Balancing interoception and exteroception: vestibular and spatial contributions to the bodily self

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Abstract

Experiencing the body as a coherent, stable, entity involves the dynamic integration of information from several internal (i.e. interoceptive) and external (i.e. exteroceptive) sensory sources, to produce a feeling that the body is mine (sense of body ownership), that I am in control (sense of agency) and I am aware of its movements (motor awareness). However, the exact contribution of these different sensory sources to self-consciousness, as well as the context in which we experience them, is still a matter of debate.

This thesis aimed to investigate the neurocognitive mechanisms of body ownership, agency and motor awareness, including interoceptive (via affective touch), proprioceptive, exteroceptive (visuo-spatial) and vestibular contributions to body representation, in both healthy subjects and brain damaged patients. To examine the role of the vestibular and interoceptive systems in body ownership, a series of studies in healthy subjects was devised, using multisensory illusions (i.e. the rubber hand illusion; RHI), that involve the integration of interoceptive and exteroceptive sensory sources, and using electrical stimulation of the vestibular system (i.e. Galvanic Vestibular Stimulation; GVS). To investigate ownership, agency and motor awareness in neuropsychological patients with disorders of ownership and/or unawareness of motor deficits, behavioural manipulation of body ownership (via a rubber hand) and visual perspective (via a mirror) were tested. Finally, to explore underlying mechanisms of awareness of one's own performance (i.e. meta-cognition), two studies were carried out in healthy subjects using behavioural manipulations of spatial reference frames (either centred on the subject, i.e. egocentric, or world-centred, i.e. allocentric).

The results of these studies indicate that the vestibular system balances vision and proprioception according to contextual relevance: when there is no tactile stimulation, visual cues are stronger than proprioceptive ones (i.e. proprioceptive drifts are greater); when touch is delivered synchronously, this effect is enhanced (even more when touch is affective rather than neutral). However, when touch is only felt but not seen, the vestibular system downregulates vision in favour of proprioception (i.e. proprioceptive drifts are smaller), whilst the opposite happens when touch is only

vicariously perceived via vision. Nevertheless, when the rubber hand is positioned in a non-biomechanically possible fashion, there appears to be no difference in proprioceptive drifts in comparison with anatomically plausible positions, suggesting that such rebalancing may be more related to basic multisensory integration processes underlying body representation. In patients with disorders of the self, visual cues seem to dominate over proprioceptive ones, leading to strong feelings of ownership of a rubber hand following mere exposure to it; however, the same is not true for agency, which seems to be more susceptible to changes in the environment (i.e. presence or absence of a visual feedback following attempted movement). Moreover, manipulating visual perspective using a mirror (from 1st to 3rd) seem to lead to a temporary remission of dis-ownership but not motor unawareness, suggesting that awareness may not be influenced by online changes in visual perspectives. Finally, when judging their own performance in a visuo-proprioceptive task from an egocentric rather than an allocentric perspective, healthy subjects appear less objective prospectively rather than during the task (i.e. their belief updating is biased when judging their ability to complete a task egocentrically).

In sum, the work described above adds to the evidence that the sense of self derives from a complex integration of several sensory modalities, flexibly adjusting to the environment. Following brain damage, such flexibility may be impaired, even though it can be influenced by spatial perspective. Similarly, the point of reference from which we perceive stimuli affects the way we judge our own perceptual choices. Hence, the way we represent our bodily self is a dynamic process, constantly updated by exteroceptive and interoceptive incoming stimuli, regulated by the vestibular system. These findings could provide new avenues in rehabilitating disorders of the self (such as unawareness and dis-ownership).

Declarations

I declare that this thesis represents my own work and it has not previously been submitted successfully for an award.

The study presented in Chapter 2 has been published in:

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The study presented in Chapter 3 is currently in press in Psychophysiology and available online in its final version:

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Table of contents

List of Tables

List of Figures

List of Appendices

Abbreviations

AHP	Anosognosia for Hemiplegia
AROC	Area under the receiver-operating characteristic (ROC) curve
CT	C-Tactile
DSO	Disturbed Sensation of limb Ownership
fMRI	functional Magnetic Resonance Imaging
FoR	Frame of Reference
GVS	Galvanic Vestibular Stimulation
HC	Healthy Controls
HP	Hemiplegic Patients
HDT	Heart-beat Detection Task
HTT	Heart-beat Tracking task
IQR	Inter-Quartile Range
LGVS	Left Galvanic Vestibular Stimulation
LMM	Linear Mixed Model
M	Mean
Mdn	Median
MRI	Magnetic Resonance Imaging
PP	Person Perspective
RGVS	Right Galvanic Vestibular Stimulation
RHI	Rubber Hand Illusion
SD	Standard Deviation
RHI	Rubber Hand Illusion
VLSM	Voxel-based Lesion-Symptom Mapping
VoC	Visual Capture of Ownership

Chapter 1

General introduction

1.1. Background

"Biological brains are first and foremost the control systems for biological bodies. Biological bodies move and act in rich real-world surroundings."

Andy Clark

The concept of embodied cognition, i.e. the idea that the mind is inherently rooted in an individual's physical body (Clark, 1998), has increasingly gained consensus among cognitive scientists in the past decades. However, despite extensive attempts to integrate the notions of mind, brain and body, few theoretical frameworks have fully embraced such holistic views as the basis for the study of cognition and behaviour (Paulus et al., 2019). The philosophical debate around whether we are a "mind in a body" started centuries ago, with Descartes' dualistic view of the mind and body as separate ontological entities. Since then, several steps have been taken to reconciliate the idea that the mind and the body are not entirely distinct features of human beings. Such debate took a turn in the late 1800/early 1900 with the James-Lange and Cannon-Bard theories of emotions, opening the discourse around whether emotions are essentially top-down (i.e. derived from higher-order cognition and ultimately leading to perception of the associated feeling) or bottom-up (i.e. from perception to higher order cognition), with James and Lange proposing that bodily states are the basis for developing emotions in humans (Lange & James, 1922). The relevance of such notions for today's concept of embodied cognition is not only confined to the emotional domain but to a more general understanding of our sense of self. As such, this thesis aims to investigate facets of our sense of self from an embodied perspective. Specifically, it examines how the integration of different sensory modalities gives rise to a conscious sense of bodily awareness.

The abovementioned debate opened the door to a newly conceptualised way of investigating the sense of self from an embodied perspective, with increased scientific interest and methodological rigour. In 1991, in “The embodied mind”, Varela posited that consciousness cannot be investigated without taking into consideration that the experience of the world, and one’s own self, is always an embodied experience (i.e. the subject is never experiencing without a body; Varela, 1996). Stemming from this, several approaches were developed in order to study consciousness in an embodied perspective. Specifically, one way to investigate how individuals develop a conscious experience of the external world, and their own body, is to look at it as the result of a multisensory integration process (i.e. the integration of different sensory modalities into a coherent percept). In this view, the bodily self is the result of the integration of sensory information conveyed by different sensory signals, weighted according to their contextual relevance (Fetsch et al., 2011; Stein et al., 2014). That is, different sensory signals contribute to the formation of a coherent perception of the outside world according to the context in which they are experienced: for instance, if we are far from an object, we rely on vision to detect its main characteristics (e.g. size or colour). If we are in reach, tactile information can inform us about additional features (e.g. texture). The same dynamic balancing of sensory information depending on context applies to how we construct a sense of self (dynamic here refers to the updating of our sense of self by using incoming sensory information available at any given moment).

