

Multisensory Representation of the Space Near the Hand: From Perception to Action and Interindividual Interactions

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Abstract

When interacting with objects and other people, the brain needs to locate our limbs and the relevant visual information surrounding them. Studies on monkeys showed that information from different sensory modalities converge at the single cell level within a set of interconnected multisensory frontoparietal areas. It is largely accepted that this network allows for multisensory processing of the space surrounding the body (peripersonal space), whose function has been linked to the sensory guidance of appetitive and defensive movements, and localization of the limbs in space. In the current review, we consider multidisciplinary findings about the processing of the space near the hands in humans and offer a convergent view of its functions and underlying neural mechanisms. We will suggest that evolution has provided the brain with a clever tool for representing visual information around the hand, which takes the hand itself as a reference for the coding of surrounding visual space. We will contend that the hand-centered representation of space, known as perihand space, is a multisensory-motor interface that allows interaction with the objects and other persons around us.

Keywords

hand-centered space, multisensory perception, sensory-motor processing, grasping, avoidance, mirror neurons, transcranial magnetic stimulation, fMRI, parietal lobe, premotor cortex

Introduction

Our everyday actions, such as grasping a glass of water to drink it, or pass it over to somebody, seem to us easy and effortless. Performing these actions, however, represent an extremely challenging task for the brain if we consider the computational effort required to control these “simple” acts. In order to interact successfully with the environment, we need to know precisely where our body parts are located in space and where the targets of our interactions are placed with respect to ours and other people’s body. Moreover, we need to keep these topographical inputs updated online as a function of ongoing and upcoming hand movements. The space near our and other people’s hands is peculiar in this respect: being the theatre of most of our interactions with the external world, it deals not only with spatial perception and action but also with their integration. We review here convergent results from nonhuman and human primates showing the existence of a spatial representation centered on the hand (perihand space, Fig. 1) arising through the activity of multisensory areas within the parietal and frontal cortex and subcortically in the putamen. We will argue in favor of a primary role of the perihand space representation in

the sensory guidance of motor behavior for interacting with objects and other people around us.

Neurophysiological Bases of the Hand-Centered Representation of Visual Events

The existence of hand-centered visual processing of nearby space has been revealed by electrophysiological research in macaque monkeys, within a network of visuo-tactile integrative areas such as the parietal and frontal premotor cortices, and subcortically the putamen (Graziano and others 1994; Hyvärinen and Poranen 1974; Rizzolatti and others 1981a, 1981b). A visuo-tactile

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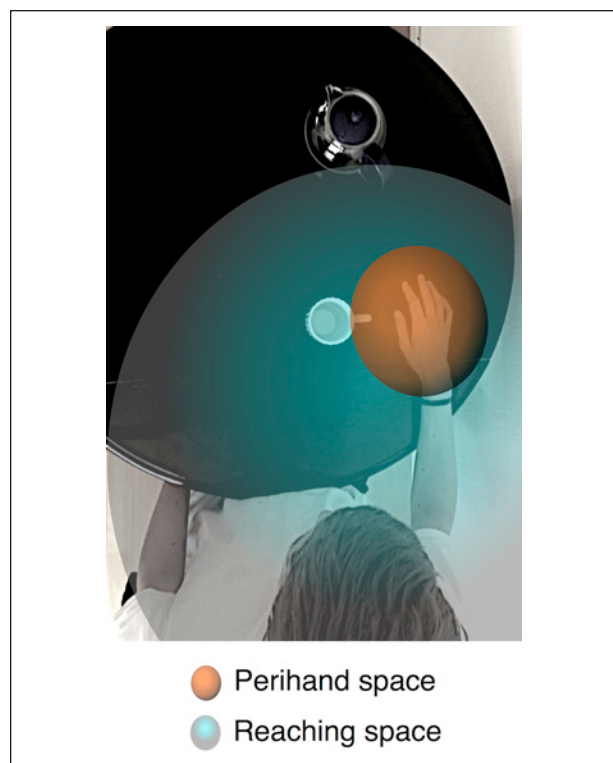


Figure 1. Perihand space representation (orange sector) with respect to reaching space (green sector).

integrative mechanism arises at the single neuron level, with individual visuo-tactile neurons having both a tactile and a visual receptive field (RF). Most of the visual RFs are limited in depth to the region of space close to the body surface (Rizzolatti and others 1981b). Interestingly, the visual responding area of the visuo-tactile neurons has been shown to be independent of the eye position (Fogassi and others 1992; Gentilucci and others 1983). The visual response of neurons presenting tactile RFs on the hand is updated instead by hand displacement (Graziano and Gross 1993; Graziano and others 1997). In other words, the visual RFs follow the hand as it moves. Such a physiological property inspired the hypothesis that the network of visuo-tactile areas can represent the visual space around the body in a body part-centered fashion (Rizzolatti and others 1997). Indeed, the integration of visual information from the space near but outside the body with tactile information arising—by definition—from the bodily surface, allows for the construction of a special representation of the space that lies in the boundary zone between objects near the body and the body itself. It is in this region of space where most of our interactions with objects take place, and where physically threatening objects are the most dangerous for the individual. The hand-centered representation has therefore been thought to play a role in the sensory guidance of

movements toward objects (Gentilucci and others 1988; Rizzolatti and others 1988) and in the sensory guidance of movements for reacting to or avoiding approaching objects (Cooke and others 2003; Graziano and others 2002). It has been suggested that the hand-centered representation of space might also assist the localization of limbs (Graziano 1999).

A detailed series of studies on the properties of visuo-tactile neurons has been performed in the premotor cortex. Neurons in the F4 subregion of the inferior area 6, identified as the ventral premotor cortex, are strongly responsive to tactile stimulation. They are characterized by relatively large tactile RFs located primarily on the monkey's face, neck, arm, hand, or both hands, and face (e.g., in the peribuccal region; Rizzolatti and others 1981a). A large proportion (85%) of the tactile neurons in this area also discharges in response to visual stimuli. According to the extent in depth of the visual RFs protruding out from the body, the so-defined bimodal neurons can be subdivided into pericutaneous (54%) and distant peripersonal neurons (46%, as reported in Rizzolatti and others 1981b). The pericutaneous neurons responded best to stimuli presented a few centimeters from the skin (10 cm or less), whereas the distant peripersonal neurons responded to stimuli within reach of the monkey's arms.

