conceived as an emotional zone around the human body that people feel like “their space” (Tajadura-Jiménez, Pantelidou, Rebacz, Västfjäll, & Tsakiris, 2011), and it is meaningful only in terms of social interaction. Hall specifically distinguished four different spatial zones as a way of placing spatial boundaries on interpersonal behaviour (see Figure 9.4): an *intimate zone*, used in very close relationships only; a *personal zone*, that correspond to the space of interaction with the other; *social* zone, that corresponds to a portion of space where more formal interactions take place and *public zone*, which is the distance kept from public figures (Hall, 1966; see Lloyd, 2008, for a review). A similar distinction between different sectors of space was first applied by Hediger (1950) to the animal behavior (see Graziano & Cooke, 2006 and Lloyd, 2008, for reviews). Hediger identified what he called a *flight zone*, a margin of safety around the animal's body: when a threatening object enters this flight zone, the animal escapes. In this sense, if we consider the Personal Space as a defensive zone, an overlapped can be found with the concept of PPS, given the sensory to motor function of PPS representation.

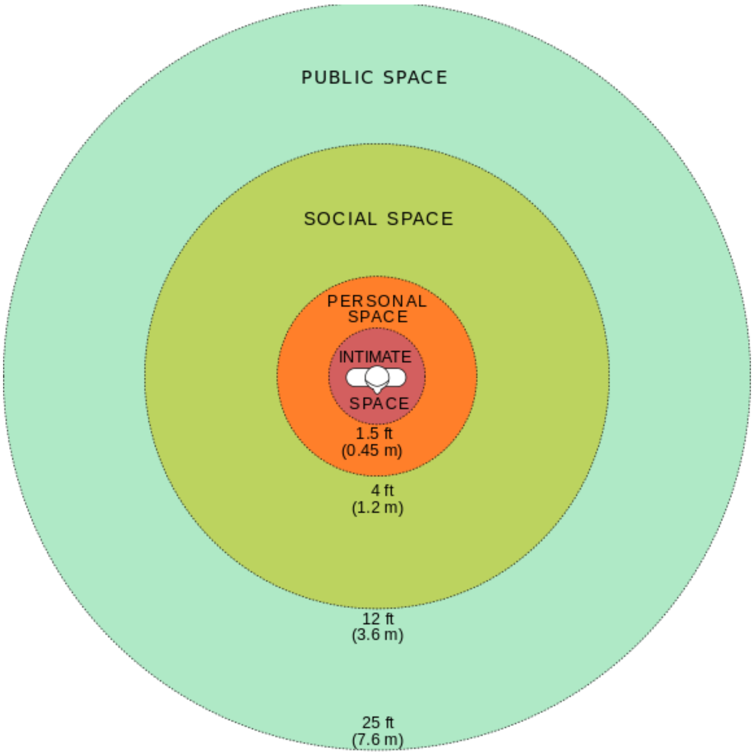


Figure 9.4 Diagram of Edward T. Hall's personal reaction bubbles. Adapted from Hall, The Hidden Dimension, 1966.

As demonstrated in this dissertation (see Chapter 3 and Paragraph 3 of the present Chapter), the human brain has evolved an adaptive mechanism that preferentially code for stimuli presented within and entering the PPS and map them onto the motor system in order to prepare an appropriate and rapid motor response.

Several studies in the literature, extensively reviewed in the present dissertation, demonstrate that PPS representation is not static, but it is dynamically updated through experiences. Similarly, also the representation of “Personal Space” in a more social context is not static, but can be updated by emotional states. A study of Tajadura-Jimenez and colleagues (Tajadura-Jiménez et al., 2011) specifically demonstrated that the extent of “Personal Space” is modified by the emotional valence of the music (positive VS negative) that people listened through personal music player when being in a social context. The extent of Personal Space in this study was measured as the distance where participants began to feel uncomfortable with the presence of another person. Specifically, their results showed that when participants listened to “positive” music (delivered through headphones), the Personal Space shrunk, allowing others to get closer. Instead, when participants listened to “negative” music, delivered through loudspeakers, the Personal Space expanded.

Taken together these results suggested that at a theoretical level an overlapping between the concept of Peripersonal Space in neuroscience and Personal Space in social psychology is possible: a common point seems to be that the social distance, that is the interpersonal distance that is considered acceptable, is not always rigidly fixed but is partially determined not only by participants internal feeling, but also by the social context (Hall, 1966; Tajadura-Jimenez et al., 2011). Interestingly, results from the study presented in this dissertation are new in showing a direct link between the extension of PPS representation and feelings generated not only by an internal state (such as happened in Tajadura-Jimenez and colleagues' study), but also by interaction with others.

In conclusion the present dissertation revealed how different types of experiences shape body and space representation. Specifically, we demonstrated how, in several contexts, changes in the structure or in the function of the physical body plastically modify mental representations of the body and of the PPS. An interaction between a perceptual representation of the body in space and high-level representations in a social context also demonstrated that other individuals shape PPS representation. Such plasticity suggests that our sense of body in space is not given at once, but it is constantly constructed and adapted through experience.

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