Being able to process information coming from both outside and inside our body is the basis for the abovementioned dynamic integration, ultimately leading to the sense that our body belongs to us (i.e. body ownership; Gallagher, 2000). In 2002, Craig proposed that interoception, i.e. the sense of the physiological state of our body, may constitute the starting point of our conscious self. He argued that individuals’ homeostatic processes, and their awareness of them, lead to a primitive, “material”, sense of self, which is then subsequently refined into more abstract and conceptualised views of the self. Craig’s theory has supported a more bodily-focused view of self-consciousness, by positing the starting point of individuals’ experience in their awareness of their own bodily states. This led to the view that, instead of being “brains in a vat” (i.e. minds disconnected from their own body which are still able to produce a sense of self, according to Putnam; see Goldberg, 2016), individuals are embodied beings, whose consciousness and perception derives from a dynamic processing of interoceptive, proprioceptive (i.e. related to the sense of position of one's own body in space) as well as exteroceptive (i.e. perception of stimuli originating outside of one's own body, including other social agents) signals (Fotopoulou & Tsakiris, 2017; Tsakiris, 2010). However, such embodied self is a multifaceted concept, encompassing body ownership, the sense of self-awareness and the sense of agency (i.e. the sense of being in control of our own actions; Haggard, 2005). The degree to which each of these aspects of the bodily self is influenced by the integration of different sensory modalities, and how these different aspects of the self relate to each other, is yet to be fully determined.

In 1998, a novel method to explore the boundaries of the bodily self was put forward by Botvinick and Cohen. Given that studying how individuals integrate different sensory modalities to obtain a sense that their own body belongs to them poses intrinsic constraints (i.e. individuals are already embodied beings and their body is always present; Tsakiris, Hesse, Boy, Haggard, & Fink, 2007), these authors exploited a multisensory conflict between touch, proprioception and vision in order to elicit an illusory sense of ownership of a realistic rubber hand. This paradigm, namely the Rubber Hand Illusion (i.e. RHI), has been at the forefront of the advances in understanding the way different sensory signals are combined to give individuals the sense that their body is, in fact, their own. Studies using conflictual sensory paradigms to investigate the sense of body ownership have been increasingly implemented following the advent of the RHI (Ehrsson, 2007; Tsakiris, 2008). Such experimental paradigms in healthy subjects aided our scientific understanding of the self as a bodily self, by providing a theoretical framework of how different sensory modalities contribute to inform distinct aspects of the self.

Similarly, the study of disorders of the self (such as feelings of dis-ownership or lack of self-awareness) in patients with brain damage (i.e. neuropsychological patients) has opened new research avenues. For instance, specific disorders, namely Anosognosia for Hemiplegia (i.e. AHP; unawareness of paralysis, Babinski, 1914) and Disturbed Sensations of limb Ownership (i.e. DSO, ranging from the sense of non-belonging of the paretic limb to the delusional attribution of the limb to somebody else; Baier & Karnath, 2008) offer a unique insight into the cognitive mechanisms underlying our embodied cognition (Caramazza & Coltheart, 2006; Fotopoulou, 2014). These patients, contrary to healthy subjects, present with unawareness or dis-ownership of their own body, thus providing researchers with the possibility of investigating what mechanisms and neural correlates are compromised, in order to better understand the intact mechanisms sub-serving the formation of a coherent bodily self. Nevertheless, the neural correlates as well as the role played by the integration of sensory signals in forming a sense of body ownership, self-awareness and agency (as well as their relationship) are not yet fully understood, and studies in patients with disorders of the self could help elucidate these aspects.

More recently, alongside classic exteroceptive modalities (e.g. vision) and recently defined interoceptive signals (e.g. pain – see Craig 2002; 2003 and Ceunen et al., 2016 for a discussion of pain as interoceptive), two understudied sensory systems have been linked to the formation and maintenance of the bodily self, with a specific focus on their role in body ownership (investigated via the RHI). The first one, namely the vestibular system, is well-known for its role in regulating balance, posture and motor coordination during self-motion (Brandt & Dieterich, 1999). However, there is increasing evidence pointing towards the vestibular system as a key modality in multisensory integration (Bense et al., 2001), body representation (Ferrè & Haggard, 2016; Been et al., 2007) and body ownership (Ferre, Berlot, & Haggard, 2015; Lopez, Lenggenhager, & Blanke, 2010). It has been suggested that the right-hemisphere vestibular network may balance different sensory signals according to their relevance during multisensory integration processes (Ferrè, et al., 2015). Nonetheless, the exact modulation of multisensory integration by the vestibular system is still a matter of debate, with conflicting findings and unexplored avenues.

The second one, namely the C-Tactile (i.e. CT) system, is a reconceptualised interoceptive modality (Ceunen, Vlaeyen, & Van Diest, 2016), recognised as such due to its shared physiological pathway with other interoceptive modalities (e.g. pain) (Björnsdotter, Morrison, & Olausson, 2010). The peculiarity of the CT system is that, despite being activated by tactile stimulation at slow velocities comprised between 1-10 cm/s, it is not involved in discriminatory aspects of touch (i.e. the ability to explore physical properties of objects via touch) but rather conveys feelings of pleasantness and affectivity (i.e. CT-optimal stimulation is correlated with perceived pleasantness; Löken et al., 2009). As such, the CT system can be considered as part of the interoceptive, rather than exteroceptive, modalities (Ceunen et al., 2016). Interestingly, the CT system has been linked to body ownership and body representation due to its role in enhancing illusory ownership of a rubber hand during the RHI (Crucianelli, Krahe, Jenkinson, & Fotopoulou, 2017; Crucianelli, Metcalf, Fotopoulou, & Jenkinson, 2013). However, the exact contribution of the CT-system to facets of the bodily self remains debated, with studies suggesting specific CT-dependent contributions to body ownership and others pointing to a more general role of the affectivity conveyed by the slow type of touch associated with CT activation (Lloyd, Gillis, Lewis, Farrell, & Morrison, 2013; van Stralen et al., 2014).

Hence, the overarching aim of this thesis is to shed light on the processing underlying bodily awareness (i.e. the sense of being aware of one's own body) in healthy subjects as well as neuropsychological patients. Specifically, the contribution of vestibular and interoceptive systems in multisensory integration processes leading to body ownership, as well as the study of different facets of the self (including agency and self-awareness) will be explored from an embodied cognition perspective to fill existing gaps in the literature. Firstly, the role of the vestibular system in balancing different sensory modalities, including interoceptive ones, will be investigated (Chapters 2-4), to provide evidence for a key role of vestibular and interoceptive signals in leading to a coherent perception of one's own body. Then, the influence of different sensory modalities, as well as different spatial perspectives, on body ownership, motor awareness (i.e. awareness of our own actions) and agency will be explored (Chapters 5 and 6), to shed light on processes underlying aspects of the self and identify potential interventions. Finally, the influence of spatial reference frames during integration of sensory signals on individuals' self-awareness will be presented in Chapter 7, with a focus on how signals arising from one's own body influence metacognitive processing and thus contribute to self-awareness. Thus, this thesis aims to explore the concept of bodily awareness via the presentation of neuromodulation, neuropsychological and behavioural studies.