Also the posterior parietal lobe of the macaque brain contains neurons with visuo-tactile properties, in two subregions: area 7b within the inferior parietal territory and the ventral section of the intraparietal sulcus (VIP). Electrophysiological studies in awake monkeys revealed that visuo-tactile responses in these areas arise from single-cell recordings, similarly to those evoked in neurons in the premotor cortex (Hyvärinen and Poranen 1974). The majority of neurons within area 7b respond to tactile stimuli, displaying a rough somatotopic organization, where it is possible to distinguish face, arm, and hand representations. Within the face and arm regions of this map, approximately a third of the cells show visual sensitivity in addition to tactile responsiveness (Hyvärinen and Poranen 1974; Leinonen and others 1979). Visual responses are typically triggered by visual objects moving toward the monkey, within about 10 cm from the tactile RF, although in some cases, stimulation presented further away, but still within a reachable distance, was also effective (Hyvärinen and Poranen 1974). Researchers initially interpreted the responses to such visual events as an "anticipatory activation" that appears before the neuron's tactile RF was touched (Hyvärinen and Poranen 1974, p. 675). The activation of visuo-tactile cells was shown to decay as a function of the distance of the effective visual event from the body-part (Leinonen and others 1979). Similar multisensory mechanisms have also been described for cells in the monkey area VIP, in the fundus of the intraparietal sulcus (Avillac and others 2005;

Duhamel and others 1998). VIP neurons respond to tactile and visual stimulations presented within a few centimeters of the tactile RFs. Unlike area 7b neurons, however, tactile RFs in VIP's multisensory neurons are primarily located on the face and head, and their visual RFs are anchored to a region of space around the face (Colby and others 1993).

Together with the cortical regions described above, the putamen seems to play a relevant role in the visuo-tactile processing of events occurring within the space around the body (Graziano and Gross 1993). Visuo-tactile neurons in the putamen display tactile RFs on the arm, hand, and face that are somatotopically organized. As for cortical visuo-tactile neurons, the visual and tactile RFs in the putamen's multisensory neurons show a rough spatial correspondence. A large portion (82%) of face neurons responds best to visual stimuli presented in a region of space within 10 to 20 cm from the tactile RF. Neurons with tactile RFs on the arm and hand present even narrower visual selectivity for the space around the hand (up to 5 cm; Graziano and Gross 1993).

Overall, the neurophysiological findings mentioned above define a set of at least four distinctive areas with broadly similar visuo-tactile responses: premotor area 6, parietal areas 7b and VIP, and the putamen. These areas are heavily interconnected, forming a set of anatomically interconnected areas (Matelli and Luppino 2001; Rizzolatti and others 1997, 1998) that we refer to hereafter as the "peripersonal space network." Neurons in the areas included in this network share common features: (1) Visual stimuli moving near the monkey's body trigger a stronger response than farther stimuli; (2) The visual responses lie primarily within a head-face or arm-hand centered somatosensory representation of the body. Such properties allows for a body part-centered coding of visual events within sectors of space adjacent to the body surface (Fogassi and others 1992; Graziano and Gross 1993; Rizzolatti and others 1997).

The Hand-Centered Representation of Space in Humans

Substantial behavioral evidence exists in favor of a functionally similar representation of the space near the body in humans. Behavioral evidence of selective representations of the space near the body and its parts has been initially provided by neuropsychological studies. The main source of information for neuropsychologists consists of the pathological behavioral changes that become manifest after a damage to the central nervous system. The association between the altered cognitive ability with the lesion affecting defined brain territories, and especially the dissociation among certain symptoms and lesion maps has greatly contributed to our understanding

of the organization of brain functions (Shallice 1991). From neuropsychological studies in humans, it became soon evident that one of the structures mainly responsible for the construction of spatial representations is the parietal lobe (Balint 1909; Gertsman 1930; Holmes 1919). The most solid evidence in favor of the existence of a selective representation for the space near the body in humans derives from the pathological conditions known as *hemispacial neglect* and *extinction* (Bender 1952; see Jacobs and others 2012 and Schenk and Karnath 2012, for recent reviews). Patients presenting neglect after right brain damage display a peculiar reduction of response and attention to sensory events occurring in the left (contralesional) hemispacial, despite the absence of any gross impairment in the primary sensory processing. Several studies have shown and confirmed that the neglect syndrome can affect selectively the space near the body (Halligan and Marshall 1991) or the space far from the body (Cowey and others 1994). The double dissociation provided by the mentioned studies constitutes evidence that the human brain must selectively represent the two regions of space. Interestingly, the representation of the space near the body presents a degree of functional plasticity. Indeed, the use of a tool that elongates the arm and therefore the reaching capabilities of the body can induce an enlargement of the peripersonal space representation. In a single case study, Berti and Frassinetti (2000) reported the performance of a patient showing a severe neglect selectively affecting the space near the body. In a line bisection task, a standard procedure for the assessment of neglect pathological rightward bias, the bias was apparent in the near, but not far space. When the patient was requested to bisect lines in the far space by means of a laser pointer, her performance was comparable to controls. However, when the same task was performed with a stick, used by the patient to bisect the line in a far position, the rightward bias reappeared, and was as severe as that observed in her near space. In other words, an artificial extension of the patient's body (the stick) caused the remapping of the far space into near space. This finding, in addition, provided some hints about the functional link existing between the representation of the space near the body and the "motor potential" of the body, which is the possible motor interaction with the close environment.

Similarly to hemispacial neglect, the neuropsychological condition called extinction provides a compelling support to the idea that the interaction between different sensory modalities plays an important role in building the representation of the space near the body. As neglect patients, extinction patients also fail to respond to a sensory event occurring in the contralesional space, but only when this is accompanied by another sensory event in the ipsilesional space. This pathological sign can appear in different sensory modalities and also cross-modally, such

as, for example, when touch delivered on the left contralesional hand is “extinguished” by visual stimulation presented to the right hand. Crucially, the visual stimulus is effective in extinguishing the contralesional tactile one only if presented in the space near the hand (di Pellegrino and others 1997). This spatial selectivity corroborates the idea that a strong visuo-tactile interaction takes place in the human peripersonal space. Furthermore, the multisensory phenomenon manifested by extinction patients has been proved to arise in hand-centered coordinates. When patients for instance are tested with the hands crossed along their body midline (i.e., the right hand in the left hemispace and the left hand in the right one) visual stimuli presented near the right hand (in the left hemispace) still extinguish tactile stimuli delivered to the left hand, despite the fact that the left hand is now in the patient’s right hemispace. Within the same spatial arrangement, visual stimuli presented farther away from the right hand produce little or no extinction. This means that visual stimuli are processed by a mechanism that takes the hand as reference for coding the space immediately outward the hand and follows it, staying anchored to this reference when the hand changes location. In more general terms, multisensory interactions revealed by extinction patients’ behavior arise in a body part-centered fashion (Làdavvas 2002). Critically, for instance, the extinction of the touch on the left hand induced by the co-occurring visual event has been shown to be less severe when the visual stimulation is presented near other body sectors, for instance, the face (Farnè and others 2005a) rather than the homologous body part (e.g., the right hand).

