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MULTISENSORY MECHANISMS OF BODY OWNERSHIP AND SELF-LOCATION

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Front cover: Arvid Guterstam demonstrating the “third arm illusion” (Guterstam, Petkova, Ehrsson, 2011, *PLoS ONE*) on neurologist and author Oliver Sacks (1933-2015), who subsequently related this experience in his book *Hallucinations* (page 300). Karolinska Institutet, Stockholm, 2012. Photo credit: Christopher Berger.

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MULTISENSORY MECHANISMS OF BODY OWNERSHIP AND SELF-LOCATION

THESIS FOR DOCTORAL DEGREE (Ph.D.)

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ABSTRACT

Having an accurate sense of the spatial boundaries of the body is a prerequisite for interacting with the environment and is thus essential for the survival of any organism with a central nervous system. Every second, our brain receives a staggering amount of information from the body across different sensory channels, each of which features a certain degree of noise. Despite the complexity of the incoming multisensory signals, the brain manages to construct and maintain a stable representation of our own body and its spatial relationships to the external environment. This natural “in-body” experience is such a fundamental subjective feeling that most of us take it for granted. However, patients with lesions in particular brain areas can experience profound disturbances in their normal sense of ownership over their body (somatoparaphrenia) or lose the feeling of being located inside their physical body (out-of-body experiences), suggesting that our “in-body” experience depends on intact neural circuitry in the temporal, frontal, and parietal brain regions. The question at the heart of this thesis relates to how the brain combines visual, tactile, and proprioceptive signals to build an internal representation of the bodily self in space.

Over the past two decades, perceptual body illusions have become an important tool for studying the mechanisms underlying our sense of body ownership and self-location. The most influential of these illusions is the rubber hand illusion, in which ownership of an artificial limb is induced via the synchronous stroking of a rubber hand and an individual’s hidden real hand. Studies of this illusion have shown that multisensory integration within the peripersonal space is a key mechanism for bodily self-attribution. In **Study I**, we showed that the default sense of ownership of one’s real hand, not just the sense of rubber hand ownership, also depends on spatial and temporal multisensory congruence principles implemented in fronto-parietal brain regions. In **Studies II and III**, we characterized two novel perceptual illusions that provide strong support for the notion that multisensory integration within the peripersonal space is intimately related to the sense of limb ownership, and we examine the role of vision in this process. In **Study IV**, we investigated a full-body version of the rubber hand illusion—the “out-of-body illusion”—and show that it can be used to induce predictable changes in one’s sense of self-location and body ownership. Finally, in **Study V**, we used the out-of-body illusion to “perceptually teleport” participants during brain imaging and identify activity patterns specific to the sense of self-location in a given position in space. Together, these findings shed light on the role of multisensory integration in building the experience of the bodily self in space and provide initial evidence for how representations of body ownership and self-location interact in the brain.

LIST OF SCIENTIFIC PUBLICATIONS

- I. Gentile, **Guterstam**, Brozzoli, Ehrsson (2013) Disintegration of multisensory signals from the real hand reduces default limb self-attribution: an fMRI study. *The Journal of Neuroscience*.
- II. **Guterstam**, Zeberg, Özçiftci, Ehrsson (2016) The magnetic touch illusion: a perceptual correlate of visuo-tactile integration in peripersonal space. *Cognition*.
- III. **Guterstam**, Gentile, Ehrsson (2013) The Invisible Hand Illusion: Multisensory Integration Leads to the Embodiment of a Discrete Volume of Empty Space. *Journal of Cognitive Neuroscience*.
- IV. **Guterstam** & Ehrsson (2012) Disowning one's seen real body during an out-of-body illusion. *Consciousness and Cognition*.
- V. **Guterstam**, Björnsdotter, Gentile, Ehrsson (2015) Posterior Cingulate Cortex Integrates the Senses of Self-Location and Body Ownership. *Current Biology*.

LIST OF ADDITIONAL PUBLICATIONS

Guterstam, Petkova, Ehrsson (2011) The illusion of owning a third arm. *PLoS ONE*.

Van der Hoort, **Guterstam**, Ehrsson (2011). Being Barbie: the size of one's own body determines the perceived size of the world. *PLoS ONE*.

Guterstam, Björnsdotter, Bergouignan, Li, Gentile, Ehrsson (2015) Decoding illusory self-location from activity in the human hippocampus. *Frontiers in Human Neuroscience*.

Guterstam, Abdulkarim, Ehrsson (2015). Illusory ownership of an invisible body reduces autonomic and subjective social anxiety responses. *Scientific Reports*.

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LIST OF ABBREVIATIONS

BOLD	blood-oxygen level dependent
fMRI	functional magnetic resonance imaging
FWHM	full-width-at-half-maximum
GLM	general linear model
HC	hippocampus
HMD	head-mounted display
IPS	intraparietal sulcus
MNI	Montreal Neurological Institute
MVPA	multivoxel pattern analysis
OBE	out-of-body experience
PCC	posterior cingulate cortex
PMv / PMd	ventral (v) and dorsal (d) premotor cortex
PPI	psychophysiological interaction
PZ	polysensory zone
RF	receptive field
ROI	region-of-interest
RSC	retrosplenial cortex
SCR	skin conductance response
SVM	support vector machine
TPJ	temporoparietal junction
VIP	ventral intraparietal area

1 INTRODUCTION

‘Listen,’ I said. ‘I don’t think you’re well. Please allow us to return you to bed. But I want to ask you one final question. If this—this leg—is not your left leg, then where is your own left leg?’

Once more he became pale—so pale that I thought he was going to faint. ‘I don’t know,’ he said. ‘I have no idea. It’s disappeared. It’s gone. It’s nowhere to be found...’

Oliver Sacks, *The Man Who Mistook his Wife for a Hat*

The body is a unique object in the world. Not only do we have access to it via our external senses—i.e., we can see it, hear it, and sometimes even smell it—we also feel it from the inside. Sensory receptors in muscles, tendons and joints convey information to the brain about the positioning of our limbs. Receptors in the skin signal sensations of touch. Feelings such as thirst, hunger, and emotional pain are diffuse and hard to spatially localize to a specific body part, but we refer them to within the boundaries of our own body. Despite the richness of our bodily awareness, it has historically attracted substantially less attention from psychologists and philosophers compared to, for instance, visual awareness. One might speculate that this state of affairs is due to the difficulty of studying bodily awareness, which, unlike vision, is not under voluntary control and is constantly present. For instance, I cannot actively choose to stop sensing my left arm, and there is no moment in our everyday lives when we are completely unaware of our body – as William James eloquently put it, “we experience a warm and intimate feeling of the same old body always there” (James, 1890). To the experimental psychologist, not being able to “turn on and off” the mental phenomenon under investigation (such as hearing a sound versus not hearing a sound) constitutes a major disadvantage to studying that phenomenon, which might explain why the brain processes underlying bodily awareness have remained relatively unexplored. Another complicating factor is that bodily awareness is a rather complex phenomenon, featuring multiple different aspects, such as modality-specific sensations (touch, proprioception, vestibular, and pain), interception (sensing the internal state of the body), bodily emotions (e.g., hunger, thirst, and tiredness), agency (the feeling of being in control of one’s actions), spatial self-perception (“where am I?”), and body ownership (“what am I?”). Because it is usually wise to start with trying to understand something simple at the

heart of a complex problem, this thesis aimed at characterizing the brain processes that underlie two basic aspects of bodily awareness: the feeling that the body belongs to the self (body ownership) and the sense of being located somewhere in space (self-location).

1.1 IS THERE A FEELING OF BODY OWNERSHIP?

When looking at our hands, we immediately recognize them as our own hands. The term “body ownership” refers to the feeling that the body belongs to the self. With the development of several paradigms of perceptual body illusions over the past two decades (Botvinick and Cohen, 1998; Ehrsson, 2007; Lenggenhager et al., 2007; Petkova and Ehrsson, 2008), bodily self-perception has become a lively research topic in experimental psychology and cognitive neuroscience. However, before delving into the neuroscientific literature on body ownership, it might be prudent to first ask a more basic and philosophical question: is there a feeling of body ownership (sometimes referred to as “mineness,” e.g., de Vignemont, 2015) in addition to the judgement of body ownership? According to de Vignemont, there are three main standpoints – the eliminativist, the reductionist, and the irreductionist view (de Vignemont, 2015). The eliminativist view (e.g., Bermúdez, 2011) argues that there is no intrinsic feeling of ownership that goes beyond the experience of the mere physical properties of the body. According to this view, I am aware of my right hand belonging to me in the sense that I know it, not in the sense that I feel it. The existence of body ownership illusions such as the rubber hand illusion, in which healthy participants report feeling ownership of an artificial limb even while acknowledging that it is not actually part of their own body (Botvinick and Cohen, 1998) (i.e., it is an illusion and not a delusion), provides a strong argument against this viewpoint. Conversely, there are cases of asomatognosia in which the patient lacks a feeling of ownership over their real limb but still acknowledges that it is indeed their own (Vallar and Ronchi, 2009). This dissociation between feelings and judgements of ownership seem to suggest that there is an experiential component of body ownership that goes beyond the mere judgement of ownership (De Vignemont, 2007; Peacocke, 2014). This argues in favor of the irreductionist view, which suggests that feelings of ownership are irreducible (Gallagher, 2005), or the reductionist view, which suggests that feelings of ownership can be reduced to other bodily experiences (De Vignemont, 2007).

The four most commonly held reductionist positions argue that feelings of ownership are grounded in (i) the sense of the spatial boundaries of one’s body within which one can feel sensations (Martin, 1995), (ii) the sense of agency (i.e., being in control) of the body (Gallese and Sinigaglia, 2010), (iii) the affective sense of familiarity with one’s own body

(de Vignemont, 2015), or (iv) a multisensory representation of the body. Position (i) seems implausible because it predicts that we cannot refer sensations to non-corporeal objects such as tools – which, in fact, we can (Maravita and Iriki, 2004)—and that asomatognosic patients would not be able to refer bodily sensations to their disowned limb—which, in some cases, they may:

Mr. S (addressing his doctor): ‘Don’t you see? This thing here [indicating his left arm]! The doctors have attached this tool to my body in order to help me move ... but it’s completely useless and very painful. I asked the nurses several times to take it away and put it in the cupboard!’ (Maravita, 2008)

In addition, the reported feelings of ownership of an artificial limb do not correlate well with recalibrations of our sense of limb position (Abdulkarim and Ehrsson, 2015; Rohde et al., 2011), which would be expected if ownership was entirely grounded in the spatial experience of one’s body. Position (ii) also appears unlikely given that the majority of paralyzed patients do not experience disownership of limbs that they are no longer in motoric control of. In addition, participants under certain conditions experience agency without ownership in the so-called moving rubber hand illusion (Kalckert and Ehrsson, 2012; Tsakiris et al., 2006). Position (iii), which states that the feeling of ownership is an “affective feeling that highlights the significance of the body for the self” and is grounded in a specific type of body schema that emphasizes bodily protection (de Vignemont, 2015), seems somewhat more plausible. This reductionist account of ownership asserts that syndromes of body disownership, such as somatoparaphrenia, could be interpreted as a bodily version of Capgras syndrome. Capgras patients can typically visually recognize their spouse for instance, but they lack the affective response of seeing their loved one and therefore believe that he or she is an impostor (Capgras and Reboul-Lachaux, 1923). In this framework, disownership associated with somatoparaphrenia results from an intact somatosensory system in the absence of an adequate affective response, while the illusory ownership of an artificial hand reflects the projection of affective significance to an external object, which is made possible by “tricking” the somatosensory system using multisensory stimulation. The observation that threatening a self-attributed artificial hand activates our affective systems in the form of increased sweating (Armel and Ramachandran, 2003) and brain activity in the cortical circuits for pain anticipation and fear (Ehrsson et al., 2007; Gentile et al., 2013; Guterstam et al., 2015a) supports an intimate relationship between reported sensations of body ownership and affective responses. The feeling of ownership of an artificial limb or full-body *per se* has consistently been associated with activity in

primarily non-affective brain regions, such as the premotor and posterior parietal cortices and the putamen (Ehrsson et al., 2004; Guterstam et al., 2015a; Petkova et al., 2011a), which could be interpreted as the dynamic updating of our “protective body schema” within this framework. However, this theory does not account for the fact that a mother holding her child does not experience the child’s body as her own body even though she probably assigns a great deal of affective significance to the child’s body and would perform automatic protective actions if the child’s body were subjected to a physical threat (e.g., an incoming projectile). This argument might speak against the view that ownership merely reflects the “affective coloring” of the experiences relating to an object. Finally, the reductionist position (iv) states that the feeling of body ownership is grounded in a multisensory representation of the body (Ehrsson, 2012), which is constructed and maintained according to specific principles of multisensory integration. Support for this model can be drawn from both the literature on neurological lesions, which shows that deficits in ownership and multisensory processing often co-occur and involve the same set of brain regions (Blanke et al., 2004; Vallar and Ronchi, 2009), and the vast body of research on ownership illusions, which has demonstrated that feelings of owning an artificial limb are determined by basic multisensory congruence rules (Botvinick and Cohen, 1998; Stein and Stanford, 2008). As the remainder of this thesis will demonstrate, the multisensory hypothesis is strongly supported by experimental data related to the process of attributing real and artificial limbs to the self.

However, we can experience ownership of our body even in the absence of multisensory integration, for instance, in cases when the brain only has access to sensory information from a single modality (e.g., when we have our eyes closed and receive no tactile input, relying solely on proprioception) or no sensory input at all (an amputee experiencing a phantom limb). Thus, the feeling of body ownership cannot be reduced to multisensory integration *per se*. Instead, these ownership sensations must emerge from an internal multisensory representation of the body that is continuously *updated* via integration processes and that is maintained even when integration is not actively taking place. A strength of this hypothesis is its simplicity and strong empirical support. However, for this model to explain, for instance, why we do not experience bodily ownership over tools, one needs to stipulate a “test-to-fit” criterion specifying that the multisensory body representation only incorporates body-like objects (Tsakiris, 2010). This *ad hoc* hypothesis reduces the explanatory value of the multisensory model because it appears to partly assume its conclusion.

In summary, feelings of body ownership cannot be easily reduced to other bodily experiences while still accounting for all of the special cases of limb ownership and disownership described in the neurological and neuropsychological literature. However, regardless of whether body ownership is an irreducible feeling or, perhaps, is reducible to a genuine multisensory percept or sense of affective significance, the enterprise of examining its underlying neural mechanisms, which sometimes involves asking participants to rate their subjective feelings of body ownership, remains meaningful. In the following sections I will summarize the neuropsychological, neurological, and neuroscientific attempts to answer the following questions: What makes us feel that our body is our own? How does this feeling relate to our sense of self-location? To understand how the brain represents the body and its spatial context, a good start is to review the basic neurophysiological research on “multisensory integration,” which has heavily influenced the modern study of perception in general and bodily self-consciousness in particular.