1.2. Exteroceptive and interoceptive sensory integration: the basis of the bodily-self

Multisensory integration is the fundamental process through which signals from different sensory modalities are combined to produce a coherent perceptual experience of the world as well as our own body (Ernst & Banks, 2002; Fetsch, Pouget, DeAngelis, & Angelaki, 2011; Stein, Stanford, & Rowland, 2014). Typically, studies exploring multisensory integration focused on the combination of sensory modalities such as vision, proprioception and touch (Folegatti, de Vignemont, Pavani, Rossetti, & Farnè, 2009; Holmes, Crozier, & Spence, 2004; Pavani, Spence, & Driver, 2000; van Beers, Wolpert, & Haggard, 2002). Moreover, in the last two decades, hundreds of experimental studies have manipulated these modalities to study not only how we perceive combined sensory input, but also how we relate such perceptions from the body to our psychological sense of the self. Specifically, the bodily self has been defined as a multi-componential phenomenon, entailing the sense that our body belongs to us (i.e. body ownership; Gallagher, 2000), the sense that we are aware of our own body and of the outcomes of our actions on the environment surroundings us (i.e. self-awareness) and the sense of being in control of such actions (i.e. agency; Haggard, 2005). The relationship between these different facets of the bodily self is yet to be determined. Whilst some posit that ownership and agency are dissociated (Kalckert & Ehrsson, 2012), others put them in relation to each other, suggesting one may inform the other (yet without a clear directional hypothesis; Asai, 2016; Burin et al., 2018; Tsakiris, Prabhu, & Haggard, 2006). As for self-awareness, which encompasses motor awareness (i.e. awareness of one's own actions; Fourneret & Jeannerod, 1998), whilst advances have been made in defining its core aspects (e.g. how planning and monitoring our own actions leads to a sense that these actions have been performed by us and what their outcome is; Wolpert, 1997), the relationship between self-awareness, body ownership and agency has not been clarified.

The implementation of bodily illusions in healthy individuals helped to shed light on how these different aspects of the self are integrated into a coherent representation of our own self. Specifically, such illusions revealed that the bodily self is modifiable and dynamic: the way we represent our body is constantly updated according to incoming stimuli. For instance, during the RHI (Botvinick & Cohen, 1998), participants watch a fake, realistic, hand being touched in synchrony or out of synchrony with their own, unseen, hand. Usually, both the rubber hand and the real hand are inserted in a box, such that during each condition participants can only see the rubber hand whilst their own hand is concealed. As a result of synchronous stroking of both the rubber hand and participant's hand, individuals may feel subjective feelings of ownership of the rubber hand, and/or a shift in the perceived location of their own real hand towards the position of the rubber hand (i.e. proprioceptive drift). When faced with such a sensory conflict, individuals have to combine the visual experience of seeing a hand that does not belong to them, whilst feeling their own hand in a different point in space. When touch is added in a synchronous fashion (i.e. delivered at the same time, speed and relative location on both real and rubber hand), individuals are confronted with a three-way conflict between vision, proprioception and touch. One way to resolve such conflict is by attributing the location of the felt touch to the one where the touch is seen (i.e. touch is felt in one place, but is seen in another) and hence perceiving the illusion of ownership of a rubber hand (Tsakiris, 2010). This model of embodiment during the RHI has provided significant insight into how conflict between vision of a synchronously touched rubber hand and proprioception of the real hand's different location is resolved by information from one modality (vision) dominating over the others (e.g. proprioception; Folegatti, de Vignemont, Pavani, Rossetti, & Farnè, 2009; Pavani, Spence, & Driver, 2000; van Beers, Wolpert, & Haggard, 2002). This "visual capture" effect, characterised by a dominance of visual cues over other modalities (Rock & Victor, 1964), occurs when vision is deemed contextually more reliable. For instance, when we process stimuli during a task performed in the horizontal spatial plane, vision is weighted more than proprioception; on the contrary, proprioceptive cues are weighted more when the task requires subjects to process sensory inputs in the vertical plane (i.e. in depth) (van Beers et al., 2002). As such, "visual capture" refers to the relative dominance of vision over other sensory modalities during multisensory conflict.

As mentioned above, one of the several sensory modalities contributing to the formation and maintenance of our sense of self, namely interoception, has gained increasing scientific interest in the past decades. The early definition of interoception only comprised visceral sensations coming from involuntary muscles' receptors (Sherrington, 1906). During the 20th and the beginning of the 21st century, the study of cardiovascular (e.g. Critchley, Wiens, Rotshtein, Ohman, & Dolan, 2004; Garfinkel, Seth, Barrett, Suzuki, & Critchley, 2015), nociceptive (e.g. von Mohr, Krahé, Beck, & Fotopoulou, 2018) and autonomic responses (such as temperature) as well as feelings of thirst and hunger, led to a redefinition of the term interoception, which now encompasses all the signals related to the sense of the physiological condition of one's own body (Craig, 2002). Several studies are now beginning to investigate the relationship between interoception, multisensory integration and our sense of self (e.g. Suzuki, Garfinkel, Critchley, & Seth, 2013; Tajadura-Jiménez & Tsakiris, 2014; Tsakiris, Tajadura-Jimenez, & Costantini, 2011).

One of the most commonly employed ways to establish interoceptive sensitivity (i.e. the ability to accurately report one's own interoceptive signals; Barrett, Quigley, Bliss-Moreau, & Aronson, 2004) is asking individuals to detect their own cardiac activity. In particular, two main tasks have been consistently used as a parameter of interoceptive sensitivity: the Heart-beat Tracking Task (i.e. HTT), during which participants are asked to count the number of perceived heartbeats in a specific time window (Schandry, 1981) or the Heart-beat Detection Task (i.e. HDT), instructing participants to report the occurrence of their own heartbeats in accordance with external stimuli (Brener & Kluvitse, 1988; Whitehead, Drescher, Heiman, & Blackwell, 1977). Research employing the HTT and HDT as a measure of interoceptive sensitivity found that low interoceptive sensitivity is linked with susceptibility to multisensory illusions (e.g. RHI; Suzuki et al., 2013; Tsakiris et al., 2011) as well as modulation of self-other distinction, with low interoceptive sensitivity leading to increased identification with others during multisensory illusions (such as the rubber hand and full-body illusions) (Tajadura-Jiménez & Tsakiris, 2014). However, other research groups have not replicated these findings (e.g. Crucianelli, Krahé, Jenkinson, & Fotopoulou, 2018), suggesting that the relationship between body ownership and different aspects of interoception is yet to be fully understood.