The functional plasticity of the boundary of the peripersonal space representation, featured after the use of an elongating tool, has also been suggested on the basis of multisensory probing of space (Farnè and Làdavvas 2000; Farnè and others 2005b, 2007; Maravita and Iriki 2004; Serino and others 2007). A seminal study on a group of patients presenting extinction tested the visuo-tactile interaction before and after the use of a tool that elongated the arm reaching capabilities. Visuo-tactile extinction was more severe after compared to before tool-use for visual stimuli presented far from the hand and near the tip of the tool. When the same patients were requested to actively point to the same distant locations without the tool, no such a remapping of space was reported. In addition, when patients were tested for visuo-tactile extinction after having paused the active use of the tool for a few minutes, the severity of their cross-modal extinction was back to pre-tool-use baseline level (Farnè and Làdavvas 2000). This dynamic modulation has been taken as evidence for the plastic properties of the human peripersonal space, similarly to what has been suggested by electrophysiological recordings in the monkey (Iriki and others 1996; Maravita and Iriki 2004).

Similarly to the neuropsychological approach described above, a series of behavioral studies in neurologically unimpaired people has measured the strength of the interference induced by visual stimuli over the performance on a tactile task to probe the layout of the peripersonal space (Spence and others 2004b). This line of research corroborates the findings described in brain-damaged patients. Indeed, the strength of the visuo-tactile interference appears (1) to decay as a function of the distance between visual and tactile information (Spence and others 2004a); (2) to follow a body part-centered system of reference frames (Spence and others 2004b); and (3) to be remapped after the use of a tool that extends the arm reaching capabilities (Holmes and others 2004).

Further behavioral evidence supporting the existence of a selective representation of the space near the hand in humans comes from a series of studies employing the rubber hand illusion (Botvinick and Cohen 1998; Ehrsson and others 2004). To elicit this illusion, the experimenter uses two small paintbrushes and applies strokes to a rubber hand in full view, and the participants’ real hand, which is hidden behind a screen, synchronizing the strokes as carefully as possible. The initial conflict between the seen location of the rubber hand and real hand is reduced by a process where the sense of touch is referred to the rubber hand, similar to the ventriloquist effect in audio-visual integration (Ehrsson 2012). The participants also develop a vivid percept of the rubber hand as one’s own hand, and in addition to this there is a change in the perceived position of the hand toward the location of the rubber hand (the so-called “proprioceptive drift”). The illusion is not elicited if the seen and felt stimuli on the hands are delivered asynchronously, the rubber hand placed in an anatomically incongruent position (Farnè and others 2000), or the rubber hand placed outside peripersonal space (Lloyd 2007). These psychological rules fit well with the proposal that the rubber hand illusion involves multisensory integration mechanisms operating in hand-centered spatial reference frames, and this would point toward a possible involvement of the peripersonal space network. On a more general note, the rubber hand illusion suggests that the visuo-tactile representation of the peripersonal space, being at the boundaries between the own body and the external world, can support the feeling of ownership of limbs and their localization in space (Makin and others 2008).

Neural Bases of the hand-Centered Representation of Space in Humans

In striking contrast to the richness of behavioral investigations, until recently, very few attempts had been made to elucidate the brain structures involved in the representation

of peripersonal space in humans (Bremmer and others 2001; Huang and others 2012; Makin and others 2007; Sereno and Huang 2006). As described by electrophysiological studies, multisensory neurons representing the space near different body sectors are intermingled in parietal and premotor areas, and these neurons are in turn intermingled with other multisensory neurons with much larger visual and tactile RFs encompassing multiple body parts. For this reason, investigations employing functional magnetic resonance imaging (fMRI), a technique that segments the brain in volumetric units (voxels) containing *several* neuronal populations can encounter problems to identify subpopulations with a strict visual selectivity. To circumvent this problem, in a series of neuroimaging studies, we decided to employ blood oxygen level-dependent (BOLD) adaptation for revealing neuronal population with a visual selective response for events occurring within the space near the hand. Adaptation is a robust phenomenon in electrophysiology (Li and others 1993) that has been extended to fMRI (Grill-Spector 2006). It is based on the premise that repeated presentation of identical stimuli leads to a reduction in the measured signal from neuronal populations selective to specific stimulus features. The main advantage of BOLD adaptation is the capacity to reveal subpopulations of neurons that exhibit selectivity to such features *within a single voxel*. Such an advantage proved to be an effective tool for investigating the spatial selectivity of the visual response in neuroimaging (Brozzoli and others 2011).

In a first study, a real object was presented (a 40-mm diameter red sphere attached onto a thin wooden stick) moving either near or far from the participant's hand. Four different combinations of visual stimuli were presented: The object could appear near the hand or far from it for the whole duration of the visual stimulation (6 seconds), or the object was first presented for 3 seconds near the hand and then for 3 seconds in the far position or the other way around (the sphere moving for 3 seconds in the far position and then for 3 seconds near the hand). These conditions were all repeated in two different contexts (implemented in separate scan runs), either with the hand placed visible in front of the participants on a table, or with the hand retracted from the table and placed on their chest. Critically the moving object stimulus was always presented in the same portion of external space but only close to the hand when the hand was outstretched on the table. Thus this experimental design allowed us to test for brain areas showing BOLD adaptation specific to the repeated visual stimulation near the hand by comparing the BOLD signal recorded during the first 3-second period versus the second 3-second period of the near-hand stimulation trial. Following a similar logic, with an alternative but convergent approach we could also look for reductions in the BOLD signal during the second 3-second period of near-hand stimulation, when this

stimulation had been preceded by near-hand stimulation versus the same stimulation but presented far from the hand (only the former case should produce adaptation). Crucially, the design allowed for direct contrasts between the conditions with the hand present and the hand absent. Collectively, the results from both approaches outlined above could reveal BOLD adaptation responses that are specific to the visual stimuli presented in the space near the hand, controlling for unspecific adaptation effects related to prolonged visual stimulation, order effects, or repeated stimulation of a particular location in external space coded in coordinates other than body part-centered coordinates.