1.2 MULTISENSORY INTEGRATION

Sensory processing and perception has long been studied in both psychology and neuroscience. Historically, most studies have focused on investigating one sensory modality at a time (e.g., vision, touch, hearing, or proprioception). However, situations in our everyday lives often stimulate multiple sensory modalities at the same time. For instance, we both see and feel a glass of water in our hand, and both see and hear a tennis ball hitting a garage door. Although our sensory systems convey a staggering amount of information—both signal and noise—to our brain, it manages to filter out the noise and integrate subsets of signals from different senses to create meaningful percepts of our body and the external world. The term multisensory integration refers to the mechanisms by which the brain merges information across sensory modalities to enhance the salience (“perceptual importance”) of biologically meaningful events (Stein and Stanford, 2008). Until relatively recently, the mechanisms by which the brain accomplishes this feat were largely unknown. However, in the 1980s, neurophysiologists Barry Stein and Alex Meredith characterized the first multisensory neurons in cats in their pioneering studies of the deep layer of the superior colliculus, which is a structure in the posterior mesencephalon that is involved in guiding eye movements. Although earlier experiments had found neurons that responded to multiple sensory modalities (Bastian, 1982; Stein and Arigbede, 1972), Stein & Meredith identified neurons that not only responded to multisensory stimuli but also integrated cross-modal signals in a very specific manner. The response of these neurons to visual and auditory stimuli greatly exceeded the sum of the responses to each

sensory modality alone provided that the stimuli occurred within a specific temporal window and that they originated from approximately the same region of external space (Meredith and Stein, 1983). This response property was referred to as superadditivity, and it is now considered a hallmark of multisensory integration because it provides a neuronal mechanism by which the brain enhances the salience of biologically meaningful events (Driver and Noesselt, 2008; Stein and Stanford, 2008).

Over the years, multisensory neurons have been identified in multiple species, including non-human primates (Avillac et al., 2005, 2007) and humans (Serenó and Huang, 2006). As a general rule, it has been shown that the signals from two sensory modalities are much more likely to be integrated if they occur within a specific time window and if they originate from the same region of the body or external space. These two principles are commonly referred to the spatial and temporal rules of multisensory integration (Stein and Stanford, 2008). Together with the rule of inverse effectiveness, which states that the magnitude of multisensory integration is proportionally the greatest when the cross-modal stimuli are the weakest (Stein and Stanford, 2008), these principles play an important role in the construction and maintenance of a stable perception of the world.

1.3 THE REPRESENTATION OF PERIPERSONAL SPACE

Several regions have been identified in the (non-human) primate brain that are related to the neuronal integration of cross-modal signals originating from the body. These neuronal populations integrate visual, tactile, and proprioceptive signals and have been found in the putamen (Graziano and Gross, 1993) and the premotor (Graziano et al., 1997; Rizzolatti et al., 1981) and posterior parietal cortices (ventral intraparietal area, VIP, and area 7B) (Avillac et al., 2007; Graziano, 2000), all of which receive convergent inputs from primary sensory areas (Figure 1) and have strong anatomical interconnections. Intriguingly, populations of neurons in these regions do not only represent the body itself but also respond to visual (and sometimes also auditory; see Graziano et al., 1999) stimuli that originates within the space surrounding the body—the region constituting the so-called peripersonal space (Brozzoli et al., 2014). Single-unit recordings in macaques have identified trimodal neurons that have visual receptive fields (RFs) that extend up to 40 cm from a tactile RF (Fogassi et al., 1996), follow changes in limb position (Graziano, 1999) and are independent of the direction of gaze (Graziano and Gross, 1998). Thus, the visual RFs of these neurons are spatially anchored to the limb (Graziano, 1999). Collectively, these neuronal populations build representations of the body and its surrounding peripersonal space and encode objects close to the body in body-centered spatial reference

frames (Graziano and Botvinick, 2002). One might ask why such a representation would be adaptive. One possible reason comes from invasive studies performed in macaques demonstrating that neurons in the VIP and the polysensory zone (PZ) in the premotor cortex respond selectively to stimuli signaling a potential threat to the body surface. In fact, electrical microstimulation of the same cortical regions evoke movements that are typical of defensive reactions (Cooke et al., 2003; Graziano and Cooke, 2006). The multisensory representation of peripersonal space is thus considered to be important for defensive behavior, the sensory guidance of limb movements and the localization of body parts (Brozzoli et al., 2014; Graziano, 1999; Graziano and Botvinick, 2002).

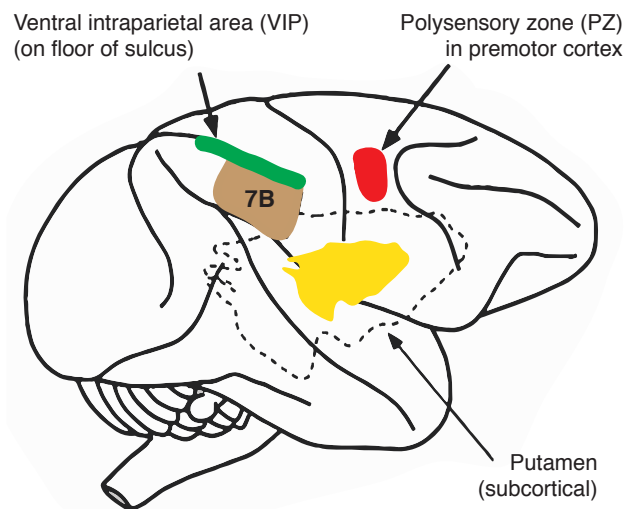


Figure 1. Multisensory regions in the macaque brain in which neurons that integrate visual, tactile, and proprioceptive signals within peripersonal space have been identified. Adapted from Graziano et al (2004).

The evidence for a similar representation of peripersonal space in humans is primarily based on results from neuropsychological studies of patients with deficits caused by brain lesions (Brozzoli et al., 2014; Làdavas and Farnè, 2004). For example, it has been shown that spatial neglect – the failure to perceive stimuli originating from the contralesional space – can selectively affect the space near or far from the body (Cowey et al., 1994; Halligan and Marshall, 1991). Furthermore, cross-modal extinction – the failure to perceive a sensory stimulus originating from the contralesional space when a stimulus for another sensory modality is presented in the ipsilesional space – can specifically affect the space close to the patient’s body (di Pellegrino et al., 1997). In healthy individuals, similar cross-modal interference effects specific to the near-personal space have been found using so-called visuo-tactile congruency tasks (Holmes et al., 2004; Serino et al., 2011; Spence et al., 2004a, 2004b), providing further support for the existence of a special representation of peripersonal space in humans. Thus, even though a wealth of research suggests that

peripersonal space has a very special representation in the brain, from a phenomenological point of view, the space close to our hands does not “feel” different than the space outside our reach, and none of the experimental paradigms listed above provide a mechanism by which a patient or participant could consciously perceive a specific perceptual “object” that corresponds to visuo-tactile integration in peripersonal space. In **Study II** of this thesis, we characterize a new perceptual illusion in which healthy participants perceive a “magnetic force” between the surface of a rubber hand and an object moving in empty space above it, and we provide converging behavioral evidence for the notion that this illusion constitutes a perceptual correlate of visuo-tactile integration in peripersonal space (see Section 5 for details).

Numerous neuroimaging studies in humans provide evidence for the convergence of visual, tactile, and proprioceptive stimuli onto fronto-parietal and subcortical regions (Beauchamp et al., 2010; Gentile et al., 2011; Hadjikhani and Roland, 1998; Huang et al., 2012; Lloyd et al., 2003; Makin et al., 2007; Saito et al., 2003; Sereno and Huang, 2006), which are thought to be homologous to the multisensory areas VIP, 7B, and PZ in the monkey brain (Figure 1; although it should be noted that direct inter-species comparisons should be interpreted with caution; see Grefkes and Fink, 2005; Culham and Valyear, 2006). However, it has remained unclear whether the integration of visual-tactile-proprioceptive stimuli in these areas follows the spatial and temporal rules of multisensory integration, which prompted us to conduct **Study I** of this thesis (see Section 5). A few studies have provided evidence for the existence of a representation of perihand space (Brozzoli et al., 2011, 2012; Makin et al., 2007). The most convincing demonstration of this was conducted by Brozzoli & Gentile and colleagues, who found that the repeated presentation of an object close to one’s hand, as opposed to “far” from the hand but still within reach, is associated with an increase in fMRI-adaptation in the intraparietal and premotor cortices and the putamen (Brozzoli et al., 2012). This fMRI-adaptation was independent of the position of the hand, as if a visual RF were anchored to the limb. These results suggest that multisensory premotor, intraparietal and putamen regions preferentially respond to visual stimuli close to one’s hand, effectively encoding the location of objects within the peripersonal space in hand-centered spatial reference frames (Brozzoli et al., 2012).

In summary, a wealth of research has demonstrated that a specific set of brain regions, namely, the premotor and intraparietal cortices and the putamen, integrate multisensory stimuli from the body and its surrounding (peripersonal) space. Because the peripersonal space represents a multisensory boundary zone between the body and the external world, it

has been suggested that the neuronal machinery underlying the representation of this space might also be involved in the self-attribution of one's limbs. Two separate lines of research are especially relevant to testing this hypothesis: the study of patients with neurological impairments in their normal sense of limb ownership following brain lesions and the study of dynamic changes in the sense of limb- and full-body ownership using perceptual illusions in healthy participants.

1.4 DISORDERS OF BODY OWNERSHIP

The notion that the feeling of body ownership is a central construct that depends on intact neural circuitry in specific brain regions is not new. In 1942, neurologist Josef Gerstmann reported two cases of patients with lesions of the right hemisphere who suffered, in addition to the well-known motor and somatosensory deficits, from delusional beliefs that the limbs on their left side were not part of their own bodies; a syndrome he named somatoparaphrenia (Gerstmann, 1942). Somatoparaphrenia has been described in numerous studies since and is characterized by delusional beliefs concerning the contralesional side of the patient's body, most commonly manifesting as disownership of the limbs on the left side (e.g., the opening quote from one of Oliver Sacks' patients) (Arzy S et al., 2006; Feinberg et al., 2010; Gerstmann, 1942; Vallar and Ronchi, 2009). This experience of disownership persists despite providing evidence to the patients that suggests otherwise, which distinguishes somatoparaphrenia from the related syndrome asomatognosia (Critchley, 1953; Feinberg et al., 2010; Vallar and Ronchi, 2009). Somatoparaphrenia is often but, importantly, *not always* accompanied by motor and somatosensory deficits, as well as hemispatial neglect (Vallar and Ronchi, 2009). The neuroanatomical basis for somatoparaphrenia and other related syndromes has been difficult to determine with great precision because of the substantial variation in the location of the lesions across studies. Limb disownership has been associated with lesions in the frontal, temporal, and parietal lobes (Feinberg et al., 2010; Vallar and Ronchi, 2009), as well as with damage in subcortical structures such as the posterior insula (Baier and Karnath, 2008) and basal ganglia (Halligan et al., 1993). However, the somatoparaphrenia is much more likely to manifest after right-brain lesions (Blanke, 2012; Feinberg et al., 2010; Vallar and Ronchi, 2009). In fact, one study using injections of amobarbital in the right carotid artery, which results in the temporary inactivation of the entire hemisphere, reliably induced somatoparaphrenia in 82% of the patients (Meador et al., 2000).

The existence of somatoparaphrenia suggests that a functioning sense of body ownership requires intact neural processing in the above-mentioned circuits. However, the most

informative results for understanding the mechanisms by which the brain attributes ownership sensations to limbs come from the study of perceptual body illusions in healthy participants.

1.5 FROM SINGLE LIMB- TO FULL-BODY ILLUSIONS

In 1998, psychologists Matthew Botvinick and Jonathan Cohen re-discovered an old magic trick in which healthy participants are made to feel that an artificial hand is part of their own body (Botvinick and Cohen, 1998). To induce this illusion, the participant observes a rubber hand being touched in synchrony with identical touches applied to their real hand, which is hidden from view behind a screen. This procedure creates an illusion that the applied touches are felt on the rubber hand and that the rubber hand is suddenly part of one's own body, while the real hand fades from consciousness. They named this phenomenon the "rubber hand illusion," and this experimental paradigm has become an important tool for investigating the mechanisms underlying the sense of body ownership over the past two decades. A wealth of behavioral and psychophysiological evidence, primarily from subjective questionnaires, skin conductance responses (SCRs) evoked by physical threats toward the rubber hand, and pointing errors in intermanual pointing tasks (see Section 4 for details), suggests that the illusion results from the integration of visual, tactile and proprioceptive signals in hand-centered reference frames within the peripersonal space (Blanke, 2012; Ehrsson, 2012; Makin et al., 2008; Tsakiris, 2010). It has been shown that to elicit the illusion, the visual stimulation of the rubber hand and the tactile stimulation of the real hand must be temporally synchronous (Botvinick and Cohen, 1998; Ehrsson et al., 2004; Tsakiris and Haggard, 2005), and the stimuli must be applied in the same directions in hand-centered coordinates (Costantini and Haggard, 2007). In addition, and the rubber hand needs to be spatially matched with the real hand in terms of laterality (Holmes et al., 2006; Tsakiris and Haggard, 2005; Tsakiris et al., 2008), anatomical orientation (Costantini and Haggard, 2007; Ehrsson et al., 2004; Pavani et al., 2000; Tsakiris and Haggard, 2005), and visual appearance (e.g., the illusion cannot be elicited using a block of wood) (Haans et al., 2008; IJsselstein et al., 2006; Tsakiris and Haggard, 2005; Tsakiris et al., 2010). The rubber hand must also be placed within the theoretical limits of the peripersonal space of the real hand (Lloyd, 2007; Preston, 2013). In accordance with these behavioral results, which suggest that ownership of the rubber hand is a consequence of multisensory integration, functional brain imaging studies have found that the illusion is associated with increased activity in multisensory areas in the premotor and posterior parietal cortices (Ehrsson et al., 2004, 2005, 2007; Limanowski and

Blankenburg, 2015), with the magnitude of the neural response in the ventral premotor cortex (PMv) best reflecting the subjective sense of ownership (Ehrsson et al., 2004). Notably, this set of areas is analogous to the regions in which multisensory neurons associated with the peripersonal space have been identified in the macaque brain, which is consistent with the hypothesis that multisensory integration within the peripersonal space is a mechanism underlying body ownership (Makin et al., 2008). In **Study I**, we extended and validated these results for the real hand by showing that decreased multisensory congruence leads to a stronger sense of hand disownership, which is reflected in a corresponding decrease in neural activity in multisensory regions. Furthermore, the results of **Study III** challenge the claim that an object with a limb-like appearance is necessary for eliciting illusory ownership by characterizing a counter-intuitive illusion in which multisensory stimulation leads to the perception of having an invisible, “phantom-like” hand.