Investigating detection of cardiac activity, however, is not the only way to explore the role of interoception in multisensory integration and body representation. In 1988, a new type of C-fibres, namely C-tactile (CT) fibres was discovered in the hairy skin of humans (Johansson, Trulsson, Olsson, & Westberg, 1988; McGlone & Reilly, 2010). CT-fibres are optimally activated by slow, dynamic (i.e.

moving across the skin), caress-like tactile stimulation at velocities between 1 and 10 cm/s (McGlone et al., 2014), which is strongly correlated with perceived feelings of pleasantness (Lӧken et al., 2009; Shaikh et al., 2015; Pawling et al., 2017). Microneurography studies (e.g. Vallbo, Olausson, & Wessberg, 1999; Watkins et al., 2017) identified a physiological difference in the pattern of activity between stimulation of C-tactile afferents and C-mechanosensitive nociceptors (i.e. C-fibres responsible for encoding of pain stimuli). By means of microneurography recordings of nervous activity in healthy subjects undergoing tactile stimulation on their left arm (i.e. stroking, to identify CT fibres, and pinching, to elicit a response in C-mechanoreceptors), Watkins and colleagues showed clear differences at the electrical level between C-tactile fibres and C-mechanoreceptors. Specifically, the former responds to low-threshold gentle stroking and conveys positive affective information, whilst the latter is high-threshold and is involved in somatosensation and pain. Furthermore, a single case of a patient with a selective loss of large, myelinated fibres, necessary to perceive discriminatory features of touch (A-class fibres rather than C, unmyelinated, fibres), provided further insight into the role of CT fibres. Despite an inability to perceive discriminative aspects of touch, this patient was able to perceive pleasantness following stimulation of CT fibres and showed a functional activation of limbic, rather than somatosensory, areas (e.g. the insular cortex; Olausson et al., 2002). In a complementary fashion, a reduced density of C-fibres due to a type of hereditary neuropathy is associated with reduced perceived pleasantness of touch delivered between 1-10 cm/s (with no effect on discriminative aspects of touch), with a concomitant reduced activation of the posterior insular cortex (Morrison et al., 2011).

Hence, these authors and other research groups have proposed that CT-afferents may be linked to affectivity rather than tactile discrimination (Björnsdotter et al., 2010; McGlone et al., 2012). This type of CT-optimal touch has been identified as a type of affective touch, due to its hypothesised contribution to bonding and affiliative behaviours in humans as well as the positive correlation between CT-fibres stimulation and pleasant sensations (McGlone et al., 2014). Functional imaging studies showed how CT-optimal touch activates multimodal areas of converging sensory and affective information regarding the state of the body (including the posterior insula, Craig, 2002; 2003; Olausson et al., 2002; McGlone et al., 2012 and the cingulate cortex, Case et al., 2017). Moreover, the pleasantness associated with CT-optimal touch is not affected by inhibition of the primary and secondary sensory cortices: in a series of repetitive Transcranial Magnetic Stimulation studies (Case et al., 2016; Case et al., 2017), Case and colleagues showed how perception of affective touch is not influenced by controlled inhibition of somatosensory areas whilst tactile intensity is, thus showing a clear dissociation between affective and discriminatory tactile systems. Taken together, these findings support the notion that the CT-system might play a unique role in conveying affective rather than discriminative aspects of touch. As such, information encoded by CT fibres is considered as contributing to the interoceptive (Ceunen et al., 2016) rather than exteroceptive, modalities (Björnsdotter et al., 2010; Crucianelli et al., 2017).

Whilst integration of visual, proprioceptive and tactile information during the RHI has been extensively studied, the influence of hedonic aspects of touch on body ownership has been only recently investigated. CT-optimal touch has been found to increase embodiment during the RHI (Crucianelli et al., 2013; Crucianelli et al., 2017; Lloyd et al., 2013; van Stralen et al., 2014). For example, Crucianelli and colleagues (2013) found increased subjective embodiment during the RHI using synchronous, CT-optimal touch, whilst van Stralen and colleagues (2014) reported increased proprioceptive drifts following affective (compared to neutral) touch. Thus, affective touch may contribute to the sense of body ownership by increasing subjective and objective measures of ownership during the RHI. However, it is not yet clear whether this contribution is due to the felt components of affective touch or if the effect relies also on its *seen*, vicarious aspects. There are no studies, to date, which investigated the contribution of seen or felt CT-optimal touch during the RHI separately (but only both aspects together). Importantly, a characteristic shared by both affective touch as well as pain is their vicarious property. Affective touch has been shown to elicit comparable feelings of pleasure, and neural activation in the posterior insula, when experienced directly on one's own skin as well as when observed on someone else's skin, i.e. vicarious affective touch (Morrison, Bjornsdotter, & Olausson, 2011a; Morrison et al., 2011b; Walker, Trotter, Woods, & McGlone, 2017). In a study investigating congruency of affective valence of stimuli felt and seen during the RHI, Filippetti and colleagues (2019) devised different conditions during which touch was delivered via objects of different affective valence (i.e. soft vs rough fabrics) either congruently (i.e. both seen and felt touch were of the same valence) or incongruently. The authors found that congruency between the touch felt and the touch seen (i.e. both touch felt and seen were of the same affective valence) enhanced subjective feelings of ownership of the rubber hand in comparison with incongruent conditions (i.e. touch was delivered via two objects of different affective valence; Filippetti, Kirsch, Crucianelli, & Fotopoulou, 2019). Thus, the enhancing effects on ownership found during the RHI may be due to the felt, the seen or both components of affective touch; nevertheless, no study to date has explored this possibility in the context of affective touch.

1.3. Balancing the body: the vestibular system and body representation

Multisensory integration comprises more than just vision, touch, interoception and proprioception. For instance, whilst sitting on a stationary train, individuals looking outside of the window may see another train beginning to move past. Often, this leads to an illusory feeling of movement. In such instances, the vestibular system, which is the system regulating balance, posture and coordination during self-motion, may provide additional information signalling an unresolved conflict between vision (i.e. “I see motion”) and proprioception (i.e. “I feel I am *not* moving”). Such multisensory conflict may result in a feeling of nausea and dizziness (Bertolini & Straumann, 2016), due to the vestibular system balancing visual-proprioceptive cues in favour of vision. In the past years, an increasing number of studies investigated the possibility that the modulatory role of the vestibular system may go beyond the regulation of posture and balance, and that it may actually play an important role also in the multisensory integration processes involved in body ownership (Brandt & Dieterich, 1999).