The results revealed that premotor and parietal cortices (anterior intraparietal sulcus [aIPS]), and subcortically the putamen, contain neuronal populations that selectively encode visual stimuli close to the hand (Fig. 2A; Brozzoli and others 2011). That is, these areas displayed a reduction in the BOLD response specifically when the object was repeatedly moved in the near location with respect to the outstretched hand (Fig. 2B). Importantly, no such significant reduction in the BOLD signal was detected when the hand was retracted. Furthermore, presenting the object in the far location did not produce a differential BOLD-adaptation across the conditions, regardless of whether the hand was stretched out in view or retracted. This finding suggests that a set of areas in humans - similar to the "peripersonal space network" defined in the macaque brain—including the IPS, the premotor cortex, and the putamen contain neurons that are selective for the visual presentation of an object in the space around the hand. In further experiments using the BOLD adaptation approach described here, we showed that the visual selectivity for the space near the hand was "anchored" to the hand, so that when the hand was moved in space across two locations the near-hand selectivity of the BOLD adaption response followed the hand (Fig. 3; Brozzoli and others 2012a). This suggests that the human premotor-posterior parietal neuronal populations encode the space near the hands in hand-centered coordinates, just as they do in the brain of macaque monkey (Graziano and others 1997). The results of these two fMRI studies contribute to fill the gap in the literature between the electrophysiological results in monkeys and the behavioral data available in humans.

Even though caution should be exerted when comparing studies in nonhuman and human primates—especially with respect to possible homology relations between areas in the association cortices—the premotor and parietal regions we found adapting to an object moving near the hand match very well the electrophysiological data in macaque monkeys. As reviewed in the previous section, these neurons have multisensory properties since they respond to visual, tactile, and proprioceptive information

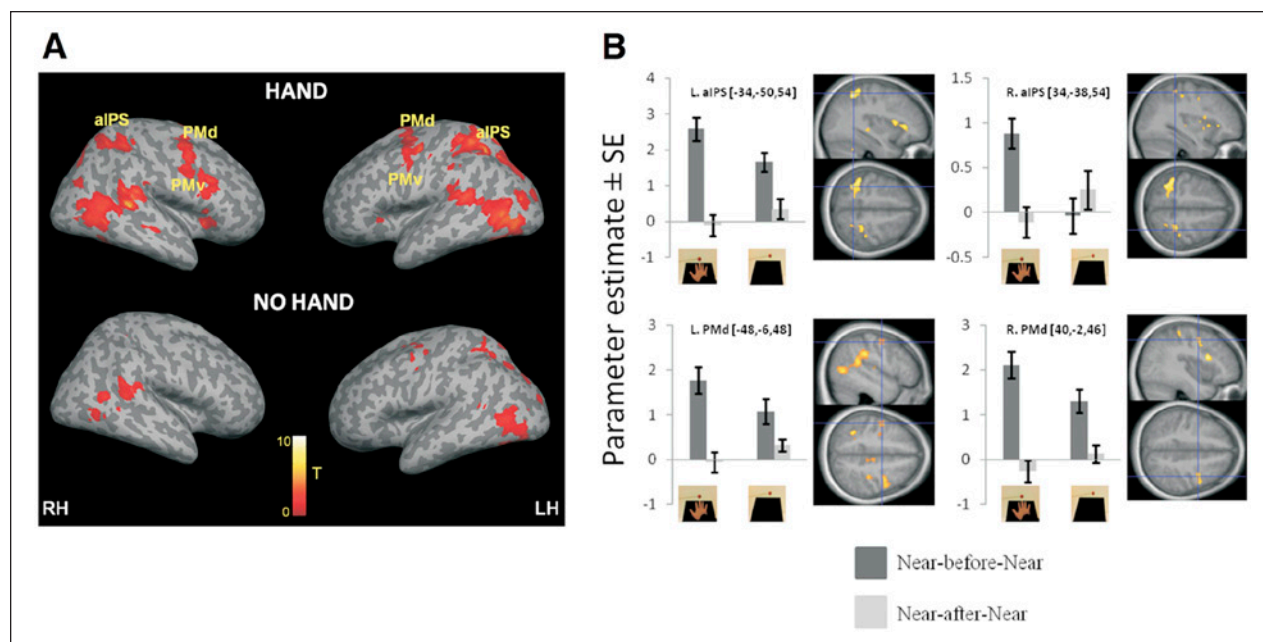


Figure 2. (A) Areas displaying visual selectivity for the space surrounding the hand. The activation maps on the whole-brain rendering represents the adaptation to an object presented in the near location when the hand was outstretched on the table, in correspondence of the stimulus location (HAND, top part of the panel) and when the hand was retracted (NO HAND, bottom part). RH = right hemisphere; LH = left hemisphere; aIPS = anterior intraparietal sulcus; PMv = ventral premotor cortex; PMd = dorsal premotor cortex. (B) Blood oxygen level-dependent (BOLD) adaptation to an object presented near the hand in parietal and premotor cortices bilaterally. The plots display the parameter estimates for the first and the second 3-second period of stimulation in the near location, when the hand was outstretched on the table (left part of each graph) and when the hand was retracted far from the near location of stimulation (right part of each graph). Error bars represent SEM. The three numbers next to the titles refer to the x, y, and z coordinates in MNI (Montreal Neurological Institute) space. Modified from Brozzoli and others (2011).