Previous studies have shown that multisensory ownership illusions are not limited to single limbs and that they can be extended to an entire artificial body, commonly referred to as “full-body illusions” (Ehrsson, 2007; Lenggenhager et al., 2007; Petkova and Ehrsson, 2008; Petkova et al., 2011a). In one such illusion, referred to here as the “mannequin illusion,” the participants observe a mannequin’s body being touched by an object through a set of head-mounted displays (HMDs) while receiving correlated tactile stimulation on their real body. This procedure results in the illusory experience that the mannequin is one’s own body (Maselli and Slater, 2013; Petkova and Ehrsson, 2008), which is reflected by increased neural activity in the same set of multisensory areas that are involved in the rubber hand illusion (Petkova et al., 2011a). In addition to following the same spatial and temporal multisensory congruence rules that govern the rubber hand illusion, the successful elicitation of the mannequin illusion is dependent on viewing the artificial body from the first-person visual perspective (Petkova et al., 2011a, 2011b). Interestingly, the specific body part of the mannequin that is stimulated (arm, belly, or foot) does not matter, since behavioral and neuroimaging results show that the ownership illusion “spreads” across body segments (Gentile et al., 2015; Petkova et al., 2011a). Phenomenologically, this finding is consistent with the notion that our sense of full-body ownership is a coherent unified experience rather than the sum of ownership-sensations over individual limbs and body parts.

In what way are these perceptual body illusions relevant to the main goal of this thesis, namely, investigating the relationship between the senses of body ownership and self-location? One way is illustrated by a particularly interesting full-body illusion, the so-called

“out-of-body illusion” (Ehrsson, 2007), in which the spatial context of the illusory body is experimentally manipulated. This offers a way to study the link between bodily and spatial self-perception. In this experiment, the participants sit on a chair and wear a set of HMDs. Through the HMDs, they view a real-time 3-D video feed from a pair of cameras located 2 m behind their backs (Figure 2). To induce the illusion, the experimenter synchronously touches the participant’s chest, which is hidden from view, and the space just below the field of view of the cameras with two identical small rods. This mode of visuo-tactile stimulation leads to the illusory experience of being physically located at the position of the cameras, which is supported by questionnaire data and by SCRs evoked by threatening the “illusory body” with a sledgehammer (Ehrsson, 2007). Crucially, the delivery of asynchronous touches significantly reduces the vividness of the illusion, allowing for the comparison of otherwise equivalent conditions (Ehrsson, 2007). In **Study IV**, we reproduced and extended the results of Ehrsson (2007) by quantifying the effect of the illusion on spatial self-perception using a behavioral self-location task and examining how the illusory experience affects the representation of the seen real body. In **Study V**, we adapted the out-of-body illusion for use in an MRI scanner and studied the neural interplay between the senses of body ownership and self-location. The results of Study V are relevant to the literature on representations of the spatial environment in the brain, which, historically, has focused mostly on spatial navigation in animals, virtual navigation during neuroimaging in humans, and a limited number of case reports on out-of-body experiences (OBEs) in patients.

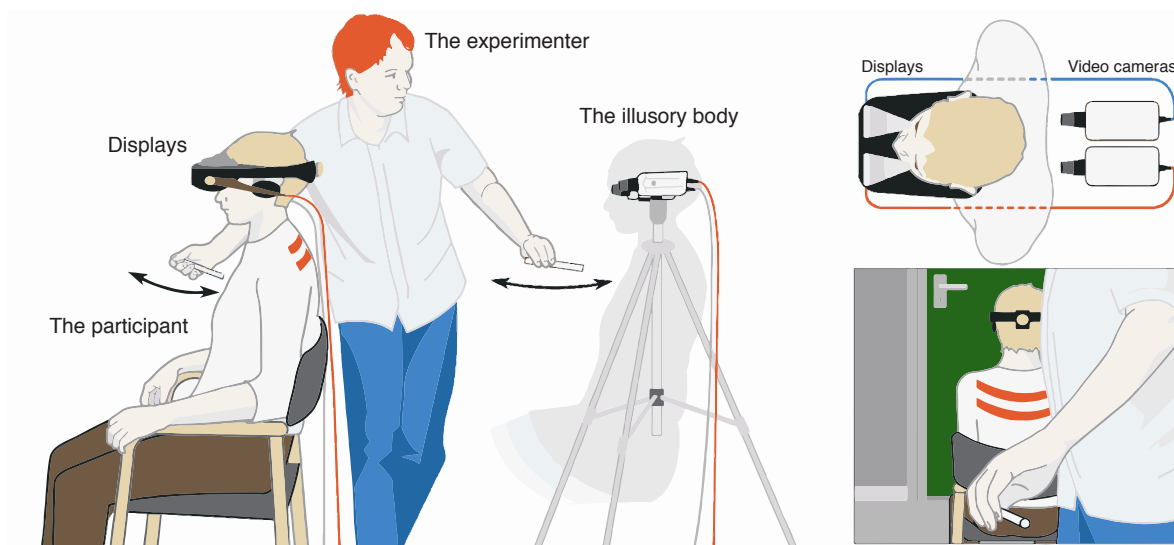


Figure 2. Experimental setup of the out-of-body illusion (Ehrsson, 2007).

1.6 THE SENSE OF SELF-LOCATION AND ITS RELATION TO BODY OWNERSHIP

We do not experience our body in isolation from its spatial environment. We experience the body as a physical entity with a specific location in the external space, and we perceive the world from within our bodies, from a spatial origin located within the skull at some distance behind the eyes. The mechanisms by which the brain builds and maintains this fundamental subjective experience of being located somewhere in space have long been a central topic of discussion for philosophers and psychologists. In the late 1800s and early 1900s, Ernst Mach emphasized the importance of our first-person visual perspective (Figure 3; Mach, 1903), which was later reiterated in the works of James Gibson (Gibson, 1986). However, they provided little empirical support for these claims. What if the first-person visual perspective could be experimentally changed—for instance, let us assume that the output signals from my retina could be wirelessly transmitted to your optical nerve—would your sense of self-location be instantly transferred to mine? Would your brain assume ownership over my body, from which you now view the world? These previously hypothetical questions have only recently become accessible to experimental psychologists and cognitive neuroscientists with the advent of advanced virtual and video reality technology and human brain imaging methods. Nevertheless, the basic mechanisms by which the brain represents the spatial environment have been a lively topic of research in neuroscience for almost half a century, probably due in large part to an unexpected discovery of specific neurons in the hippocampus of freely moving rats.

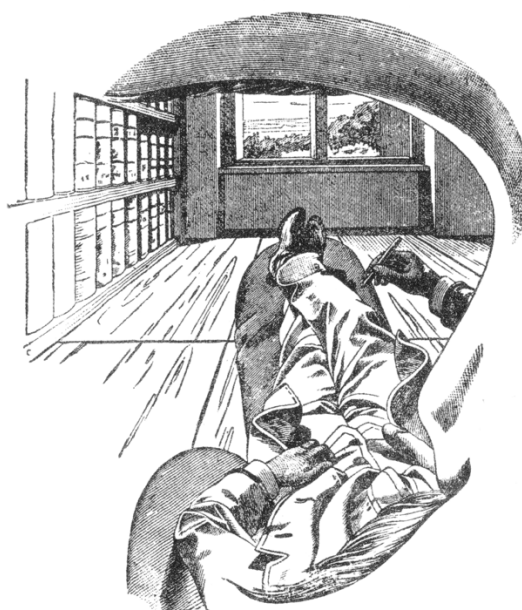


Figure 3. "Picturing the Visual Field" by Ernst Mach (Mach, 1903).

In 1971, neurophysiologists John O'Keefe and Jonathan Dostrovsky published a seminal paper in which they described neurons in the rat hippocampus that fired when the animal occupied a particular location in a spatial environment (O'Keefe and Dostrovsky, 1971). The activity of these neurons, appropriately named "place cells," was GPS-like; they fired at a given spatial location regardless of the rat's head orientation or visual input. It was therefore proposed that the hippocampus is involved in building a cognitive map of the spatial environment, in which the individual's location is represented in an allocentric (i.e., with respect to external or world-based coordinates) fashion (O'Keefe and Nadel, 1978). The behavioral advantage of this representation was later demonstrated in the famous Morris water maze experiment, in which hippocampal lesions resulted in dramatically impaired performance in a task where freely swimming rats tried to find a hidden platform that could normally be located using memory of spatial landmarks (Morris, 1981; Morris et al., 1982). These results suggest that the spatial representation in the hippocampus plays a role in facilitating ecological behaviors such as spatial navigation and memory (Andersen, 2007). In addition to place cells, other neurons coding for different aspects of spatial localization have been identified, the most important being the "grid cells" in the entorhinal cortex (Hafting et al., 2005) and the "head-direction cells" in the subiculum (Chen et al., 1994; Sargolini et al., 2006). One of the main functions of this neuronal machinery in the medial temporal lobe is considered to be the support of "path integration," which refers to the process of keeping track of the individual's position in the environment by integrating linear and angular self-motion cues (Moser et al., 2008) (i.e., the brain mechanism that allows you to keep track of your spatial location if you were to close your eyes and walk around in the room you are currently in). Over the recent decades, a large body of research in multiple species, including humans, has shown that the hippocampus plays an important role in episodic and spatial memory (Burgess et al., 2002; O'Keefe and Nadel, 1978), spatial navigation (Hassabis et al., 2009; Howard et al., 2014; Maguire et al., 1997), and spatial mental imagery (Lambrey et al., 2012; Marchette et al., 2014).

In addition to the hippocampus and entorhinal cortex, a number of regions that are anatomically highly interconnected with the medial temporal lobe (Kravitz et al., 2011) have been shown to play important roles in building a representation of the spatial environment. These include posterior midline structures such as the precuneus, the retrosplenial (RSC) and posterior cingulate cortices (PCC), and the intraparietal sulcus (IPS) (Burgess, 2008; Maguire et al., 1998; Moser et al., 2008). Studies on spatial memory and navigation have shown that the human brain uses both egocentric (i.e., body-centered spatial coordinates) and allocentric representations of space and that regions in the medial

temporal lobe contribute primarily to allocentric representations, parietal areas contribute to egocentric representations, and the posterior cingulate cortex seems to be involved in transitioning between the parietal egocentric and medial temporal allocentric reference frames (Burgess, 2006, 2008; Vann et al., 2009).

The vast majority of neuroimaging studies in humans have been based on virtual navigation, mental imagery, or spatial memory tasks. A few of these studies have specifically examined representations of self-location. For instance, two studies decoded the target locations in a virtual navigation task and found significant activity in the hippocampus and the posterior parietal region (Hassabis et al., 2009; Rodriguez, 2010). However, it remains unclear how these spatial representations relate to the perceptual experience of self-location and how they interact with the multisensory representations of one's own body. Important clues related to this question can be found in the literature on OBEs of neurological origin. Studies of patients suffering from focal epilepsy or undergoing electrical brain stimulation during neurosurgery have shown that abnormal activity in the temporal and parietal areas, most commonly in the posterior superior temporal and angular gyri, can sometimes result in the experience of seeing one's body and the world from a location outside the physical body, which defines an OBE (Blanke, 2012; Blanke et al., 2002, 2004, 2015; Brugger et al., 1997; De Ridder et al., 2007; Heydrich and Blanke, 2013). In addition to a change in the origin of their visuo-spatial perspective, these patients almost invariably report some type of vestibular sensation, such as rotating in space (Blanke et al., 2004). Interestingly, a previous fMRI study using a perceptual illusion in healthy participants based on visuo-tactile stimulation examined the interaction between self-location and the perceived directionality of the first-person visual perspective and presented evidence for the involvement of the bilateral temporoparietal junction (TPJ) (Ionta et al., 2011). However, this study did not specifically address the interplay between the senses of ownership and self-location, and studies on lesions are seldom informative with respect to the underlying perceptual mechanisms because the lesions are typically large and damage multiple areas of interest along with the underlying white matter. In **Study V**, we investigated the relationship between representations of self-location and body ownership by making use of an out-of-body illusion (Ehrsson, 2007). The behavioral results from **Study IV** demonstrate that the manipulation of visuo-tactile synchrony results in predictable changes in the senses of ownership and self-location. Specifically, synchronous visuo-tactile stimulation was associated with a strong sense of ownership of the new "illusory body," disownership of the seen real body, and a strong sense of self-location at the position of the cameras, whereas asynchronous stimulation was coupled with a

decreased sense of ownership of the new “illusory body,” less disownership of the real body, and a strong sense of self-location at the actual position of the physical body (Figure 2). These behavioral properties of the out-of-body illusion, in conjunction with the observation that the strength of the ownership and self-location illusions varied across participants (Guterstam and Ehrsson, 2012), allowed us to examine the neural activity related to ownership and self-location and the interaction between these perceptions in **Study V**.

2 AIMS

The general aim of this thesis was to investigate the role of multisensory integration in generating the feeling that the body is part of the self (body ownership) and the experience of being located in a given position in the environment (self-location).

2.1 STUDY I AIM

- Study I examined whether specific multisensory regions in the human brain integrate visual, tactile, and proprioceptive signals from one's real hand according to basic multisensory integration principles relating to spatial and temporal congruence and how this integration process relates to the default feeling of limb ownership.

2.2 STUDY II AIM

- Study II aimed at elucidating the relationship between multisensory integration within peripersonal space and the sense of limb ownership by studying a new perceptual illusion that allows healthy participants to experience an illusory magnetic force in the space close to an artificial hand.

2.3 STUDY III AIM

- Study III investigated the role of vision in bodily self-attribution. Specifically, this study characterized a novel perceptual illusion in which healthy participants are made to experience an invisible hand as part of themselves, challenging the assumption that visual input from a limb-like object is necessary for inducing changes in the sense of limb ownership.

2.4 STUDY IV AIM

- The goal of Study IV was to estimate the effects of the out-of-body illusion on the sense of self-location and feelings of (dis)ownership of the seen real body.

2.5 STUDY V AIM

- Study V aimed at characterizing the neural correlates of full-body ownership, the sense of self-location, and their functional interplay. Specifically, we used the out-of-body illusion to perceptually teleport participants during high-resolution brain imaging and employed a multivoxel pattern analysis (MVPA) to decode their perceived self-location from neural activity patterns across the whole brain.

3 METHODS

3.1 PARTICIPANTS

A total of 360 healthy human volunteers participated in the **Studies I-V**. All participants were naïve to the purpose and specific hypotheses of the experiment in question. Informed consent was obtained prior to the experimental sessions. The Regional Ethical Review Board of Stockholm approved all of the experimental procedures.