Information about acceleration, rotation and gravity is captured by vestibular receptors in the inner ears in a continuous flow, and it is then conveyed to the central nervous system via the vestibular nerves (Day & Fitzpatrick, 2005). Interestingly, the vestibular system is one of the few sensory modalities that does not have a primary unimodal cortex (Been, Ngo, Miller, & Fitzgerald, 2007; Ferrè & Haggard, 2016). Functional imaging findings (Fasold et al., 2002; zu Eulenburg, Caspers, Roski, &

Eickhoff, 2012) suggest the presence of a distributed network of areas receiving input from vestibular signals as well as other sensory modalities, such as vision (Brandt et al., 2002; Seemungal et al., 2013; Della-Justina et al., 2015), touch and proprioception (Dijkerman & de Haan, 2007; Lackner & DiZio, 2005). Furthermore, areas of the vestibular network partially overlap with multisensory integration areas, such as the temporoparietal junction, inferior parietal lobule, insula and cingulate cortex (Lopez et al., 2012; Lopez, 2016). Such overlap may represent the neural correlate of vestibular contributions to different aspects of body representation (i.e. the way we combine knowledge, experiences and beliefs to give rise to the representation of our own body; Longo, Azanon, & Haggard, 2010). Accordingly, the vestibular system has been shown to influence lower-level perception of body features (such as shape and size, Lopez et al., 2012c) as well as the sense of body ownership (Lopez, 2015).

In order to explore the influence of vestibular signals on body representation and body ownership, several studies implemented artificial vestibular stimulation to activate the peripheral vestibular organs. For example, excitation of the semi-circular canals of the internal ear by insertion of cold or warm water (i.e. Caloric vestibular stimulation, CVS) activates contralateral vestibular areas. In patients affected by right-hemisphere stroke and disorders of the self (see section "1.4. Dis-ownership, motor awareness and agency in right hemisphere stroke patients" for further details), CVS targeting the right hemisphere has led to improvements in self-awareness (Cappa et al., 1987; Vallar et al.,1993; Bottini et al., 2005) as well as body ownership (Bisiach et al., 1991). A novel, less invasive, and more controlled way of stimulating the vestibular network is via Galvanic Vestibular Stimulation (GVS). GVS has been proven to be a useful tool in both experimental paradigms and rehabilitative contexts (Utz, Dimova, Oppenländer, & Kerkhoff, 2010). A small electrical current (up to 2 mA) applied using two electrodes (one anode and one cathode) positioned on the mastoids influence the electrical excitability of the underlying vestibular nerves. When the anode is located on the left mastoid and the cathode on the right (i.e. LGVS), the right-hemisphere vestibular network is activated, whilst the opposite configuration (i.e. RGVS) leads to bilateral activation (Eickhoff, Weiss, Amunts, Fink, & Zilles, 2006; Kammermeier, Singh, & Bötzel, 2017; Lopez et al., 2012; Stephan et al., 2005; Stephan, Bense, Yousry, Brandt, & Dieterich, 2000; zu Eulenburg et al., 2012).

GVS has been increasingly employed in order to study vestibular contributions to body ownership and body representation. However, findings of studies combining the RHI with GVS have not been always consistent. Specifically, LGVS seems to differentially influence subjective embodiment and proprioceptive drifts during the RHI. Ferrè and colleagues (2015) devised an RHI paradigm during which participants underwent brief bursts of vestibular stimulation. The authors found a decrease in proprioceptive drifts following synchronous stroking conditions in LGVS only, suggesting that vestibular stimulation of the right-hemisphere would lead to an enhancement of proprioceptive signals over visual ones (Ferrè et al., 2015). Conversely, in an RHI study with longer stimulation windows (i.e. 1 minute) Lopez and colleagues (2010) found increased subjective embodiment and a trend for increased proprioceptive drifts following LGVS. This points to an opposite pattern in respect to Ferrè and colleagues' study, with vision dominating over proprioception during the RHI by enhancing a "visual capture" of ownership (Lopez et al., 2010). Regardless, both studies indicate that vestibular signals may regulate multisensory integration according to the contextual relevance of each different sensory modality. Hence, the vestibular system may act as a balancing factor in order to solve sensory conflicts, by either enhancing vision (see Lopez et al., 2010) or proprioception (see Ferrè et al., 2015).

However, there are several alternative explanations of how the vestibular system might affect multisensory integration, other than its balancing role in weighting visual versus proprioceptive signals. For instance, the vestibular system may act on the primary somatosensory cortex by attenuating proprioceptive signals, instead of balancing the different sensory modalities in a later stage of multisensory processing. This could, in turn, lead to a subsequent enhancement of visual cues. Accordingly, Schmidt and colleagues (Schmidt, Artinger, Stumpf, & Kerkhoff, 2013) found that LGVS impairs proprioceptive processing during an arm positioning task, in which individuals are asked to estimate the location of their arm whilst undergoing vestibular stimulation. Furthermore, another possibility is that vestibular stimulation of the right hemisphere may induce a compensatory shift towards the left in the lateral space (Ferrè, Longo, Fiori, & Haggard, 2013; Utz, Keller, Kardinal, & Kerkhoff, 2011; Wilkinson et al., 2014): following this idea, the effects seen during the RHI coupled with

GVS may be linked to a remapping of external visual space rather than to changes in body representation.

Hence, the first three chapters of this thesis will be exploring different, possible effects of GVS on body ownership during the RHI. Specifically, using different variants of the Rubber Hand Illusion, combined with GVS, the role of the vestibular system in balancing sensory conflict and body representation will be explored. Furthermore, the influence of vestibular stimulation on multisensory integration of both exteroceptive and interoceptive signals will be examined. Specifically, in Chapter 2, the previously unexplored question of how the vestibular system might influence the already reported role of exteroceptive (vision) and interoceptive (affective touch) signals in body ownership will be investigated. In Chapter 3, the unanswered question of whether the seen versus felt aspects of affective touch are the cause of previously observed effects on body ownership (e.g. Crucianelli et al., 2013; Lloyd et al., 2013; van Stralen et al., 2014) will be addressed, with a specific focus on the effects of vestbular stimulation on different aspects of touch. Finally, in Chapter 4 the extent to which the previously observed effects of vestibular stimulation can be attributed to a weighting mechanism of different sensory signals during multisensory integration (as hypothesised by Ferrè et al., 2015) will be assessed via investigation of alternative hypotheses.

1.4. Dis-ownership, motor awareness and agency in right hemisphere stroke patients

"If a man has lost a leg or an eye, he knows he has lost a leg or an eye; but if he has lost a self —himself— he cannot know it, because he is no longer there to know it."

Oliver Sacks

As outlined in the sections above, far from being a static process, our sense of self-awareness and body ownership rely on the continuous integration of several sensory signals (Tsakiris, 2010).