from a body part and its surrounding space (Avillac and others 2005, 2007; Graziano and others 1997; Rizzolatti and others 1981a, 1981b). In this regard, it is noticeable that several previous fMRI studies have shown that the intraparietal areas and premotor regions of the human brain respond to multisensory stimuli in peripersonal space (Bremmer and others 2001; Ehrsson and others 2004; Gentile and others 2011; Lloyd and others 2003; Macaluso and Driver 2005; Makin and others 2007). The study by Gentile and colleagues (2011) provides evidence regarding the multisensory properties of the “perihand space network.” In this study unimodal visual, unimodal tactile, and congruent bimodal visuo-tactile stimulation were delivered to the hand placed on a table in direct view of the participants (stimuli was a small ball mounted on a stick). Interestingly, both premotor and intraparietal cortices displayed greater activity for bimodal visuo-tactile stimulation of the right hand compared to unimodal visual stimulation near the hand (but not touching it) and unimodal tactile stimulation on the hand (when participants closed their eyes). More specifically, super-additive effects were identified in the aIPS and portions of the premotor cortex. A more recent follow-up study demonstrated

that the visuo-tactile responses in the same premotor-posterior parietal areas depended on the spatial and temporal congruence of the visual and tactile stimuli, and moreover, that the visuo-tactile integration requires a concurrent match between the seen and felt orientations of the upper limb. These observations fit well with the notion that the visuo-tactile integration on the hand takes place in hand-centered reference frames (Gentile and others 2013). These findings are important as they demonstrate the multisensory coding of the peripersonal space network in the human brain.

Recent fMRI studies have also provided support for the hypothesis that the multisensory processing in perihand space is related to the feeling of ownership over hands. Importantly, a recent imaging experiment provides direct evidence for a link between the hand-centered encoding of space and the explicit perception of the hand as one’s own and its location (Brozzoli and others 2012a). In this study, the rubber hand illusion (Botvinick and Cohen 1998) was used to experimentally manipulate the perceived ownership of a model right hand and trigger the associated changes in hand localization. The former can be assessed with questionnaires where the participants

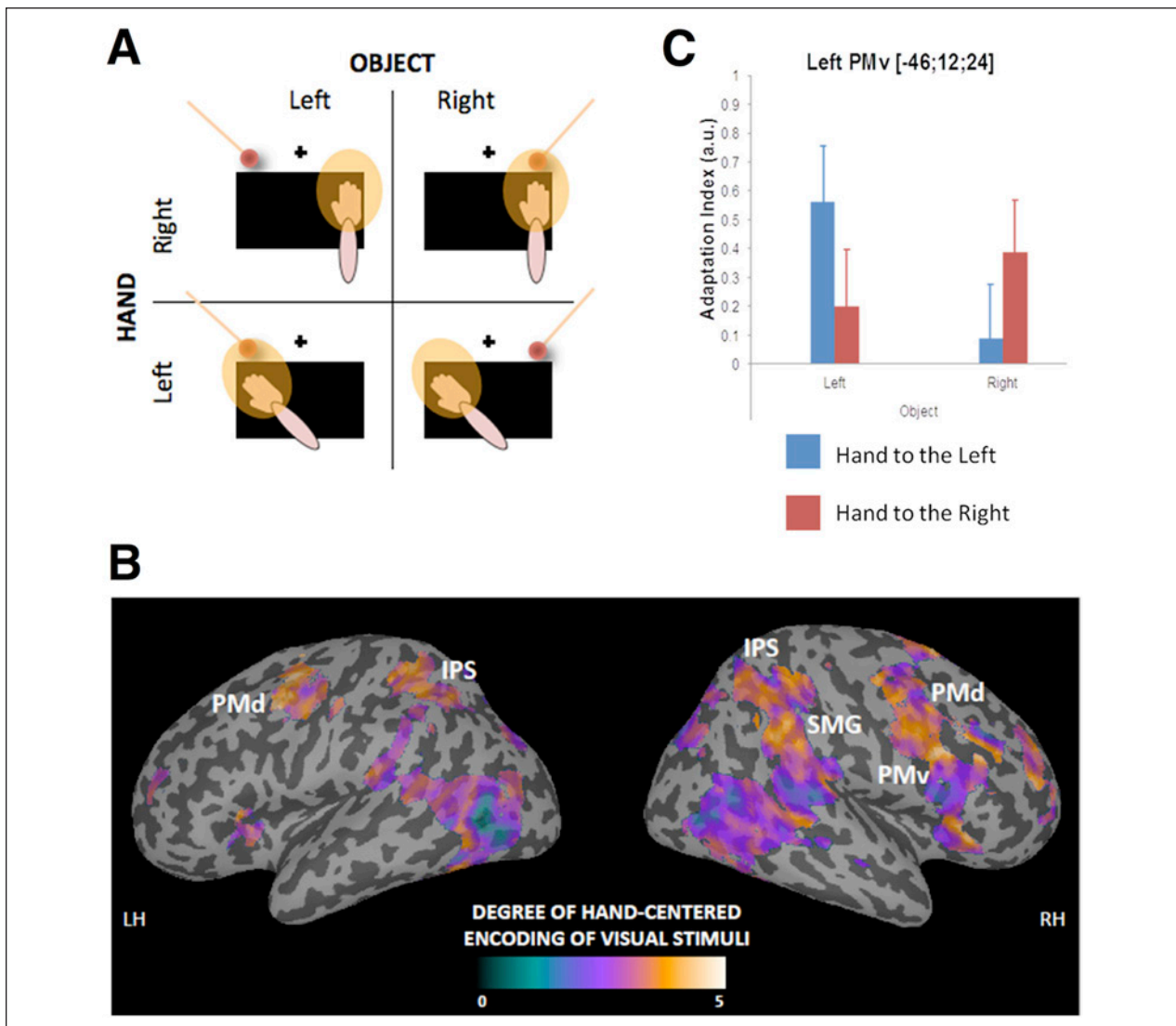


Figure 3. (A) The participant's right hand was placed on a tilted table in front of them, on either the left or the right of a central fixation point (black cross). A three-dimensional object was presented to either the left or the right of the fixation point. The resulting 2×2 factorial design allowed direct testing for the hand-centered selective encoding of the object. (B) The figure displays areas showing BOLD adaptation to a visual stimulus moving near the hand, using a gradient indexing the degree of hand-centered encoding (0 represents absence of hand-centered responses, whereas larger values represent stronger hand-centered encoding). Although early visual areas adapted to the object independently of its position relative to the hand, the posterior parietal and premotor cortices showed a high degree of hand-centered encoding. RH = right hemisphere; LH = left hemisphere; IPS = intraparietal sulcus; SMG = supramarginal gyrus; PMv = ventral premotor cortex; PMd = dorsal premotor cortex; BOLD = blood oxygen level–dependent. (C) Example of BOLD adaptation responses for individual conditions in the left ventral premotor cortex. The bar graphs report the adaptation index, calculated as the difference in contrast estimates between the first and the second presentation of the object, for each of the four conditions used to define the interaction contrast in the factorial design (blue bars refer to the conditions with the hand to the left and red bars to the conditions with the hand to the right; error bars represent SEM). Modified from Brozzoli and others (2012a).