3.2 QUESTIONNAIRES

Arguably, the most direct method of quantifying conscious experiences are verbal reports by the subjects themselves. In **Studies I-V**, we quantified the subjective experiences associated with the illusions under investigation by using questionnaires that were presented at the end of each experimental condition. In the brain imaging experiments in **Studies I, III, and V**, in which each experimental condition was repeated multiple times during the scanning sessions, we administered the questionnaires immediately after the conclusion of the brain imaging acquisition in a separate session in which we repeated each condition once. The design of the questionnaires was based on the original rubber hand illusion study (Botvinick and Cohen, 1998), which has been widely used and validated in studies of body ownership illusions (Ehrsson, 2007; Ehrsson et al., 2004; Ionta et al., 2011; Longo et al., 2008; Moseley et al., 2008; Tsakiris and Haggard, 2005). In general, the participants were asked to affirm or deny different statements reflecting potential perceptual effects using a seven-point Likert scale that ranged from -3 to +3. The participants were informed that -3 indicated “I completely disagree,” +3, indicated “I agree completely,” and 0 indicated “I do not know, I can neither agree nor disagree.” Half of the statements were designed to probe the perceptual effects of the illusion in question (referred to as “illusion” or “test” statements); the other half of the statements were used to control for suggestibility and task-compliance (“control” statements). By statistically analyzing the difference in ratings between the illusion and control statements and comparing this difference across conditions, we were able to achieve a robust estimate of the illusion-specific effects, correcting for the more general effects of suggestibility and task-compliance.

Subjective evaluations are susceptible to task-compliance (the participants tend to report what they believe the experimenter wants them to report) and suggestibility (the behavior of the experimenter influencing the reports of the participants). To minimize these effects, we carefully designed the experiments and the questionnaires to include appropriate control statements, control conditions, and importantly, we always combined questionnaire data

with more “objective” behavioral measurements, such as the degree of proprioceptive drift or threat-evoked SCRs detailed below. The control statements were designed to be as semantically similar to the illusion statements as possible, but they described a perceptual effect that we did not expect to occur. The aim of the control conditions was to alter one key factor (e.g., the synchrony or spatial congruence of the seen and felt touches) that we hypothesized would be crucial for eliciting the illusion, while keeping all other experimental factors constant.

3.3 PROPRIOCEPTIVE DRIFT

One of the most commonly used behavioral proxies of ownership in the context of the rubber hand illusion is the so-called proprioceptive drift. This refers to the systematic pointing errors toward the position of the rubber hand that participants make when they are blindfolded after the illusion has been induced and are asked to point to where their hand is located using the contralateral hand (i.e., the hand that is not involved in the experiment). It has been shown that the classical rubber hand illusion is associated with a proprioceptive drift toward the location of the rubber hand (Botvinick and Cohen, 1998; Tsakiris and Haggard, 2005) and that greater proprioceptive drift is associated with higher ratings of feelings of ownership for the observed hand (Botvinick & Cohen, 1998; Tsakiris & Haggard, 2005). However, recent studies have observed a dissociation between subjectively reported feelings of ownership and proprioceptive drift responses, suggesting that the two phenomena rely on separate underlying mechanisms (Rohde, Di Luca, & Ernst, 2011).

We used measurements of proprioceptive drift to provide additional behavioral evidence for the magnetic touch illusion in **Study II** and the invisible hand illusion in **Study III**. In both studies, each experimental condition was repeated three times. Between each period of stroking, there was a resting period of one minute. Immediately before and after each period of brushing, the participants were asked to close their eyes and indicate the position of their right index finger by pointing at it with their left hand (we always used a right rubber hand). Prior to obtaining this response, the experimenter placed the participant’s left index finger at one of three fixed starting points (the starting points were different for each repetition of a given condition, and the order was balanced across subjects) on a 1-m metal ruler (the ruler’s markings were visible only to the experimenter) positioned at a fixed distance above the table and in front of the participant’s body. Next, the experimenter asked the participants to move their finger briskly along the ruler (which contained a shallow groove) and stop when their finger was immediately above where they felt their right index finger was located.

In the statistical analyses, we computed the differences in pointing errors (toward the rubber or invisible hand) between the measurements obtained before and after each stimulation period. The average of these differences over the three repetitions constituted the proprioceptive drift for a given experimental condition within each participant. We analyzed the differences between conditions at the group-level by comparing the mean proprioceptive drift values between the conditions of interest using paired *t*-tests or repeated measures ANOVAs when the data were parametrically distributed and Wilcoxon-signed rank tests or Friedman tests when the data were non-parametrically distributed.

3.4 THREAT-EVOKED SKIN CONDUCTANCE RESPONSES

An established psychophysiological proxy of illusory body ownership is the threat-evoked SCR. The use of this measure is based on the assumption that if an artificial limb is truly incorporated into one's body representation, an increased fear response should occur when viewing the now self-attributed limb being subjected to a physical threat, such as a needle penetrating the skin (Ehrsson et al., 2007), the rubber finger being bent backwards (Armell and Ramachandran, 2003), or a knife sliding over the rubber hand (Guterstam et al., 2011, 2013). In fact, increased threat-evoked SCRs have been observed in numerous studies of limb- and full-body illusions, and this measure has therefore emerged as a reliable index of feelings of body ownership (Armell and Ramachandran, 2003; Ehrsson et al., 2007; Guterstam and Ehrsson, 2012; Guterstam et al., 2011; Petkova and Ehrsson, 2009). Viewing a self-attributed artificial limb being threatened is also associated with increased BOLD responses in regions of the brain related to fear processing and pain anticipation (Ehrsson et al., 2007), which the fMRI results from **Studies I** and **V** in the current thesis confirmed. In **Studies I, III, IV, and V**, we applied physical "threats" to the illusory body or limb (in **Study IV** and **V**, we also threatened the seen real body to test for disownership) in the form of an approaching knife (in **Study V**, we also used a sledgehammer to threaten the visual representation of the real body), and we measured the brief increases evoked in skin conductance. In **Study V**, we also included a control threat in which we substituted the knife with a wooden kitchen spoon, which allowed us to exclude any effect of merely viewing an object moving within the near-personal space during an ownership-illusion. We always balanced the stimulation order and included appropriate control conditions so that we could relate changes in the SCR to changes in illusory ownership and exclude the effect of more general factors, such as surprise, general arousal or non-specific emotional responses related to the presentation of the knife. SCR values were recorded with a Biopac

System MP150 (Goleta, USA) following standard published guidelines (Dawson et al., 2007).

Care was taken to perform the same movements with the knife from trial to trial, i.e., controlling the velocity and acceleration of the movement. In the studies in which we used pre-recorded videos (**Studies I and V**), the threat events were identical. Before the experiments commenced, all participants were shown one example of a knife threat to ensure that the procedure was not perceived as too frightening and to reduce any effects on the SCR that were related to seeing the knife for the first time. In all of the SCR experiments outside of the fMRI scanner, each experimental condition was repeated three times, and there was a one-minute resting period between each period of stroking. In the fMRI experiments (**Studies I and V**), each condition was repeated multiple times.

The threat-evoked SCR was defined as the peak in conductance that occurred within five seconds of the onset of the threat stimulus (i.e., from the first moment that the knife entered the participant's visual field). The amplitude of the SCR was calculated as the difference between the maximum and minimum values of the identified response. The investigator performing the analysis was blind to the condition (i.e., illusion or control). The average of all responses for each participant, including those in which no increase in amplitude was apparent, was separately calculated for each condition, and this value was taken as the magnitude of the SCR (Dawson et al., 2007). Thereafter, the SCR magnitudes for all participants were compared statistically across the different conditions of interest. The participants who did not display any threat-evoked SCR in at least half of the trials were considered to be non-responders and were excluded from the analysis in **Studies II and IV** in accordance with previously published protocols (Guterstam et al., 2011; van der Hoort et al., 2011; Petkova and Ehrsson, 2008). The rationale behind this exclusion criterion was based on the theoretical argument that non-responders would "dilute" the data and decrease the signal-to-noise ratio. However, this exclusion also increases the number of assumptions, and the 50 percent cut-off value is arbitrary. In the subsequently published studies (**I and V**), we based our estimates on all of the participants including the so-called non-responders. In fact, this approach generated reliable threat-evoked SCRs related to changes in ownership, similar to the ones observed in the previous studies in which we employed the non-responder exclusion criterion.

3.5 FUNCTIONAL MAGNETIC RESONANCE IMAGING

3.5.1 General methodological considerations

In **Studies I, III, and V**, we examined the neural activity associated with the experimental conditions using fMRI. The signal protocol underlying fMRI was discovered in 1990 (Ogawa et al., 1990), and soon thereafter, it became the most widely used functional brain imaging technique in humans. In contrast to other functional brain imaging methods such as PET and SPECT imaging, fMRI is non-invasive and does not require the administration of radioactive ligands or the exposure of the individual to ionizing radiation, which are associated with increased risks of cancer. The principle of fMRI is built on the so-called neurovascular reflex, which was originally proposed in 1890 by Roy and Sherrington:

“The brain possesses an intrinsic mechanism by which its vascular supply can be varied locally in correspondence with local variations of functional activity.” (Roy and Sherrington, 1890)

For instance, when you speak, neuronal populations in Broca’s area in your left prefrontal cortex increase their firing to perform the computations necessary to instruct your vocal muscles to produce the sound of the words, resulting in an increased demand for oxygen in this cortical region as the neurons consume more energy. Shortly after (approximately 0.5 s) the increase in neuronal activity, the concentration of oxygenated hemoglobin therefore decreases, while the concentration of deoxygenated hemoglobin increases. However, the neurovascular reflex ensures that the local arterioles in Broca’s area dilate, leading to an increase in blood flow to this brain region. In fact, the increase in blood flow is supercompensatory, resulting in a relative increase in the concentration of oxygenated hemoglobin, which peaks 4-6 s after the initial neuronal activation. This initial short dip and subsequent supercompensation in blood oxygenation is called the hemodynamic response function (HRF). Because oxygenated and deoxygenated hemoglobin have different ferromagnetic properties (diamagnetic versus paramagnetic), changes in their ratio affect the local homogeneity of the strong magnetic field inside an MR magnet, which can be detected with an MR machine by measuring the response to a radio frequency (RF) pulse using an RF coil placed around the participant’s head. This response signal is called the blood-oxygen-level dependent (BOLD) response, and it allows researchers to obtain a snapshot of the cerebral blood flow distribution every 2-3 s across the whole brain at a spatial resolution of 2-3 mm³ three-dimensional pixels, referred to as voxels. One can thus detect the changes in the BOLD signal over time, which constitute an indirect measure of

electrical neural activity due to the neurovascular reflex (Goense et al., 2012; Logothetis et al., 2001).

Whereas fMRI has been very useful for examining the neural correlates of perceptual, sensory, and task-related effects, it has several important limitations. In the following paragraphs, I will discuss a few of the methodological issues related to fMRI that need to be addressed when acquiring and statistically analyzing fMRI data, and how we corrected for these issues in the studies included in this thesis.

One important methodological consideration is the issue of head movement. If the participant makes drastic head movements during the scanning, the voxels will not align with the same corresponding brain tissue throughout the experiment, resulting in a violation of one of the basic principles of the statistical analysis of fMRI data (namely, that one given voxel corresponds to the neural activity in one given volume of brain tissue). To remedy this problem, we instructed the participants to keep their head and body as still as possible throughout the experiments. In addition, we fixed each participant's head in the head coil using foam pads and pillows to help them keep their heads still. Furthermore, the fMRI analysis software package we used (SPM8, Statistical Parametric Mapping, Wellcome Trust Centre for Neuroimaging, University College London, UK) employs a motion correction algorithm as part of the preprocessing of the data. This algorithm performs better when the head motion is continuous than when it is abrupt, and when the movement is, as a rule of thumb, of a magnitude less than the voxel size of the fMRI protocol. The most detrimental type of head motion is task-related head motion (e.g., if the participant nods every time a stimulus of interest is presented). To ensure that this was not the case in our studies, we always inspected the estimated realignment parameters. Figure 4 shows the average motion parameter estimates (\pm standard deviation) for all of the participants in the two experiments in **Study I**, showing that head motions were well within the safety limits. We did not need to exclude any participants from the fMRI studies due to excessive head movement or task-related head motion.

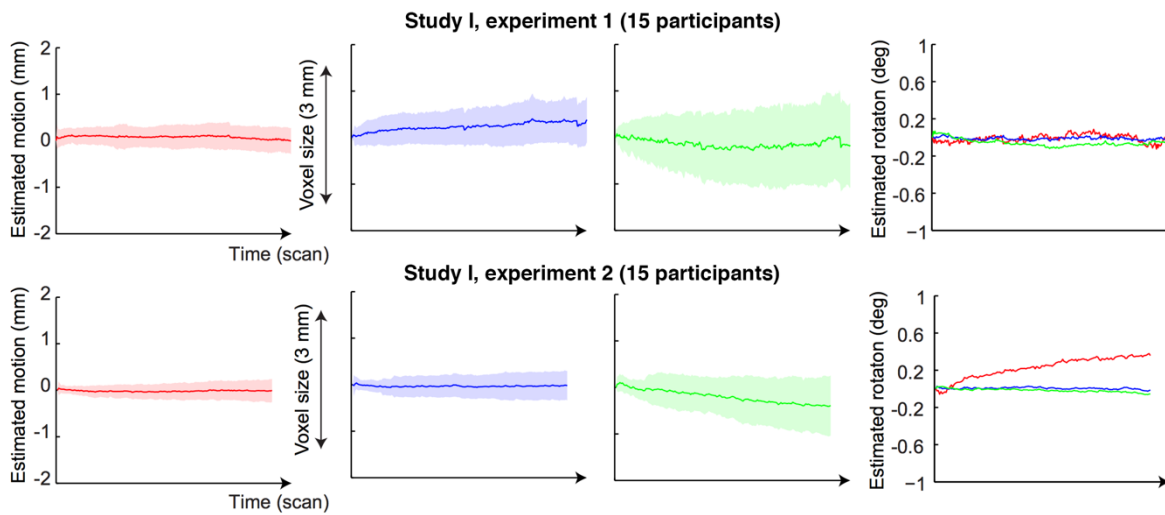


Figure 4. Head motion parameters for the two experiments included in **Study I**. The average motion in the *x*, *y*, and *z* directions, and well as the estimated rotational motion (red=Pitch, blue=Roll, green=Yaw)

Another major challenge with fMRI relates to the individual differences in brain anatomy. To make group-level inferences about changes in activity in a specific brain region, it is necessary to align the corresponding cortical areas across participants. To this end, we used the brain normalization algorithm featured in SPM8, which normalizes each individual brain to the Montreal Neurological Institute (MNI) standard brain. This procedure allowed us to compare results across participants and studies using spatial coordinates in a standardized space.

3.5.2 Preprocessing of the fMRI data

In all studies, we analyzed the fMRI data using SPM8. The first three volumes of each run were discarded from further analysis due to non-steady-state magnetization. Following slice timing correction, the functional images were realigned to correct for head movements (see above) and co-registered with the high-resolution structural scan of each participant (3-D MP-RAGE sequence, 1 mm³ voxel size). The anatomical image was subsequently segmented into white matter, gray matter, and cerebrospinal fluid partitions, and it was then normalized to the MNI standard brain.