However, following a stroke in the fronto-parietal areas of the right-hemisphere, this dynamic updating can be severely compromised (Feinberg et al., 2010; Moro et al., 2016). In 1914, Babinski coined the term “anosognosia” to describe right-hemisphere stroke patients with a left-sided paralysis and seemingly unawareness of such paralysis (it was later defined as Anosognosia for Hemiplegia to distinguish it from other deficit-specific forms of unawareness; Vossel et al., 2013; Fotopoulou, 2014). In 1942, Gerstmann observed, for the first time, two right-hemisphere stroke patients asserting that their left side limbs did not belong to them (Gerstmann, 1942). More recently, the term Disturbed Sensations of limb Ownership (i.e. DSO; Baier and Karnath, 2008) has been put forward to encapsulate different phenomena regarding distorted representation of patients’ left side limb: from strong feelings of denial of ownership (i.e. asomatognosia; see Jenkinson et al, 2018), to a delusional attribution of the limb to somebody else (i.e. somatoparaphrenia, as Gerstmann labelled it; Feinberg and Venneri, 2014; Vallar and Ronchi, 2009). These conditions can offer a unique insight into our understanding of different aspects of body representation: studying the bodily self in healthy subjects only has a reduced possibility to look at the mechanisms necessary for ownership, agency and self-awareness to arise (i.e. effects are temporary and often small) as well as their neural correlates. Conversely, studying patients lacking specific aspects of the bodily self can improve our understanding of how this sense of self is formed and maintained: patients’ compromised bodily self-awareness can be studied in longer time-windows and lesion analyses can indicate which areas sub-serve specific mechanisms. In particular, using clinico-anatomical (e.g. Berti et al., 2005; Vocat, Staub, Stroppini, & Vuilleumier, 2010) as well as behavioural experimental paradigms (e.g. the RHI) with AHP and DSO patients, several studies over the past decades aimed to investigate the mechanisms underlying body ownership (e.g. Martinaud et al., 2017; van Stralen, van Zandvoort, Kappelle, & Dijkerman, 2013; Zeller, Gross, Bartsch, Johansen-Berg, & Classen, 2011), motor awareness (i.e. awareness of one’s own actions; e.g. Fotopoulou et al., 2008) and the sense of agency (i.e. the sense of being in control of our own actions; Haggard, 2005).

As mentioned above, several aspects of the bodily self can be compromised following a stroke in areas responsible for the integration of different sensory signals, and their combination into a coherent sense of selfhood. Specifically, areas in the fronto-parietal network of the right hemisphere seem to be responsible for the formation and maintenance of body ownership feelings (Cappa et al., 1987; Bisiach et al., 1991; Naito et al., 2005; Tsakiris et al., 2007; Tsakiris, 2010). Patients with right hemisphere stroke and left-sided hemiplegia seem to present with stronger feelings of ownership during classic RHI paradigms in comparison with non-hemiplegic patients (Burin et al., 2015). Additional evidence suggests that establishment of illusory ownership following stroke may be linked to lesions of specific areas, such as the ventral premotor cortex (Zeller, Gross, Bartsch, Johansen-Berg, & Classen, 2011) as well as limbic and multisensory areas (e.g. insular cortex; Martinaud et al., 2017). Even if the majority of right-hemisphere stroke patients present with a more malleable body representation in comparison with healthy subjects, the neural correlates of such phenomena remain unclear. Thus, the question of what areas are responsible for the establishment and maintenance of a coherent sense of body ownership remains unanswered.

Furthermore, in line with the idea that right-hemisphere stroke patients may present with higher malleability of their body representation, research shows that these patients may develop subjective feelings of ownership of a rubber hand just by looking at it (Fotopoulou et al., 2008; Martinaud et al., 2017; van Stralen et al., 2013). When a rubber hand is positioned congruently with patients' own left, paralysed hand (while the latter is hidden), the majority of right-hemisphere stroke patients automatically embody it, even when they deny ownership of their own, paralysed, limb. Such Visual Capture of Ownership (i.e. VoC; Martinaud et al., 2017) may depend on a dominance of visual cues over proprioceptive ones. When there is a lesion in areas related to proprioceptive processing, visual signals may be deemed reliable enough to elicit hand ownership. This mechanism is in line with established model of body ownership in the healthy population (Tsakiris, 2010), whereby conflict between different sensory modalities can be solved by dominance of vision over proprioception when vision is deemed as most reliable. However, in healthy subjects, only a few studies investigated ownership in visual only conditions (i.e. without concomitant tactile stimulation) and even fewer in elderly populations. Hence, it remains unclear whether VoC may represent a pathological exacerbation of normal multisensory integration processes deteriorating with age or if it is specific to the lesion in right fronto-parietal areas.

Moreover, in Martinaud and colleagues' study (2017), even patients with dis-ownership of their own hand automatically embodied a rubber hand in visual only conditions. That is, the majority of the right-hemisphere patients, regardless of their clinical presentation, embodied the rubber hand just by observing it. The authors suggested that patients may be experiencing aberrant sensations incoming from their paralysed arm, preventing them from integrating it in their body representation. Such sensations would hence be in contrast with how patients expect to perceive their arm and would hence lead to a sense of dis-ownership. As mentioned above, this could be due to a disruption in normal multisensory processes, leading to a pathological enhancement of vision over proprioception, as well as to the additional presence of error signals from other sensory modalities. The latter possibility has not yet been investigated and open new questions about what these additional modalities might be and how could these errors be reduced.

It may be possible that the lack of integration between the "subjectively felt" (i.e. DSO patient's own hand) and "objectively seen" (i.e. the rubber hand) body (Fotopoulou et al., 2011) may underlie the inability of DSO patients to incorporate their own arm into their body representation, whilst still being able to feel ownership of a rubber hand. Accordingly, studies investigating DSO patients' ownership in 1st person perspective (i.e. processed from the point of view of the individual) versus 3rd person one (i.e. as experienced from the outside, such as by looking in a mirror) found that DSO patients seem to temporarily regain ownership of their own left limb whilst looking at it in a mirror (i.e. in a 3rd person perspective; Fotopoulou et al., 2011; Jenkinson, Haggard, Ferreira, & Fotopoulou, 2013). In order to maintain a coherent representation of one's own body, individuals constantly integrate information incoming from their own 1st person, as well as the external, 3rd person, perspective. One possibility is that these patients present with an impaired 1st person, subjective representation of their own body, which cannot be updated by incoming sensory signals. For instance, in Martinaud and colleagues' study, this may have translated into the dissociation between VoC for a rubber hand and dis-ownership for their own hand. When presented with an external perspective (i.e. when they look at their own arm in a mirror, instead of directly), DSO patients disengage from their impaired 1st person perspective and perceive their left limb in an objective, free from error signals, way. Nevertheless, the duration and extent of the effect of mirrors in re-establishing body ownership has not been determined, with studies using single cases or very small sample sizes. Thus, further research is needed in order to better characterise and define the extent to which mirrors can be used to reinstate ownership feelings.

As mentioned above, alongside the sense of body ownership, right-hemisphere stroke patients can offer insight into other aspects of body representation, such as motor awareness. The main symptom of Anosognosia for Hemiplegia (i.e. AHP) is the blatant disregard towards sensory feedback (i.e. the lack of movement of their own hand) when patients intend to move their paralysed limb. This has been explained by several different theoretical accounts over the past decades. Originally, AHP was thought to be the result of a denial mechanism, supported by pre-morbid personality traits (i.e. the use of denial as a coping mechanism) (Weinstein & Kahn, 1953), or an active repression (i.e. a mechanism used to maintain deficit-related processes out of the consciousness domain) of traumatic emotional content related to their current disability (Nardone, Ward, Fotopoulou, & Turnbull, 2007). However, despite being one of the possible mechanisms at play, denial and repression cannot explain the multifaceted presentation of anosognosia (Fotopoulou, 2014; Heilman, 2014). The same holds true for accounts associating the presence of anosognosia with concomitant neglect (i.e. inattention towards the contra-lesional side of space despite lack of pure sensory impairments; Vallar & Ronchi, 2006), as several studies highlighted dissociations between these two disorders (Ronchi et al., 2013). Furthermore, AHP cannot be explained by loss of sensory signals (e.g. proprioception) informing body representation or by a global cognitive impairment (as suggested, for instance, by Levine, Calvanio, & Rinn, 1991), as the above have been shown to dissociate (Coslett, 2005; Heilman, 2014; Orfei et al., 2007). Hence, the abovementioned explanatory attempts could not fully account for the symptomatology behind AHP.