have to rate how strongly they experience the model hand as their own, and the latter is registered using a behavior index where, after experiencing the illusion, people had to manually indicate changes in the perceived location of the hand (proprioceptive drift test). Brushstrokes applied

to the two hands asynchronously, and therefore not eliciting the illusion, served as a control for otherwise equivalent conditions. The key analyses focused on examining the remapping of the hand-centered space onto the prosthetic hand directly after a period of experiencing the

rubber hand illusion by employing the BOLD adaptation approach described above (i.e., by repeated presentation of a moving small ball near the model hand). Since the illusion involves both a subjective feeling of owning the prosthetic hand and a drift in the perceived location of the hand (Botvinick and Cohen 1998), we investigated how these two key percepts related to the neural hand-centered remapping responses. As predicted, the presentation of the object near the prosthetic hand led to stronger BOLD adaptation in the premotor, posterior parietal, and putaminal regions after the synchronous compared with the asynchronous stimulation periods. This pattern of BOLD adaptation responses is compatible with the encoding of the moving object in a spatial reference frame remapped onto the rubber hand. Furthermore, the results showed how the perihand space remapping relates to changes in position sense and limb ownership, respectively. By using proprioceptive drift test as a measure of changes in perceived limb position and the questionnaire ratings as a measure of subjective ownership, we regressed these parameters, respectively, with the effect size of the perihand-specific BOLD adaption and look for significant relationships in all voxels of the whole brain. We found that the stronger the participants rated the feeling of ownership over the rubber hand, the stronger the rubber hand-centered adaptation in the left ventral premotor cortex. In other words, the degree of “rubber hand-centered” spatial encoding correlated with the subjective sense of hand ownership. This finding is consistent with previous studies that related ventral premotor activity to the subjective level of ownership during congruent visuo-tactile stimulation applied directly onto the limb(s) (Ehrsson and others 2004, 2005). Importantly, the new observation provides a direct link between the representation of the perihand space and the self attribution of the limb, suggesting that the peripersonal space operates as a crucial boundary zone between self and nonself.

Interestingly, the proprioceptive drift also turned out to be predictive of the remapping of perihand space toward the rubber hand as measured by the amount of BOLD adaptation. Crucially, however, such a correspondence occurred in a different node of the peripersonal space network. The more individual participants mislocalized their right hand toward the location of the rubber hand, the stronger the adaptation responses indicative of hand-centered remapping of space in the right posterior parietal cortex. This is in keeping with the known neurophysiological functions of the posterior parietal cortex and its role in planning manual actions (Culham and Valyear 2006). Neurons in area 5 of the macaque brain encode the hand position by integrating visual and proprioceptive signals (Graziano and others 2000; Graziano and Botvinick 2002). Similarly, the human intraparietal cortex integrates visual and proprioceptive information

about the upper limb (Gentile and others 2011; Lloyd and others 2003). The finding of a tight link between perihand space representation and sense of position of the hand within the posterior parietal cortex provides evidence for the role of this area in constructing a “proprioceptive skeleton” for the representation of peripersonal space, onto which selective visual responses can be grounded (Cardinali and others 2009). In other words, these findings concur supporting a tight link between the multisensory peripersonal space representation and the body schema, a body representation for motor aims (Cardinali and others 2009, 2011; Head and Holmes 1911; Kammers and others 2009). The existence of such a functional relationship between multisensory perception of space and motor representation of the body corroborates the idea that the peripersonal space might play a crucial role in the planning and the sensory guidance of our motor behavior (Brozzoli and others 2012b; Makin and others 2012).

A Motor Frame for the Hand-Centered Representation of Space: Avoidance and Reaching

As reviewed in the previous sections, a pool of reciprocally interconnected multisensory areas integrating visual, tactile and proprioceptive signals is devoted to the representation of the space surrounding the body. Similarly in human and nonhuman primates, such a network includes areas in the parietal lobe, the premotor cortex and the putamen. Solid evidence supports the view that the cortical visuomotor grasping circuit, comprising the IPS, ventral premotor and primary motor cortex allows for the “translation” of the physical properties of an object into a suitable motor command for grasping (Castiello 2005; Ehrsson and others 2000; Murata and others 2000; see Davare and others 2011, for a review on both human and nonhuman primates data). In humans, activity in the aIPS and premotor regions is associated with the preparation and execution of object-directed actions (Culham and Valyear 2006; Ehrsson and others 2000; Fogassi and Luppino 2005; Grefkes and Fink 2005). Brain stimulation studies targeting the aIPS, for example, have shown its crucial role in the preparation phase of grasping an object; transcranial magnetic stimulation disrupting neuronal activity in the aIPS has been shown to affect the correct selection of precision or power grip, as a function of the visual information made available during action unfolding, and to be updated in case of sudden changes (Davare and others 2010). This set of results is compatible with electrophysiological results identifying the neural circuits for grasping and reaching within a parieto-frontal network of the macaque brain (Fattori and others 2010; Fogassi and Luppino 2005). This suggests that in humans, as in primates, the selective

perihand mechanism based on visuo-tactile integration might be used as an interface for correctly planning and guiding free-hand actions toward objects within reaching distance (Brozzoli and others 2012b; Graziano and others 1994; Rizzolatti and others 1997). Indeed, in order to interact successfully with the objects in the surrounding of our body, it is necessary to represent the position of the target object relative to the observer's body or body parts. Given that our hands can move simultaneously with and independently from our eyes, the brain needs to integrate and constantly update information arising in an eye-centered reference frame with information about the current position of the hand relative to the body and to nearby potential target objects. The perihand space representation provides an effective mechanism to support such a fundamental function.