3.5.3 Univariate fMRI analyses

For the univariate analyses in **Studies I**, **III**, and **V**, the functional images were normalized to the MNI standard brain and spatially smoothed with an 8-mm full-width-at-half-maximum (FWHM) isotropic Gaussian kernel. In the first-level analysis we defined separate regressors for each main experimental condition, one regressor for the threat events (**Studies I** and **V**), and one regressor-of-no-interest to model the catch trials. Each condition was modeled with a boxcar function and convolved with the standard SPM8

hemodynamic response function. We defined linear contrasts using a general linear model (GLM) to test our hypotheses, and the contrast images from all subjects were entered into a random effects group analysis (second-level analysis).

3.5.4 Multivariate fMRI analyses

For the multivariate analyses in **Study V**, we analyzed the functional data in native space and performed spatial smoothing using a 3-mm FWHM isotropic Gaussian kernel in SPM8. We defined separate regressors for each block of stimulation and each experimental condition. The resulting maps of the parameter (beta) estimates were used as the MVPA input. Within each participant, we used local multivariate mapping to identify multivoxel patterns (the so-called “searchlight” approach) (Kriegeskorte et al., 2006). The brain was partitioned into overlapping voxel clusters, and in each of these clusters, we used linear support vector machines (SVMs) with the fixed regularization parameter of $C=1$ to compute the decoding accuracies for the analyses of interest. The experimental design was optimized for an SVM decoding analysis, in contrast to alternative MVPA approaches such as representational similarity analyses (Vass and Epstein, 2013), because the SVM decoding approach allows for more exploratory whole-brain analyses (Kriegeskorte et al., 2006) and the direct use of the asynchronous condition as a rigorous control for visual input. We used a ten-fold leave-one-run-out cross-validation approach to ensure independent training and testing data. For details about the MVPA, see the supplementary material for **Study V**.

3.5.5 Effective connectivity analyses

In **Studies I, III, and V**, we evaluated changes in the degree of neural connectivity using psychophysiological interaction (PPI) analyses. The PPI measures context-induced changes in the strength of connectivity between two brain regions, as measured by a change in the magnitude of the linear regression slope that relates their underlying activities. A significant PPI indicates that the contribution of one area to another changes significantly with the experimental or psychological context (Friston et al., 1997). In our analyses, we assessed connectivity changes between a pre-defined seed region and the rest of the brain. Specifically, the seed was defined for each subject and consisted of the peak voxel within a 10-mm radius from the group peak coordinate in a main analysis of interest (e.g., in **Study V**, we defined the seed based on the main self-location decoding contrast). Having identified the subject-specific seed coordinates, we extracted the time series (first eigenvariate) of activity from the seed and adjusted for effects of no interest, such as head motion parameters, threat events, and catch trials. In all of the studies, we sought to examine ownership-related changes in connectivity, and therefore performed a PPI analysis using the contrast of synchronous versus

asynchronous as the psychological factor. At the individual level, three regressors were created in a GLM that represented the time course of activity in the seed region (the physiological factor), the psychological factor, and their product (the PPI). In **Study V**, the parameter estimates for the PPI regressor from each participant were entered into a second-level analysis using the decoding accuracy in the seed region (one per participant) as a covariate. We then analyzed the contrast estimates for the covariate by using a one-sample t-test. Notably, by estimating the covariate (which was derived from the MVPA analysis) and not the PPI regressor itself, any voxel revealed by this analysis reflects ownership-related connectivity increases (i.e., increased connectivity in the synchronous condition across position) that significantly scaled with the self-location decoding accuracy in the PCC. This analysis brought together the univariate GLM findings related to the feeling of ownership of the stranger's body and the multivariate decoding results related to the representation of the perceived self-location. As such, this effective connectivity analysis allowed us to examine the interplay between the neural representations of the body and the perceived self-location.

3.5.6 Accounting for the problem of multiple comparisons

The analysis of fMRI data faces a massive problem of multiple comparisons because one human brain consists of hundreds of thousands of voxels, and standard statistical methods perform the same analysis for each and every voxel (the so-called massive univariate approach) (Friston et al., 1995, 1997). However, every well-designed fMRI study has specific neuroanatomical hypotheses, and in the analyses of interest, it would be overly conservative to correct for all the voxels in the brain (including those representing white matter) or in regions outside the regions-of-interest (ROIs). There are several ways to define ROIs, such as using MNI coordinates from previous studies, anatomical masks, or functional localizers. In our studies, we combined an exploratory approach with stricter criteria for statistical significance (whole-brain corrections for multiple comparisons) with a hypothesis-driven approach using small-volume corrections based on coordinates from previous studies.

First, all of our fMRI analyses were performed using the whole brain as the search space. For exploratory purposes, we first thresholded the resulting whole-brain activation maps at an uncorrected threshold. For the appropriate statistical inferences, we then performed correction for multiple comparisons using the family-wise error (FWE) correction, with a threshold of $P < 0.05$ corrected as the statistical criterion for significance. For the brain regions for which we had *a priori* neuroanatomical hypotheses, we corrected for multiple comparisons using small-volume corrections (SVCs) within spheres centered on the

activation peaks derived from previous relevant studies. For the rest of the search space, we corrected for the total number of voxels in the whole brain. Importantly, both approaches result in adequate corrections for multiple comparisons. In **Study III**, we observed extremely strong levels of activation in the *a priori* hypothesized regions that survived corrections for multiple comparisons at the whole-brain level, and we therefore reported the whole-brain statistics in this study.

For activations that were located outside the regions for which we had *a priori* hypotheses—and that did not survive the whole-brain correction for multiple comparisons—we report the *T*-value, MNI peak coordinate, and the uncorrected *P*-value in a purely descriptive manner (see supplementary tables). This procedure is common practice and ensures a description of the activation maps that is unbiased with respect to *a priori* hypotheses. These results can contribute to the generation of new hypotheses for future studies and are relevant with respect to the issue of null-effects and the question of the anatomical specificity of the observed effects. The sections displayed in the figures always represent the whole-brain activation map, which has been thresholded at an uncorrected level for display purposes only. This brain mapping approach has been used in many previous publications from our group (Brozzoli et al., 2011, 2012; Ehrsson et al., 2004; Gentile et al., 2011, 2013; Petkova et al., 2011a) and from other groups (Mobbs et al., 2007; Singer et al., 2004; Tsakiris et al., 2007).

It is worth emphasizing that we did not use a conventional ROI approach. The conventional ROI approach involves pre-defining search volumes based on neuroanatomy or independent functional imaging results (functional localizers). Typically, the mean activation of the whole ROI is extracted and evaluated via a univariate analysis, while multivariate analyses typically involve the training and testing of a classifier on all of the voxels within the ROI. In these cases, one usually adopts the rather liberal threshold of an uncorrected $P < 0.05$ for the ROI, making it necessary to perform a correction for multiple comparisons when a large number (typically > 4) of ROIs are studied. Thus, the conventional ROI approach only involves corrections for multiple comparisons based on the number of ROIs tested. In contrast, the voxel-based brain mapping approach that we employed in the studies included in this thesis involves corrections for multiple comparisons across all the voxels within the appropriate search space, be it a predefined small volume or the whole brain. Similarly, for the multivariate analyses in **Study V**, we used the standard “Searchlight” approach (Kriegeskorte et al., 2006), in which a classifier is trained and tested within a subset of voxels (a 3-mm-radius sphere) centered around a given

voxel. This process is then repeated for all of the voxels in the whole brain, thus generating whole-brain decoding maps that are fed into conventional second-level random effect analyses in SPM8. In the analysis of the decoding maps, we used small-volume-corrections to control for the problem of multiple comparisons in the whole-brain data in the same manner by which the univariate analyses were performed and evaluated.

There are several advantages to using a whole-brain voxel-wise approach compared to standard ROI approaches. First, voxel-wise peak statistics provides higher anatomical specificity because information about the topology of the activation maps, which is lost when averaging the BOLD signal across an entire ROI, is retained. Second, a whole-brain approach allows for the detection of unexpected activations outside the regions for which one has *a priori* hypotheses. This typically leads to a more accurate and transparent characterization of the findings from neuroimaging experiments. For these reasons, we chose a combination of voxel-wise SVCs for activations in the anatomical regions for which we had *a priori* hypotheses and reported the uncorrected *P* values for activations outside these regions using a purely descriptive approach.

4 MAIN RESULTS AND CONCLUSIONS

In the following section, I briefly summarize the main findings and conclusions of the individual studies. For details, I refer the reader to the full manuscripts attached at the end of this thesis.

4.1 STUDY I

The goal of Study I was to determine whether neuronal populations in the premotor, parietal, and cerebellar cortices integrate visual, tactile, and proprioceptive signals from the hand according to basic temporal and spatial congruence principles of multisensory integration. Neurophysiological studies in monkeys have shown that these areas perform visuo-tactile-proprioceptive integration (Graziano, 1999; Hyvärinen and Poranen, 1974; Rizzolatti et al., 1981), and neuroimaging studies in humans using the rubber hand illusion (Ehrsson et al., 2004) suggest that this integration process might underlie our sense of limb ownership. However, it remains to be shown whether this integrative process obeys basic multisensory congruence rules for the real hand in humans, and if it is relevant for the default feeling of limb ownership. To address these questions, we developed a setup based on 3-D video technology that allowed us to manipulate the spatiotemporal relationships of the visuo-tactile (VT) stimuli delivered to a participant's real hand during fMRI and to investigate the ensuing neural and perceptual correlates. The participants were positioned inside the scanner in a posture with their head tilted and looking into a set of HMDs in which they observed their real right hand in 3-D being touched by an object (see Figure 5). In Experiment 1, we manipulated the temporal synchrony and spatial congruence (spatial incongruence consisted of seeing the back of the hand being stroked, but feeling a stroke on the index finger, or vice versa) of the seen and felt touches. In Experiment 2, we manipulated the temporal synchrony and visuo-proprioceptive congruence of the stimuli, such that in half of the trials, the seen position of the arm did not match the felt position of the arm (i.e., the participant's hand was retracted). To assess the sense of ownership of the virtual representation of the seen limb, we used a combination of post-scan questionnaires, threat-evoked SCRs and BOLD-responses during the scanning sessions.

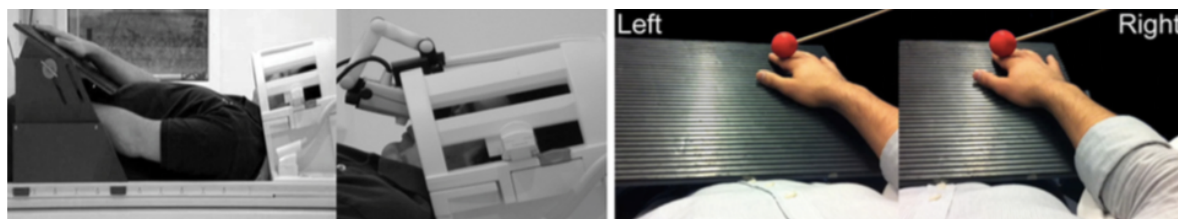


Figure 5. Experimental setup of Study I. The positioning of the participant in the scanner is shown on the left, and the stereoscopic visual stimuli is shown on the right.

The experiments revealed two main findings. First, the results of Experiment 1 show responses in the premotor, parietal, and cerebellar regions that were dependent on the spatial and temporal congruence of VT stimuli (Figure 6A). The results of Experiment 2 demonstrate that this multisensory integration effect requires a simultaneous match between the seen and felt postures of the hand (Figure 6B), which suggests that congruent visuo-proprioceptive signals from the upper limb are essential for successful VT integration. Second, we observed that multisensory conflicts significantly disrupted the feeling of ownership of the seen real limb, as quantified by complementary subjective questionnaire responses, threat-evoked SCRs, and BOLD-signal responses (Figure 6C). Furthermore, the degree to which self-attribution was impaired could be predicted from the attenuation of neural responses in key multisensory areas. Together, the results of Study I shed light on the neural basis of the integration of multisensory hand signals in accord with basic spatiotemporal congruence principles, and they demonstrate that the *dis*integration of these signals leads to feelings of “disownership” of the seen real hand. Thus, these findings suggest that not only feelings of ownership of artificial limbs but also the default feeling of ownership of one’s real limbs is dependent on basic multisensory integration principles.

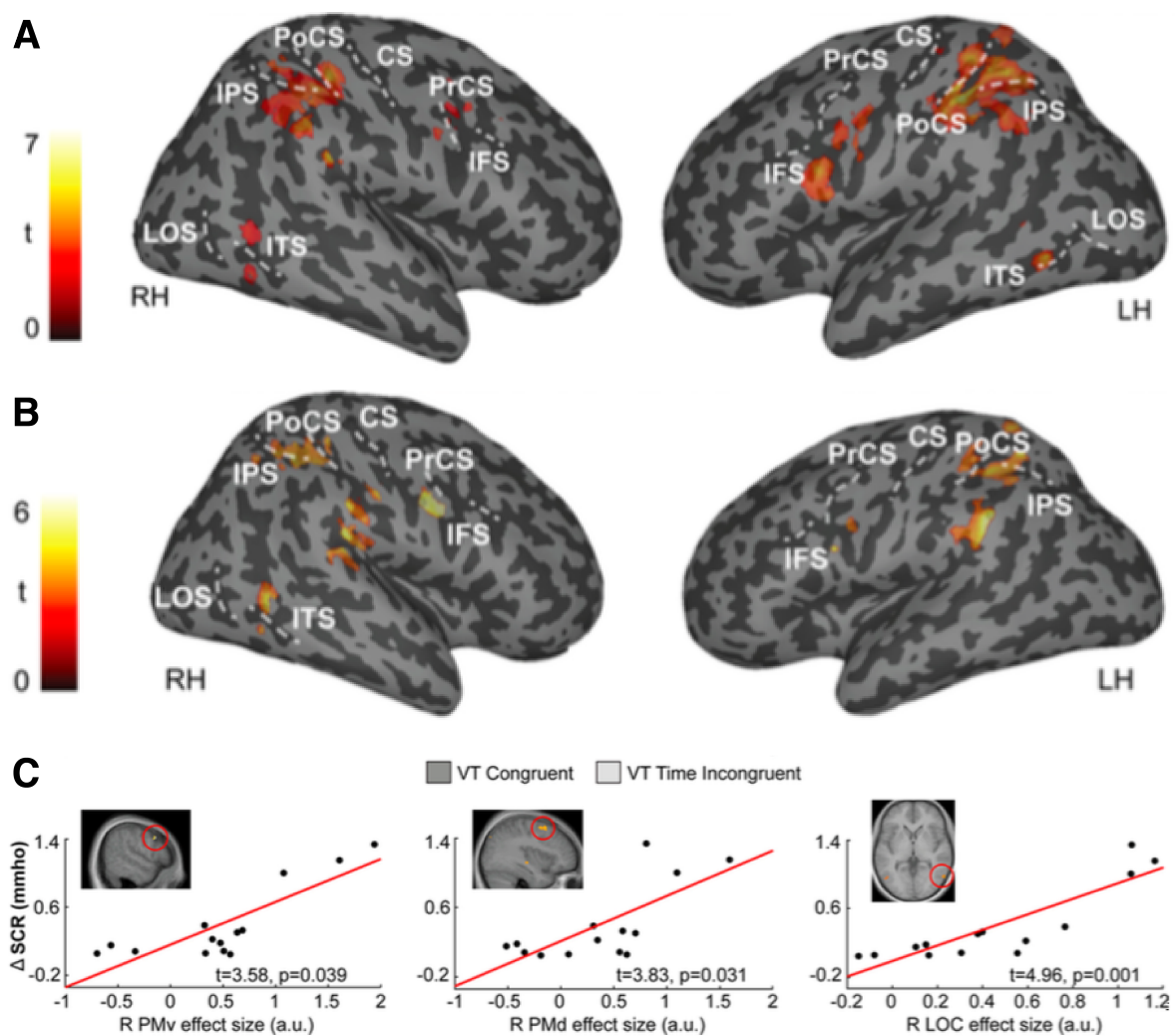


Figure 6. Study I results. **A.** Temporal and spatial VT congruence was associated with significantly increased activity in the premotor, posterior parietal, and cerebellar regions. **B.** The VT integration response in this set of areas was dependent on the congruence between the seen and felt position of the arm (visuo-proprioceptive congruence). **C.** The magnitude of the BOLD response in the premotor and lateral occipital cortices correlated significantly with the threat-evoked SCR, which is a well-established proxy of limb ownership (see Section 4.3).