One of the major advances in our understanding of motor awareness, and as a consequence AHP, has been the conceptualisation of a forward model for motor control (Wolpert & Miall, 1996). The fundamental idea behind this computational model is that, when a motor command is issued, it produces an efferent copy of such command, which is subsequently compared with the actual incoming sensory feedback. A discrepancy between the expected and the observed movement hence signals the presence of an error, prompting individuals to correct their movements. Thus, AHP could be explained as an inability of these patients to gain awareness of the errors arising from the comparison between the intended movement and the actual outcome. Such unawareness would lead these patients to rely on their original motor intentions rather than on the actual output of their actions. This overriding of motor intentions over sensory signals could explain why, when AHP patients have the intention to move and are asked to express a judgement on whether the movement occurred or not, they tend to rely on their motor expectations, which then prevent them from updating their prediction using available sensory information (Berti et al., 2005; Fotopoulou, 2014). There is some evidence that this disturbance in motor awareness seems to extend to the non-paretic limb, thus suggesting the presence of a global impairment in motor awareness beyond the affected limb in anosognosic patients (Preston, Jenkinson, & Newport, 2010). Previous research (Fotopoulou et al 2008) tried to investigate the extent to which the intention to move influences AHP patients' motor awareness by using an adapted rubber hand paradigm by the bedside (see section 5.1. Introduction, Chapter 5 for details on the methodology). The authors found that AHP patients tended to report occurrence of movement, even when there was none, but only when they had the intention to move (i.e. they showed lack of motor awareness). As such, the replication of these findings in a larger sample size would allow firmer conclusions in terms of the role of dominance of motor intentions in motor awareness.

Furthermore, the aforementioned difference in perception between the "subjectively felt" and "objectively seen" body in DSO patients, may not only affect the sense of body ownership but other aspects of bodily awareness as well. AHP patients seem to be unable to disengage from their 1st person perspective when asked to move their paralysed limb, which in turn leads to their inability to recognise a failure of the intended action. When AHP patients are confronted with their motor weakness, they may create confabulatory accounts and alternative explanations (e.g. "I don't feel like moving right now") to justify the absence of movement of their left arm (Bisiach & Geminiani, 1991; Ramachandran, 1996). However, some AHP patients seem to be able to recognise paralysis in other patients (Ramachandran & Rogers-Ramachandran, 1996) and, whilst unable to acknowledge their weaknesses when confronted with them directly (e.g. "Can you move your arm?"), their awareness improves when questions are asked from the examiner's point of view (Marcel, Tegnér, & Nimmo-Smith, 2004). On these premises, some pioneering studies investigated the possibility that a shift from the 1st person, impaired, perspective to a 3rd, intact, one could improve motor awareness in AHP patients. Specifically, two different studies recorded AHP patients during a motor awareness assessment and then showed the video to the same patients afterwards (Besharati, Kopelman, Avesani, Moro, & Fotopoulou, 2014; Fotopoulou, Rudd, Holmes, & Kopelman, 2009). As a result, one of the AHP patient showed a complete remission of her symptoms (Fotopoulou et al., 2009) whilst two more patients showed significant improvement in awareness of their motor deficits (Besharati et al., 2014). Hence, video self-observation seems to be promising in reinstating motor awareness. However, whether or not such improvement is due to the change in perspectives alone or if it is also influenced by the absence of intention to move remains to be clarified. Given the theorised importance of motor expectations in the emergence of AHP symptoms, the absence of intention to move during self-observation in videoclips (i.e. "offline") might be linked to such dramatic gain of insight. This hypothesis, i.e. that the absence of motor intention may underlie patients' improvement during video self-observation, could be tested using alternative forms of perspective-taking, such as self-observation in mirrors (which allows patients to look at themselves from the outside whilst actively trying to perform a movement, i.e. "online").

Finally, attempts to better define the relationship between the sense of body ownership and the sense of agency have been put forward in healthy subjects via "active" variants of the RHI (i.e. with subjects moving in contrast with the more "passive" experience of the classic RHI) in both real (Kalckert & Ehrsson, 2014; Tsakiris, Schütz-Bosbach, & Gallagher, 2007; Tsakiris et al., 2006) and virtual reality environments (Burin et al., 2019). Specifically, Tsakiris and colleagues (2006) found that active movements of participants' fingers during the RHI elicited widespread proprioceptive drifts extending to the whole hand rather than proprioceptive displacements localised to the finger performing the movement (in comparison with when the finger was passively moved). These findings suggest that, while ownership may be localised to a specific portion of the body (e.g. the stimulated finger), feelings of agency seem to encompass larger portions of the body, thus pointing towards a unifying role of agency in bodily awareness. Nevertheless, a subsequent review from Tsakiris and colleagues (2007) further defined the relationship between agency and ownership, by suggesting that while ownership relies on processing of sensory signals coupled with top-down representations of one's own body, agency may be the result of the integration of sensory input as well as motor outputs in a more bottom-up process (Tsakiris et al., 2007). However, whether ownership modulates agency or vice-versa is still debated. Some suggest that these two dimensions of the bodily self are dissociated (Kalckert & Ehrsson, 2012), while others posit a relationship between them, with ownership driving feelings of agency (Burin et al., 2018; Burin, Pyasik, Salatino, & Pia, 2017), or agency leading to ownership feelings (Asai, 2016).

Hence, Chapter 5 and Chapter 6 will focus on investigating body ownership, motor awareness and agency in patients with right-hemisphere stroke, in order to shed light on the mechanisms underlying these aspects of the bodily self in healthy subjects. In particular, in Chapter 5, the role of visual capture on body ownership in right-hemisphere stroke patients, as well as the influence of motor intentions in AHP patients on motor awareness and agency, will be investigated. In Chapter 6, the extent to which 1st and 3rd person perspective, together with their integration, influence ownership, motor awareness and agency in right-hemisphere stroke patients will be assessed.

1.5. Awareness of one's own bodily self: metacognition and spatial cognition

"Many people think they are thinking when they are merely rearranging their prejudices."