Recent experiments have demonstrated a rapid hand-centered processing of visual information relevant for motor control (Makin and others 2009). The participants performed a simple button-press motor response with the right index finger, while a task-irrelevant three-dimensional ball suddenly fell just above the participants' responding hand (near condition), or at a distance (far condition). Using single-pulse transcranial magnetic stimulation over the contralateral primary motor cortex, it has been reported that the sudden appearance of this potentially threatening visual stimulus was associated with a reduction in corticospinal excitability at the very early and specific time window of 70 to 80 ms following its appearance. This inhibition might reflect the proactive suppression of an automatic avoidance-related response, during the execution of the task-related response. Indeed, when the two motor behaviors (the avoidance- and the task-related responses) were uncoupled, the approaching ball had an opposite, facilitatory effect on corticospinal excitability. Crucially, both the rapid inhibition and facilitation of corticospinal excitability were hand-centered, depending mostly on the distance of the ball from the hand (near vs. far condition), regardless of the location of both overt gaze and covert spatial attention. These findings reveal a direct and fast connection between the visual processing of information in the space near the hand and the on-going motor behavior, suggesting a role for peripersonal space representation in motor responses, for example to avoid rapidly approaching objects (Makin and others 2012). Such a possibility has also been tested in monkeys through direct cortical microstimulation. Cooke and Graziano (2003) studied macaque motor activity during defensive movements evoked by aversive cutaneous stimulation, identifying a startle-related muscular activity occurring as early as ~20 to 30 ms after stimulus onset and a later muscle response starting ~70 ms after stimulus onset. Most importantly, very similar motor responses were also evoked by electrical microstimulation of

multisensory regions of the premotor cortex (Graziano and others 2002).

Could the peripersonal space representation also serve for appetitive actions, such as grasping an object? One could indeed theorize that the same anticipatory function featured by the peripersonal space network in the case of avoidance reactions, may also have evolved to guide voluntary object-oriented actions. In support to this view are the results of electrophysiological studies showing the motor properties of both parietal and periarculate visuo-tactile neurons, whose discharges are mostly correlated with reaching and grasping movements (Gardner and others 2007; Rizzolatti and others 1981a, 1981b, 1997). The two hypotheses are not mutually exclusive and one could argue that a more sophisticated grasping function could have developed from a more primordial defensive machinery, using the same body-part centered coding of visual space (in line with the "neuronal recycling hypothesis," as proposed by Dehaene (2005)). Only recently, though, research started investigating the link between the perihand space representation and voluntary motor behavior in humans. The rationale behind this line of studies is that if the perihand space representation guides the execution of voluntary free-hand actions, for instance reaching toward an object, the motor program should induce a rapid online remapping of visuo-tactile spatial interactions (Fig. 4A). To test this hypothesis in humans, multisensory interactions have been assessed during the execution of a reach-to-grasp action. A group of healthy participants were requested to solve a perceptual task while grasping an object. The perceptual task consisted in discriminating the elevation (up or down) of a tactile stimulus delivered to either of two digits (index or thumb) of the acting hand, trying to ignore a task-irrelevant visual distractor that was concurrently presented on the target object. The results showed that when participants performed the action with the tactually stimulated hand, the visuo-tactile interaction was enhanced as compared with a static phase before action execution (Fig. 4B). Crucially, if the same action was performed with the nonstimulated hand, no multisensory modulation was observed. The concurrent kinematic recording ensured that participants could grasp the object with similar movements, and therefore attentional demands, across hands (Brozzoli and others 2009). This result constitutes evidence in favor of the fact that the execution of a grasping movement triggers a motor-evoked remapping of the perihand space. In other words, the brain updates the relationship between visual and tactile information well before the hand comes into contact with the object. The finding that only actions performed by the tactually probed hand produced such a visuo-tactile remapping confirms the hand-centered nature of the perihand space. It is interesting to note that the increase in the strength of the visuo-tactile interaction

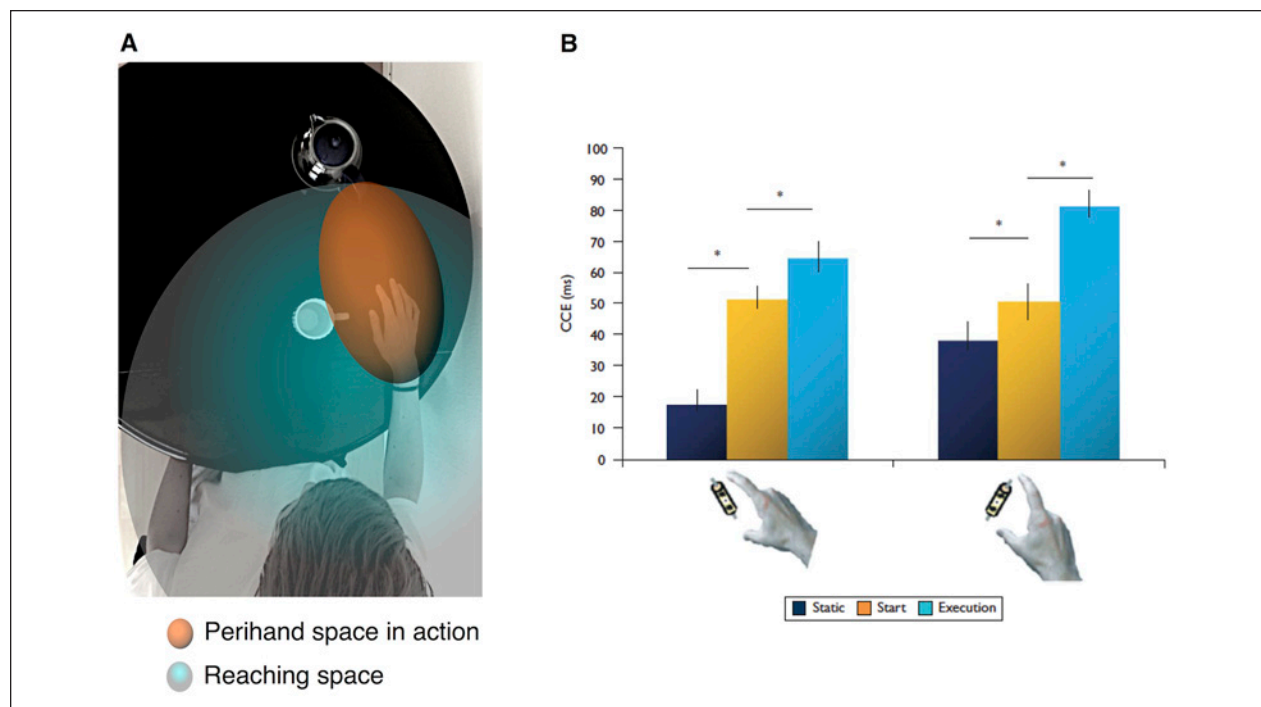


Figure 4. (A) Schematic representation of the modulation of the perihand space induced by an action. When reaching toward the tea pot in the figure, the motor program induces an online remapping of the hand-centered representation of space (orange halo in the figure). As a consequence, the visual information on the target location is interacting with the tactile information on the effector of the action. (B) The action induces a reweighting of multisensory processing as shown by a stronger visuo-tactile interaction measured at the onset of the action compared to a static condition. The increase is even more important when the visuo-tactile stimulation occurs in the early execution phase (200 ms after action starts). Modified from Brozzoli and others (2009).