4.2 STUDY II

Study II aimed to elucidate the relationship between multisensory integration within the peripersonal space and the sense of limb ownership by characterizing a novel perceptual illusion: the “magnetic touch illusion.” This rather unexpected illusion demonstrates that it is possible to induce ownership of a rubber hand without actually touching its surface. In this case, the illusion was elicited by applying brushstrokes in mid-air at some distance above the hand (Figure 7A). Intriguingly, this mode of stimulation resulted not only in the illusory experience of owning the rubber hand but also in the perception of a “magnetic force” or “force field” between the brush and the rubber hand. In a series of eight experiments, we used a combination of questionnaires, proprioceptive drift measurements, and motion tracking of the brush in mid-air to systematically examine the hypothesis that

this illusory magnetic force reflected multisensory integration mechanisms operating in peripersonal space. As mentioned in Section 1.3, trimodal peripersonal space neurons characterized in macaques have specific RF properties, namely, they feature visual RFs that extend up to 40 cm from a tactile RF (Fogassi et al., 1996), follow changes in limb position (Graziano, 1999) and are independent of the direction of gaze (Graziano and Gross, 1998). Our results show that in each of the questionnaire-based experiments (Experiments 1a, 1b, 2a, and 3a), the magnetic touch sensation correlated strongly with the reported sense of rubber hand ownership. Furthermore, the magnetic touch sensation exhibited a nonlinear decline in illusory strength at approximately 40 cm (Experiment 1a; Figure 7B), which was independent of gaze direction (Experiment 1b). We also found that “tactile expectations” (Ferri et al., 2013) elicited by merely observing an object moving near the hand did not contribute to the illusion (Experiment 2a and 2b) and that the perceived magnetic force did not penetrate physical barriers (Experiment 3a and 3b), thus further linking this phenomenon to the multisensory body representation. In Experiment 4, we combined motion tracking with a continuous real-time assessment of the strength of the illusion to map out the extension of the magnetic touch illusion in 3-D space for two different rubber hand positions and found that the illusion volume was spatially anchored to the rubber hand (Figure 7C-D). Together, these findings led us to propose that the illusory sense of magnetic touch constitutes a perceptual correlate of visuo-tactile integration in peripersonal space. Furthermore, the results provide strong support for the notion that multisensory integration within peripersonal space is key for the emergence of body ownership.

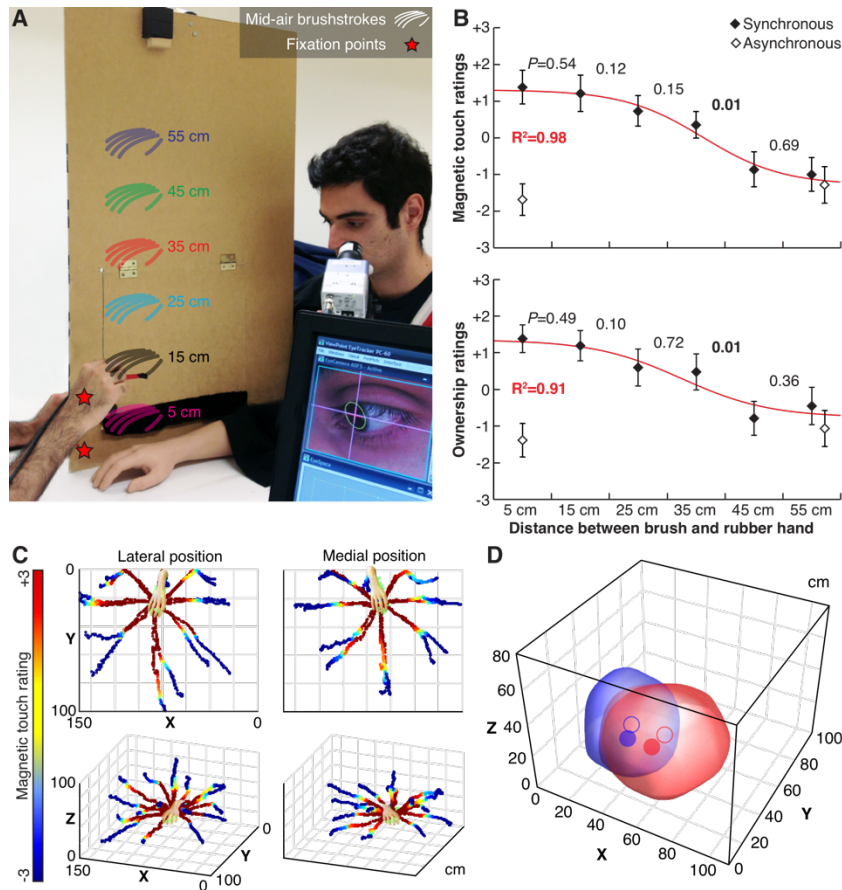


Figure 7. Results of Study II. **A.** Experimental setup of Experiment 1A and 1B. Mid-air brushstrokes were performed at different distances from the rubber hand as indicated (5 cm-55 cm). **B.** The mean ratings of the sensations of magnetic touch and rubber hand ownership. In both cases, there was a non-linear decline in the strength of the illusion between the distances 35 cm and 45 cm. **C.** In Experiment 4, we mapped out the 3-D spatial extension of the illusion for two different rubber hand positions. To this end, we synchronized motion tracking of the brush moving in mid-air (in 17 different directions) with real-time ratings of illusion vividness. Here, we show all the data from one individual participant, in which each spatial coordinate is color-coded according to the reported subjective strength of the magnetic touch sensation. **D.** By extrapolating the data, we were able to map the illusion volumes for each of the two rubber hand positions, the result of which clearly demonstrate that the illusion volume follows changes in rubber hand position.

4.3 STUDY III

The goal of Study III was to examine the role of vision in the multisensory process of self-attributing limbs. Specifically, we undertook a systematic investigation of a novel perceptual illusion, which we named the “invisible hand illusion,” demonstrating that it is possible to elicit ownership sensations of a discrete volume of empty space. In essence, we adopted the classical rubber hand illusion paradigm but removed the rubber hand and, instead, applied the brushstrokes in empty space, “painting the contours” of an invisible hand. The results show that within a short period of brushing, participants started to refer the sensation of touch to empty space and also experienced having an invisible hand in this position. By evaluating questionnaires and measuring proprioceptive drift, threat-evoked SCRs, and BOLD responses in a total of 234 participants, we showed that the invisible hand illusion follows the same perceptual rules as the rubber hand illusion and is associated

with increased activity in premotor and intraparietal multisensory regions (Figure 8). The illusion was dependent on the application of temporally synchronous and spatially congruent (with respect to hand-centered reference frames and within near-personal space) brushstrokes in mid-air and on the hidden real hand. In short, these results demonstrate that multisensory integration can result in the perception of a phantom-like invisible limb and that the *visuo*-tactile integration mechanisms in the premotor-intraparietal regions that underlie changes in limb ownership are not dependent on *visual* input from a limb-like object.

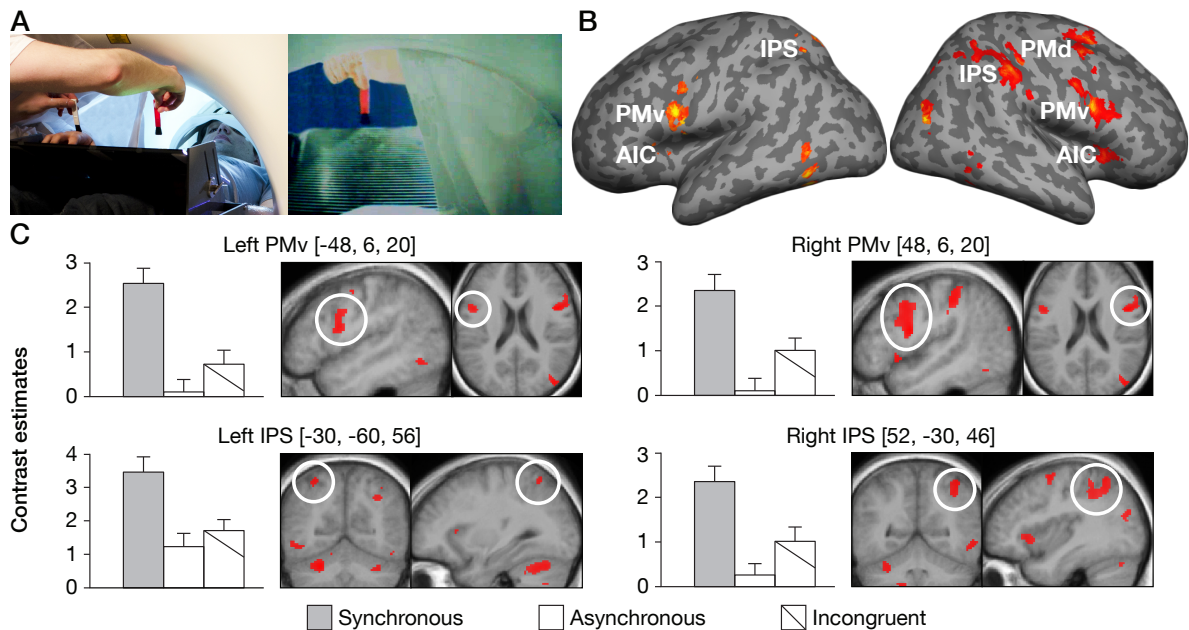


Figure 8. FMRI setup and results of **Study III**. **A.** Experimental setup used to induce the illusion within the constrained scanner environment, as observed from the outside (left) and from the participant's perspective inside the magnet (right). **B-C.** Significant activations in the ventral and dorsal premotor cortices (PMv/d), the intraparietal sulcus (IPS) and the anterior insula (AIC), reflecting the experience of having an invisible hand. All activation maps correspond with the contrast synchronous versus asynchronous ($p < 0.05$, corrected), which was masked inclusively with the contrast synchronous versus spatially incongruent ($p < 0.001$, uncorrected), a control condition in which the brushstrokes were applied synchronously but in opposite directions. The plots display the parameter estimates for the synchronous, asynchronous, and spatially incongruent conditions for the main areas of interest. The peak coordinates are reported in MNI space. Error bars denote the SEM.

4.4 STUDY IV

Study IV investigated the effect of the out-of-body illusion (Ehrsson, 2007) on the subjects' perceived self-location and the sense of (dis)ownership of the real body viewed from a third-person perspective. To estimate the effect on perceived self-location, we induced the illusion using the application of synchronous visuo-tactile stimulation for one min, after which we administered a behavioral self-location task. In this task, we asked participants to rate how strongly they perceived themselves to be located in two candidate positions: at their veridical location in the chair and at the location of the cameras (Figure 9A). We used asynchronous visuo-tactile stimulation as the control condition. The results show that

participants in the synchronous condition reported a strong sense of self-location at the cameras and a weak sense of self-location at their veridical self-location (Figure 9C). In the asynchronous condition, the participants reported a strong sense of self-location at their veridical location and only a weak sense of self-location at the position of the cameras (Figure 9C). Thus, by manipulating the temporal congruence of the seen and felt touches on the body, we were able to change the perceived self-location in a predictable and controlled manner.

To test for potential effects of disownership of the seen real body, we measured the SCR evoked by a knife approaching the participants back after a period of synchronous or asynchronous stimulation (Figure 9A, cut-in frame). In the synchronous condition, we observed a significantly lower threat-evoked SCR than in the asynchronous condition, which is consistent with the notion that the real body is disowned during the out-of-body illusion and no longer perceived as part of the self. In a control experiment, we substituted the participant's body with a "stranger's body" and performed the same knife threatening procedure (Figure 9B). The results show no significant difference in threat-evoked SCR (Figure 9D), suggesting that differences in the SCR observed in the main experiment were indeed related to perceptions of seeing the knife approaching one's real body and not any nonspecific reduction of the SCR related to changes in visuo-spatial attention while experiencing the illusion.

In summary, the behavioral results of Study IV show that the out-of-body illusion can be used to induce predictable changes in perceived self-location and body ownership. These findings encouraged us to undertake **Study V**, which involved adapting the illusion for use in the MRI scanner.

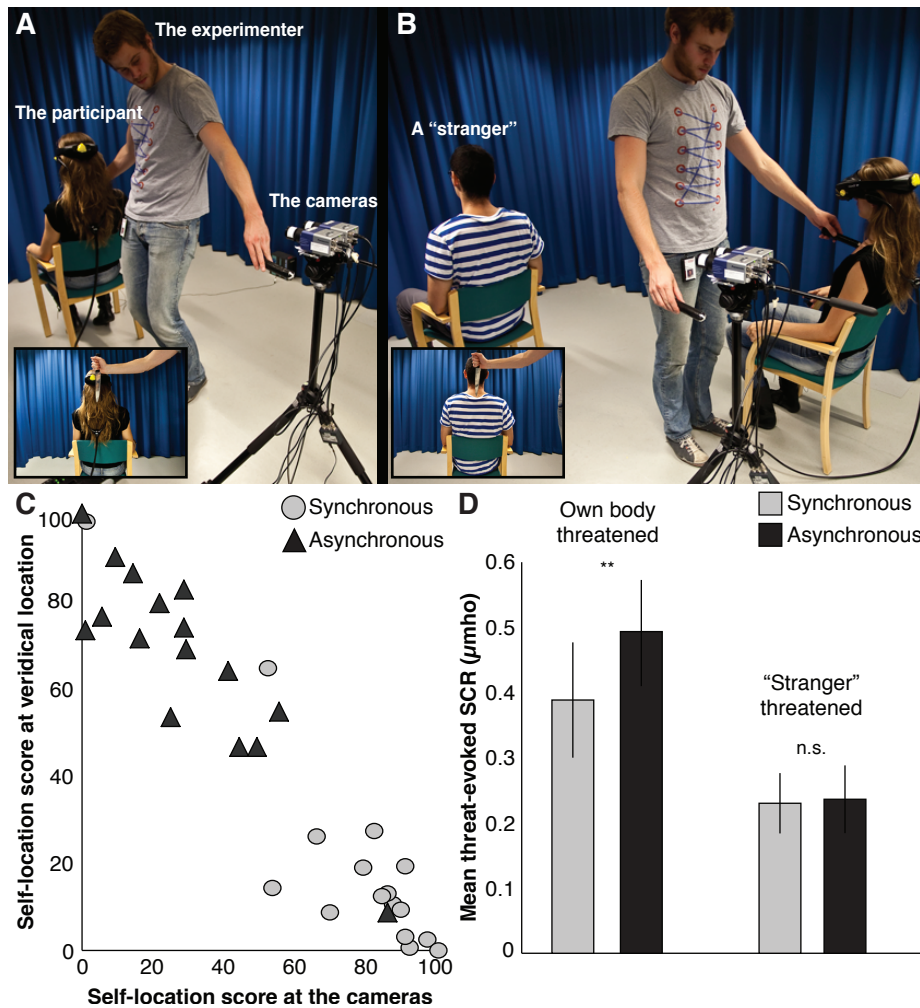


Figure 10. Setup and results of Study IV. *A-B.* The experimental setups of the main experiment (panel A) and the control experiment (panel B). The knife-threat procedure is illustrated in the sample frame in the lower left corners. *C.* Results of the self-location task. *D.* Results of the threat-evoked SCR, showing decreased stress responses to real body threats during the synchronous illusion condition compared to the response in the asynchronous control condition. These results suggest that the real body is disowned during the out-of-body illusion.

4.5 STUDY V

Study V investigated how the brain represents one’s own body with respect to the spatial environment. To this end, we adapted the out-of-body illusion to the constrained environment of an MRI scanner and studied 15 healthy participants. By using MRI-compatible HMDs, pre-recorded 3-D videos custom-edited for each participant, and multisensory stimulation, we induced the out-of-body illusion for different spatial locations in the actual scanner room (Figure 11A). To induce the illusion, the participants viewed a stranger’s body being touched by an object from the first-person perspective while receiving tactile stimulation on the corresponding parts of their real body (they observed their real body lying in the scanner from a third-person perspective). Again, asynchronous visuo-tactile stimulation was used as the control condition because the results of **Study IV** show that this mode of stimulation reliably reduces the strength of the self-location and

body ownership illusions. During the course of the experiment, we induced the illusion in several different locations (for simplicity, only positions A and B are discussed here), effectively “teleporting” the participants perceptually, while their brain activity was recorded using fMRI.

The behavioral and psychophysiological results (i.e., threat-evoked SCR, post-scan self-location task and “body ownership” questionnaire results) agreed with the findings of **Study IV**, showing that synchronous visuo-tactile stimulation was associated with an unambiguous sense of self-location in the out-of-body position and a strong sense of ownership of the stranger’s body. In the asynchronous condition, the participants had a stronger sense of being located at their veridical location inside the magnet and experienced less ownership of the stranger’s body. Furthermore, when contrasting the synchronous and asynchronous conditions across spatial locations, we found significantly stronger activity levels in key multisensory areas that have previously been found to be associated with illusory full-body ownership (Figure 11B) (Petkova et al., 2011a). Thus, these results demonstrate the feasibility of our approach.

To identify neural activity patterns that reflected the sense of self-location, we used MVPA to decode positions A versus B in the synchronous condition, using the asynchronous condition as a control for effects not specific to the illusion, such as visual input. We found significant decoding of self-location in the hippocampus, PCC, and IPS (Figure 11C). Interestingly, the decoding accuracy in the PCC and IPS scaled significantly with the subjectively reported self-location scores (Figure 11D), suggesting that activity patterns in these areas reflect one’s subjective sense of self-location.

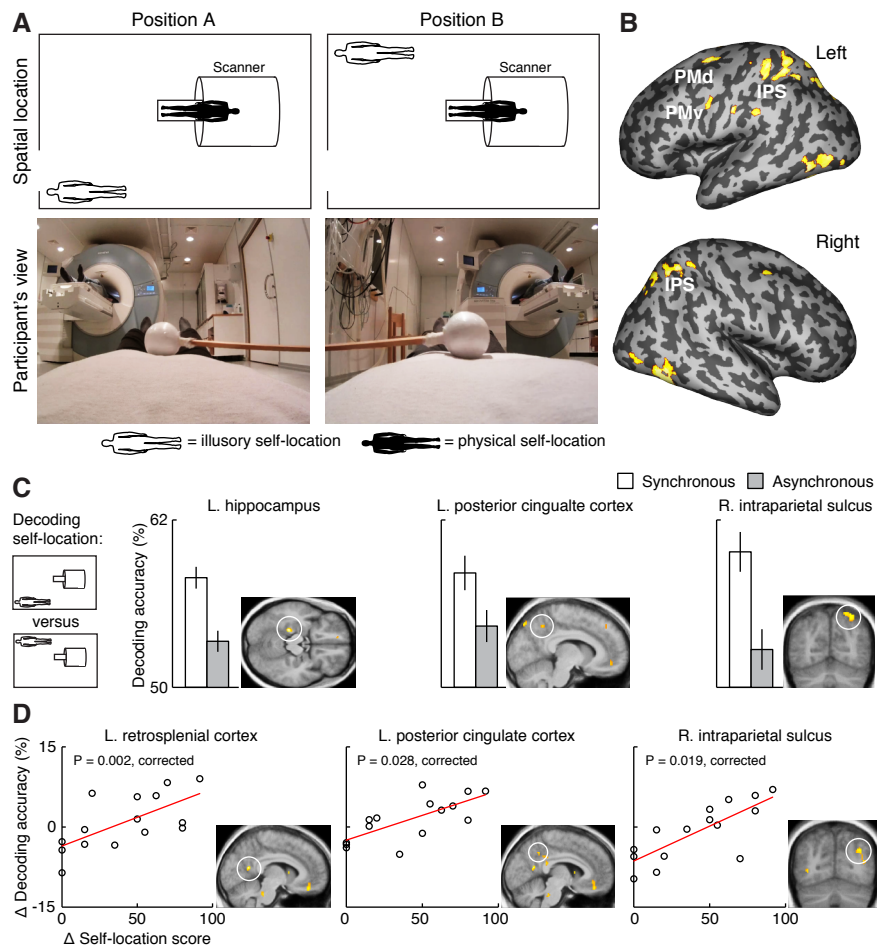


Figure 11. Setup and results of Study V. **A.** Overview of the scanner environment (upper panels) and a sample frame of the visual stimuli (lower panels) for positions A and B. **B.** Illusory ownership of the stranger's body was associated with increased activity in key multisensory regions. **C.** Significant decoding of self-location was observed in the hippocampus, posterior cingulate cortex, and the intraparietal sulcus. **D.** The decoding accuracy in the retrosplenial cortex, posterior cingulate cortex, and intraparietal sulcus significantly scaled with the behavioral self-location scores. L = left. R = right.

We investigated the interplay between the neural representations of body ownership and self-location by performing an analysis of effective connectivity. In brief, we first identified the PCC as a candidate key node in combining these two representations because previous studies have shown that the PCC is involved in translating spatial reference frames (Burgess, 2008), and PCC activity in our study both decoded self-location and significantly scaled with behavioral self-location scores. We then searched for areas showing increased connectivity to the PCC in relation to experiencing ownership of the stranger's body (i.e., in the synchronous condition) that scaled with the self-location decoding accuracy in the PCC. The results show that the higher the self-location decoding accuracy in the PCC the stronger the ownership-related connectivity was to the hippocampus, retrosplenial cortex and the IPS.

In summary, the findings of **Study V** are consistent with the notion that the PCC plays a key role in integrating the senses of self-location and body ownership, and show that the hippocampus, IPS, and PCC are not only involved in supporting ecological behaviors such

as spatial navigation and memory, but are also important for the perceptual experience of being physically located in a specific location in the environment.

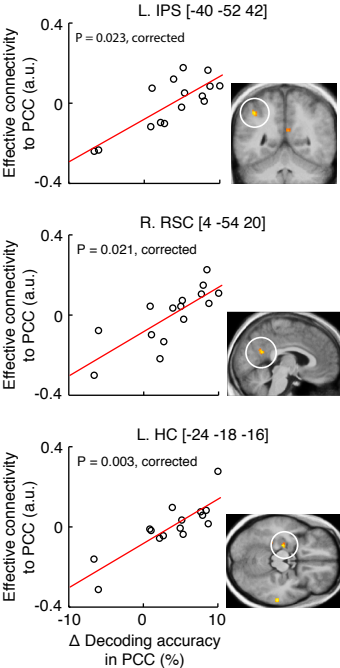


Figure 12. Results of the effective connectivity analysis examining the interplay between neural representations of body ownership and self-location. *IPS*=intraparietal sulcus. *RSC*=retrosplenial cortex. *HC*=hippocampus.

5 DISCUSSION

How does the brain combine signals across sensory modalities to build and maintain a coherent representation of the bodily self in space? The experiments included in this thesis show that basic multisensory congruence principles can be used to manipulate specific aspects of body ownership and self-location in a controlled and predictable manner. By using various behavioral measurements and functional brain imaging, we characterized the perceptual rules and the neural correlates of these manipulations of bodily and spatial self-perception. It must be noted that we are not the first to propose that multisensory integration is involved in building internal representations of the body. Decades of neurophysiological research on non-human primates have demonstrated that specific brain regions merge sensory signals across modalities and construct higher representations of the body (Graziano and Botvinick, 2002). However, because non-human primates cannot report their subjective experiences, the results of these experiments tell us little about the neural foundations of bodily and spatial perceptions in humans. To address these questions, a great deal of research over the past two decades has focused on body ownership illusions such as the rubber hand illusion, the results of which are consistent with the notion that ownership of an artificial limb or full-body relies on multisensory integration of signals originating within the near-personal space (Blanke, 2012; Ehrsson, 2012; Makin et al., 2008). Each of the studies included in this thesis aimed at filling a knowledge gap or challenging an assumption made in the literature. In **Study I**, we demonstrate that the spatial and temporal multisensory congruence principles that have previously been shown to govern the perception of an artificial limb as belonging to the self also determine the default sense of ownership of one's real hand. Furthermore, our fMRI results show that this multisensory integration process is implemented by fronto-parietal-cerebellar circuits, which is consistent with the findings from single-cell recordings in non-human primates (Graziano and Botvinick, 2002). In **Study II**, we report a new perceptual effect consisting of the illusory experience of a magnetic force between a brush moving in mid-air at some distance above a rubber hand. This magnetic touch sensation was strongly correlated with feelings of rubber hand ownership and exhibited striking similarities to the RF properties of peripersonal space neurons, providing strong support for the notion that multisensory integration within peripersonal space is intimately involved in the sense of body ownership. The results of **Study III**, in which we characterized the invisible hand illusion, show that correlated dynamic visuo-tactile signals are more important than the mere visual input from a limb-like object in the process of attributing limbs to the self, suggesting the need for an update of previous proposals in the literature regarding the role of vision in bodily self-attribution

(Tsakiris et al., 2010). In **Studies IV** and **V**, we examined the role of multisensory integration in the process of constructing a coherent, unified perception of one's body in space. The behavioral results of **Study IV** show that the out-of-body illusion (Ehrsson, 2007) can be used to elicit predictable changes in feelings of full-body ownership and the sense of self-location. Importantly, our findings demonstrate that a change in first-person visual perspective in conjunction with temporally congruent tactile stimulation is sufficient to induce a change in perceived self-location; however, if the tactile stimulation is asynchronous, participants report that their self-location is unaltered. We made use of this observation in **Study V**, in which we adapted the out-of-body illusion to the MRI environment and used it to perceptually “teleport” participants between different spatial locations while undergoing fMRI. We employed MVPA to decode perceived self-location (using the asynchronous condition as the control for visual input) and found significant decoding in the hippocampal, posterior cingulate, and intraparietal areas. Furthermore, the results of an effective connectivity analysis using the PCC as the seed region, found that this region is involved in integrating representations of body ownership and self-location. Together, the results of **Studies I-V** go beyond earlier work on body illusions because they provide unprecedented support for the notion that multisensory integration within the peripersonal space is key for the self-attribution of real and artificial limbs, and they reveal a dynamic interaction between fronto-parietal representations of body ownership and parieto-cingulate-hippocampal representations of self-location, in which the PCC might play an integrative role.

What do the results of this thesis tell us about the multisensory mechanisms that underlie feelings of body ownership and one's sense of self-location in the environment? In **Study V**, we found that illusory ownership of a stranger's body viewed from the first-person perspective was coupled with increased activity in the premotor, intraparietal, and lateral occipital cortices and that the magnitude of the BOLD response in the left PMv scaled significantly with the reported strength of the illusion. These results are consistent with the fMRI findings of **Study I** and **III**, which investigated ownership of a virtual representation of one's real hand or the perception of having an invisible hand, and with the results of previous studies on single-limb (Brozzoli et al., 2012; Ehrsson et al., 2004) and full-body ownership (Gentile et al., 2015; Petkova et al., 2011a). As previously mentioned, studies in macaques have shown that the premotor and intraparietal cortices feature neuronal populations with visuo-tactile RFs covering the skin surface and its immediate surrounding space (Graziano, 1999, 2000; Graziano et al., 1997; Rizzolatti et al., 1981), which collectively represent a multisensory buffer zone between the body and the environment. In

addition, these neurons have the capacity to integrate spatiotemporally congruent visual, tactile, and proprioceptive signals from the body (Avillac et al., 2007; Gentile et al., 2011, 2013; Graziano, 1999). Together, these properties make the IPS and PMv ideal candidates for mediating feelings of body ownership (Brozzoli et al., 2012; Ehrsson, 2012; Makin et al., 2008). The existence of the magnetic touch phenomena detailed in **Study II**, in conjunction with the results of a recent study that revealed BOLD-adaptation responses in the IPS and PMv specific to visual stimulation close to a self-attributed rubber hand (Brozzoli et al., 2012), suggests that the observed activity in premotor-intraparietal regions reflects the remapping of the peripersonal space onto a body part perceived as belonging to the self. Furthermore, **Study I** shows that premotor-intraparietal activity reflects the integration of spatiotemporally congruent visual, tactile, and proprioceptive information from the seen upper limb (consistent with the results of Gentile et al., 2011) and that this multisensory integrative activity is intimately related to the sense of limb ownership. Moreover, the unified experience of owning an entire body, as demonstrated in the full-body illusion featured in **Study V**, has been associated with the integration of visual and tactile signals across multiple body segments in the same set of fronto-parietal areas (Gentile et al., 2015; Petkova et al., 2011a). In light of these findings, I propose that feelings of body ownership are reflected in two closely related processes implemented by neuronal populations in the premotor-intraparietal cortices: the remapping of peripersonal space from being centered on the real body to being centered on an artificial body and the integration of visuo-tactile-proprioceptive information in body-centered spatial reference frames. This idea is in accordance with the decrease in SCRs (observed in **Study IV** and **V**) and BOLD activity in cortical regions related to pain anticipation and fear processing (**Study V**) in response to threats directed toward the seen real body, indicating that ownership of an illusory body is associated with the disownership of the real body.