was triggered by action execution, but also kept increasing during the early execution phase. This further online modulation of visuo-tactile performance suggests that the multisensory representation of the space around the hand might guide the action as it unfolds in time and space (Brozzoli and others 2010). In light of the scientific evidence described above, we suggest that the perihand space representation serves as a multisensory-motor interface for the hand-object interactions.

A Social Frame for the Hand-Centered Representation of Space: An Emerging New Perspective

Our everyday interactions with objects in the environment also include other people and their body, emotions and psychological state. Our peripersonal and perihand space are inevitably going to contact and overlap at least partially during simple transitive actions (i.e., action involving an object, like to put a glass of water into somebody's hand). To date, only few indirect attempts have shown a possible involvement of the multisensory peripersonal space representation in the guidance of motor interactions

between individuals (see de Vignemont 2013, for a recent review). The difficulty of such an investigation in animal models consists in training the monkeys to engage effectively in structured and experimentally valid social interactions. The challenging series of studies performed by Iriki's group is however very encouraging in showing an involvement of multisensory parietal areas in representing the space available for motor and social interactions between two monkeys (Fujii and others 2008; Yoshida and others 2011). In humans, the data available are even more sparse and limited to indirect behavioral evidence of the influence exerted by multisensory perception over social processing of others (Paladino and others 2010) and vice versa, of the influence of social variables on multisensory perception (Teneggi and others 2013). A behavioral study measuring the strength of the audio-tactile interaction in peripersonal space revealed that the representation of the region of space surrounding the body might be modulated by the presence of another person. Interesting, this modulation depended on the pleasantness of the interaction that occurred between the two individuals which is suggestive of a functional link to social cognitive processes (Teneggi and others 2013).

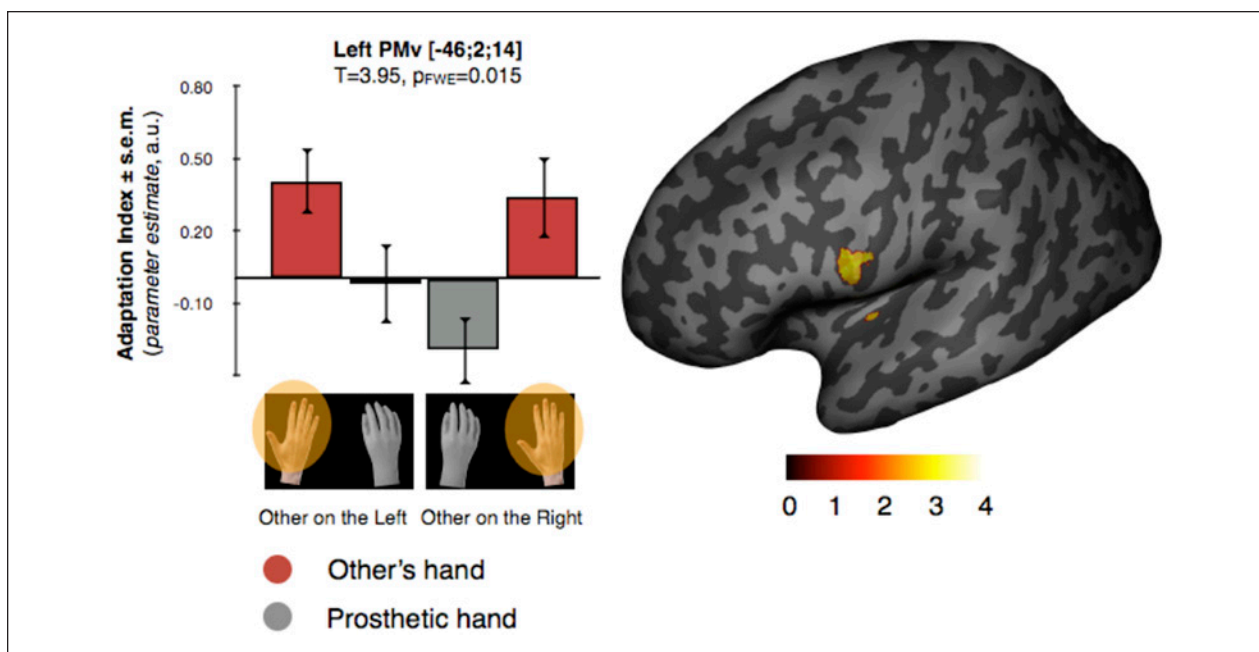


Figure 5. A shared neuronal representation of the perihand space for self and other in the left ventral premotor cortex (PMv). The left PMv showed stronger blood oxygen level–dependent (BOLD) adaptation to repeated perihand visual stimulation between self and other than between self and a prosthetic hand. The plots in the graph display the adaptation index for each condition, and error bars represent the SEM. Modified from Brozzoli and others (2013).

Recently, a neuroimaging study provided evidence of the existence of a shared representation of the peripersonal space for oneself and another person (Brozzoli and others 2013). By employing BOLD adaptation, a subset of neurons was discovered in the left ventral premotor cortex of the human brain displaying mirror properties. In other words, a subset of the neuronal populations in this area that display selectivity for an object near a person's own hand also displays the same selectivity for representing an object close to another person's hand (Fig. 5). This finding is in line with the discovery in the macaque of visuo-tactile populations of parietal neurons discharging when the monkey sees an object moving close to another individual's body (Ishida and others 2010). The shared premotor representation of perihand space could provide a common reference frame to interactively deploy spatial attention ("joint attention"; Williams and others 2005) and anticipate others' movements (Flanagan and Johansson 2003; Kilner and others 2004). Future studies should attempt demonstrate a functional link between the activity of these "peripersonal space mirror neurons" to changes in social cognitive functions.

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