One might rightfully ask how this rather complicated system for bodily self-attribution could have evolved? I speculate that the system for establishing a multisensory peripersonal space initially evolved in response to the ecological need to efficiently reach and grasp near-by objects (Graziano, 1999, 2001; Graziano and Botvinick, 2002) and to defend one's body from physical harm (Cooke et al., 2003; Graziano and Cooke, 2006). Because this multisensory system represents a swift and relatively accurate way of distinguishing the body from external objects, it might have been "recycled" by our perceptual systems for the purpose of assigning ownership sensations to limbs in accordance with the neuronal recycling hypothesis (Dehaene and Cohen, 2007). This interpretation fits well with the notion that the feeling of ownership reflects the affective significance of the body to the self

and that it is grounded in a specific type of body schema dedicated to bodily protection (de Vignemont, 2015) (see Section 1.1). The multisensory peripersonal space representation in the PMv is an ideal candidate for harboring this proposed “protective body schema” because it is involved in planning protective movements, and the neural activity in the PMv is tightly linked to the subjectively reported vividness of body ownership sensations (unlike activity in the IPS, LOC, or the cerebellum). Future studies using the magnetic touch illusion to quantify ownership sensations and map out the extent of the peripersonal space around artificial limbs, real limbs, tools, and even the limbs of other people might shed light on the relationships between the representation of the peripersonal space, the sense of limb ownership, and our sense of the affective significance of seen limb-like objects.

In the process of localizing one’s own body with respect to the surrounding spatial environment, the brain needs to combine information concerning the representation of the body – processed via multisensory peripersonal space mechanisms in the IPS and PMv – with information concerning self-location, which the decoding results in **Study V** suggest is encoded in parieto-cingulate-hippocampal regions. In **Study V**, we hypothesized that the PCC plays a central role in this integrative process based on its strong anatomical connections to both intraparietal and medial temporal areas (Kobayashi and Amaral, 2007) and its involvement in processing transformations between body-centered and allocentric spatial reference frames, which has been observed in studies of spatial perception and navigation (Burgess, 2008; Epstein, 2008; Kravitz et al., 2011). Indeed, the effective connectivity results in **Study V** show that the higher the self-location decoding accuracy in the PCC the stronger its ownership-related connectivity to regions in the IPS and the hippocampus, which is consistent with the hypothesized integrative role of the PCC. However, it should be noted that the involvement of other areas in this process cannot be ruled out, such as the posterior parietal cortex, which has been implicated in numerous studies of spatial navigation and mental imagery (Maguire et al., 1998; Rodriguez, 2010; Spiers and Maguire, 2007; Zacks and Michelon, 2005) and in which we observed an overlap between the self-location decoding cluster and the body ownership activation cluster (see Supplementary Figure 4E in **Study V**).

It is interesting to speculate in what way, if any, the mechanisms underlying the out-of-body illusion under investigation are similar to the ones responsible for OBEs of neurological origin (see Section 1.6). In OBEs described by patients, focal epilepsy or electrical brain stimulation induce the sensation of viewing one’s body and the world from a location outside the physical body, coupled with vestibular sensations such as floating,

flying, elevation, and rotation (Blanke et al., 2004; De Ridder et al., 2007; Penfield and Erickson, 1941). Out-of-body illusions and clinical OBEs share the characteristic that the perceived self-location is referred to an extracorporeal position. In contrast to OBEs, the participants experiencing the out-of-body illusion in **Study IV** and **V** denied feeling any type of illusory vestibular sensations. Interestingly, a previous fMRI study examining another full-body illusion (Lenggenhager et al., 2007) showed that the participants experienced illusory vestibular percepts in association with the illusion (Ionta et al., 2011). In this experiment, the participants were lying face up and observing, from a third-person perspective, the back of an avatar's body being touched while they received synchronous tactile stimulation of their real backs, resulting in illusory changes in their perceived self-location and feelings of looking upwards or downwards. The authors found evidence for the involvement of the bilateral posterior superior temporal gyrus (pSTG) in representing self-location with respect to the perceived direction of the first-person perspective and the gravitational field (Ionta et al., 2011). Intriguingly, this cortical region shows a stronger correspondence to the areas in which electrical stimulation have been shown to induce OBEs in patients (the pSTG and angular gyrus) (Blanke et al., 2004) compared to the set of areas that we revealed in **Study V**. Therefore, I speculate that the pSTG and angular gyrus are involved in representing self-location with respect to the gravitational field (explaining why Study V, in which the participants denied feeling any illusory vestibular sensations, failed to find significant self-location decoding in these regions), while the parieto-cingulate-hippocampal circuit identified in Study V is involved in representing self-location with three degrees of freedom (along the x, y, and z axis). The unified experience of being physically located in a given location with six degrees of freedom (i.e., x, y, z, pitch, roll, and yaw) might require an interplay between the TPJ and parieto-cingulate-hippocampal circuits. Moreover, it is interesting to consider the possibility that focal epileptic activity in the inferior parietal and superior temporal lobes in patients with neurological disorders (Blanke, 2012; Blanke et al., 2004, 2015) could be associated with the spread of abnormal neural activity to the parieto-cingulate-hippocampal areas, contributing to the false sense of self-location in OBEs of neurological origin.

Neural activity related to illusory body ownership was also found in regions outside the posterior parietal and premotor cortices in the fMRI studies presented in this thesis, the most notable being in the LOC and the cerebellum. In **Studies I, III, and V**, we found robust activations in the bilateral LOC, corresponding well with the standardized coordinates of the extrastriate body area (EBA), which is involved in the visual processing of human limbs and body parts (Downing and Peelen, 2011; Downing et al., 2001). I

speculate that the bilateral LOC activity observed across the studies in this thesis represents an ownership-induced modulation of the processing of visual information from the artificial body, possibly reflecting top-down modulatory effects (Driver and Noesselt, 2008; Macaluso et al., 2000) on the LOC from the multisensory body representation in the IPS. This interpretation is in accordance with previous studies on limb ownership that have shown illusion-induced increases in connectivity between the LOC and the IPS (Limanowski and Blankenburg, 2015; Limanowski et al., 2014), and the observation that tactile, proprioceptive, and motor signals from a limb can modulate the processing of visual information from the same body part in the LOC (Astafiev et al., 2004; Costantini et al., 2011; Orlov et al., 2010). Moreover, in **Studies I and III**^{*}, we observed strong activations in a section of the lateral cerebellum that is anatomically connected to the posterior parietal and premotor cortices (Clower et al., 2001; Orioli and Strick, 1989). This region is involved in integrating visual, tactile and proprioceptive signals from the body (Dum et al., 2002) and is activated in the classical rubber hand illusion (Ehrsson et al., 2004, 2005) and when temporally congruent visuo-tactile stimulation is delivered to a person's real hand (Gentile et al., 2011). It is also considered to compute the temporal relationship between sensory and motor signals (Ito, 2000; Miall et al., 1993) and is involved in the generation of sensory predictions (Blakemore et al., 2001). I speculate that the cerebellar activations observed in **Studies I and III** reflect the neuronal computations underlying the generation of tactile predictions based on visual impressions from an object moving close to and about to touch an artificial limb that is perceived as part of the self. The observed increase in connectivity between the cerebellum and premotor-intraparietal cortices during the invisible hand illusion supports the notion that this cerebellar information is made available to the fronto-parietal circuits responsible for establishing multisensory body representations.

In all of the studies included in this thesis, we used the classical approach in psychology of studying perceptual illusions to understand how the brain's normal perceptual processes work. A general limitation of this approach is that patterns of brain activation and behavioral/physiological responses (e.g., threat-evoked SCRs) observed in subjects while experiencing an illusion could potentially reflect nonspecific effects related to arousal or the experience of an unusual percept. For instance, it is theoretically possible that the synchronous visuo-tactile stimulation used to induce the illusions in **Studies I, III, IV, and V** led to an increase in the level of attention paid to a certain portion of the visual field, which could potentially confound the analysis of illusion-related neural activation identified

* All of the participants in Study V did not have cerebellar coverage due to the high-resolution, narrow field-of-view fMRI protocol used, and activations in the cerebellum could thus not be examined in this study.

via BOLD responses or threat-evoked SCRs. However, we took several measures to exclude these potential confounders in our studies, and there are very strong arguments against a purely attentional explanation of our findings. First, we controlled for visuo-tactile synchrony in all of the studies by including appropriate experimental control conditions (e.g., temporally synchronous but spatially incongruent visuo-tactile stimulation), which excludes the possibility that visuo-tactile synchrony *per se* or associated attentional differences can explain the observed illusion-related BOLD-signal or SCR differences. Second, the experimenter who was manually delivering the stimuli ensured that the participants always kept their hands in a fixed position in all of the experimental conditions. The observation that there were no differences in hand movements between the illusion and control conditions is supported by the lack of any significant illusion-associated BOLD activity in primary motor areas in **Studies I, III, and V**. Third, there were no significant differences in eye movements across the conditions (see the eye-tracking results of **Study V**; Supplementary Figure 5), which would be expected had there been substantial differences in the where subjects were directing their attention between illusory and non-illusory conditions. Fourth, we observed significant correlations between neural and behavioral measures in all of the fMRI studies (e.g., between the magnitudes of BOLD responses and threat-evoked SCRs in **Study I** and between self-location decoding accuracy and reported self-location scores in **Study V**). These findings support the notion that the neural activity in our regions-of-interest were related to changes in the sense of ownership or self-location rather than to changes in attention brought about by the synchrony of the visual and tactile stimuli or to nonspecific effects of arousal. This is further supported by the results of **Study I** in which we found ownership-related BOLD activity in multisensory regions even though the experiment involved ownership of the participants' real hand, which presumably constitutes a less exciting and unusual experience than ownership of an artificial hand. Finally, in **Study I**, we conducted a separate control experiment to specifically address the issue of attentional effects. Here, we employed an explicit visual attention task in the context of experiencing illusory ownership of a virtual hand elicited via synchronous visuo-tactile stimulation or in a non-illusory context in which the stimulation was asynchronous. The results show that the participants' level of performance ($P=0.59$) and their reaction times ($P=0.48$) did not significantly differ between the synchronous and asynchronous conditions. In addition, the ownership-related BOLD-responses in multisensory regions were preserved in spite of the explicit attentional task being performed. Together, these findings suggest that experiencing body ownership illusions in general does not lead to impaired visual attention or shifts in attention to portions of the visual field that are not

subject to the visuo-tactile stimulation, and they suggest that nonspecific attentional effects or arousal do not explain the ownership-related patterns of brain activation observed in our fMRI studies.

The results presented in this thesis are relevant to areas of research in applied neuroscience, in particular to the fields of neuroprosthetics and telepresence. One of the major goals in neuroprosthetics is to create artificial limb devices that not only move according to the user's intentions and relay sensations of touch but also feel as though they were the user's own limbs. Although previous studies on amputees have shown that it is possible to induce ownership of a prosthesis by using peripheral somatosensory stimulation, either in the form of tactile stimulation of the stump (Ehrsson et al., 2008; Schmalzl et al., 2011), a reinnervated patch of skin (Marasco et al., 2011) or, possibly, electrical stimulation of cuff electrodes chronically implanted in peripheral nerves (Ortiz-Catalan et al., 2014; Tan et al., 2014), it remains unknown whether it is possible to elicit ownership sensations through electrical brain stimulation. The induction of ownership sensations via cortical stimulation would have important implications for the development of advanced prosthetics devices and exoskeletons based on brain-computer interfaces in patients who lack peripheral sensory input for reasons such as lesions of the spinal cord, peripheral nerves, or subcortical structures. Characterizing the neural correlates of limb ownership and the underlying psychological processes could facilitate the identification of suitable cortical targets for neural stimulation. Given the results of previous studies on the rubber hand illusion (Botvinick and Cohen, 1998; Ehrsson et al., 2004) and those of **Study I** showing that ownership of an artificial limb as well as one's real limbs depend on the integration of multisensory input in the premotor-intraparietal regions, I hypothesize that spatially and temporally congruent visual stimulation of an artificial hand and electrical stimulation of the primary somatosensory cortex can be integrated in these multisensory areas to create ownership sensations. This prediction presupposes a flexible model of multisensory integration for bodily self-attribution that allows crude electrically induced somatosensory signals to be integrated with natural high-quality visual signals from a rubber hand being touched. This supposition could potentially be tested using electrocorticographic stimulation.

Another possible application of the present results is the development of enhanced virtual environments in which the user experiences ownership of a virtual body and a strong sense of presence (Slater et al., 2008, 2009). The development of such realistic virtual environments in combination with body ownership illusions could have relevant clinical

applications (e.g., treating social anxiety disorders [Guterstam et al., 2015b; Slater et al., 2006], motor rehabilitation in neurological patients [Sveistrup, 2004], or enhanced control over surgical robots [Seymour et al., 2002]). Furthermore, characterizing the neural mechanisms underlying body ownership and self-location has important implications for the development of true telepresence—an interface that would allow the user to experience being physically located outside the real body in another part of the world—which could have relevant applications in education, communication, travel, and entertainment.

In conclusion, this thesis sheds light on two fundamental aspects of bodily awareness: the process of attributing the body to the self (body ownership) and of representing the location of one's body with respect to the environment (self-location). Together, the results of **Studies I-V** provide converging evidence for the notion that multisensory integration within the peripersonal space is key for the emergence of body ownership and establishing the sense of self-location. Increasing our understanding of the neural mechanisms underlying bodily and spatial aspects of the self is at the heart of cognitive neuroscience because these processes define the origin of the egocentric reference frame that is necessary for self-consciousness (Blanke and Metzinger, 2009; Vogeley and Fink, 2003) and our ability to interact with the outside world (Graziano and Botvinick, 2002).

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