William James

As mentioned above, self-awareness is a multifaceted, long-debated concept, necessary to obtain and maintain a coherent sense of self. It is defined as one's awareness of one's own mental states (Newen & Vogeley, 2003) and it has been extended to comprise bodily awareness (i.e. awareness of one's own body). In AHP patients, bodily self-awareness is deeply compromised: when faced with their own disability, patients are unable to recognise the failure of their intended action (Fotopoulou et al., 2008). This is possibly due to a failure in updating prior beliefs (i.e. internal models of the world, arising from experiences and genetics; Friston, 2010) about their own body (i.e. “I can move”) in light of counterfactual evidence (i.e. the fact that my arm is paralysed) (Fotopoulou, 2014). Specifically, as mentioned in the above paragraphs, AHP patients may lack an “online” (i.e. while the action is happening) ability to monitor their own actions, which in turn prevents successful sensory updating of their body representation. Such updating, as discussed above, may be prevented by an overriding of motor intentions over sensory incoming signals. In healthy subjects, awareness of one’s own actions seems to be already relative inaccessible: when subjects are asked to perform an action (i.e. draw a straight line to a visual target) and are provided with erroneous visual feedback, they will tend to disregard sensori-motor feedback in favour of visual one (Fourneret & Jeannerod, 1998). If asked to judge their own performance, they will then rely on their motor plan rather than on the actual outcome: given they intended to draw a straight line towards a target, and visual feedback was congruent with their plan, they would be certain of having done so. Hence, in healthy subjects, and pathologically more so in AHP, awareness of one’s own motor outputs is not necessarily available to individuals.

The abovementioned lack of awareness of motor outputs may be also accompanied by a more general compromised monitoring and belief updating ability. AHP patients seem to form beliefs based on limited knowledge and are resistant to change their belief once they are formed (Vocat, Saj, & Vuilleumier, 2013). In a study by Vocat and colleagues, AHP and hemiplegic control patients were asked to perform a “riddle” task, in which they had to guess a target word with the aid of incremental clues. The clues began ambiguous enough to have multiple initial possible answers, and became increasingly specific as the task progressed, so that alternative answers became less likely. Following each clue the patient was asked to guess the target word and rate the confidence in their answer. Results showed that AHP patients, in comparison with controls, were more confident after their initial guess and remained more confident even when clues became less ambiguous. This overconfidence was present in all AHP patients relative to controls. In addition, the quality of answers provided by AHP patients was poorer, with AHP patients giving fewer correct answers and failing to update their answer when provided with more, better evidence. Another study by Jenkinson et al (2009) supports the idea of a self-monitoring deficit in patients with AHP. Jenkinson and colleagues (2009) used a 'reality monitoring' task in which patients were asked to either imagine an object or observe its pictorial representation and were subsequently asked to discriminate between imagined and perceived objects. In a second experiment, participants were asked to do the same, but in relation to movements. Specifically, they were asked to either perform, imagine or observe a movement and then discriminate between these three categories. Results showed that AHP patients, in comparison with both hemiplegic and healthy controls, showed a deficit in monitoring imagined versus perceived objects (i.e. non-motor information), whereas both AHP and hemiplegic controls were impaired in motor-related monitoring (i.e. when the information related to movements, patients would produce more erroneous responses; Jenkinson, Edelstyn, Drakeford & Ellis, 2009). Thus, AHP patients monitoring deficits seems to encompass a more global, not necessarily domain-specific, awareness impairment. These results have since been replicated and extended by Saj et al (2014). In this study, the authors asked AHP and hemiplegic controls to perform or imagine a movement with either their right or left limb. Subsequently, they had to discriminated between imagined and performed movement as well as identify whether the movement pertained the right or the left arm. Findings from this study revealed, in line with Jenkinson and colleagues (2009), that AHP patients were unable to monitor their own actions with both the left and the right limb (even though errors were higher for the left, paralised arm) (Saj, Vocat & Vuilleumier, 2014). Taken together, these findings suggest a general impairment in motor monitoring, that extends to the healthy limb (as also suggested by Preston et al., 2010) as well as a domain-general monitoring deficit.

The ability to monitor one's own cognitive processes is broadly defined as metacognition (Deroy, Spence, & Noppeney, 2016; Flavell, 1979; Fleming & Dolan, 2012) and it is often indexed by confidence judgements in individuals' perceptual choices in a behavioural task (Fleming & Lau, 2014). Several studies investigated metacognition in healthy subjects in a variety of perceptual and memory paradigms. For instance, studies investigating whether metacognition is domain-specific (i.e. whether we have separate metacognitive processes dedicated to each cognitive function, specifically memory and visual perception; Fleming et al., 2014; Morales, Lau, & Fleming, 2018), global (Faivre, Filevich, Solovey, Kuhn, & Blanke, 2018) or whether different processes sub-serve both domain-specific as well as global awareness (Morales et al., 2018), furthered our understanding of how self-awareness emerges. Using lesion mapping coupled with visual or memory discrimination tasks, Fleming and colleagues (2014) showed a dissociation between metacognitive abilities for vision (compromised) and memory (intact) in patients with lesions in the anterior pre-frontal cortex. Furthermore, in an fMRI study, Morales et al. (2018) replicated these findings of a domain-specific metacognitive processing for visual perception and memory in healthy subjects and also revealed the presence of a domain-general (i.e. related to both tasks and able to predict confidence levels) metacognitive process. Hence, findings from these studies revealed that domain-specific processes are involved in memory and perceptual metacognitive judgements, and yet, alongside these, a global, multisensory and wide-spread fronto-parietal network has been identified as the neural correlate of a general metacognitive ability.

Moreover, a key aspect of metacognitive judgements is related to when subjects are asked to express them. A lower accuracy (Siedlecka, Paulewicz, & Wierzchon, 2016) as well as the implementation of different strategy (Fleming, Massoni, Gajdos, & Vergnaud, 2016) have been linked to prospective, rather than retrospective, judgements. Prospective judgements are given before subjects are presented with a trial, i.e. they are based either on preceding trials and/or on subjects' own knowledge of how good they would be at performing the task; retrospective ones are judgements expressed after the trial has finished. Hence, it is not surprising that subjects are less able to monitor their own awareness when asked to give a judgement before having been able to collect all the information needed on the task at hand (Siedlecka et al. 2016). Both the idea of a domain-specific and global metacognition, as well as the dissociation between prospective and retrospective judgements may be linked to unawareness in clinical populations: in AHP patients, for instance, a domain-specific impairment (i.e. related to their motor disability) could be accompanied by a more global compromised metacognitive ability (Jenkinson et al., 2009; Vocat et al., 2013), which in turn does not allow information collected retrospectively to inform future prospective judgements. Nevertheless, and despite these advances in metacognition research, metacognitive abilities on aspects of the bodily self have not yet been investigated.

A crucial aspect of monitoring abilities regarding one's own body is to weight incoming information according to the context in which individuals experience and subsequently act on it. In order to successfully act on the world and therefore minimise unexpected outcomes, individuals rely on the integration of information coming from a body-centred representation of space (i.e. egocentric frame of reference) with a world-based one (e.g. Maguire et al., 1998; Burgess, 2006), in which the reference point is in the extra-personal space and independent from the perceiver (i.e. allocentric frame of reference; Ball, Birch, Lane, Ellison, & Schenk, 2017; Camors, Jouffrais, Cottereau, & Durand, 2015; Chen et al., 2018). Given that we perceive our own self in space, the way we integrate information processed in different spatial coordinates that are either egocentric (Fogassi et al., 1992; Graziano and Gross, 1998) or allocentric (Maguire et al., 1998; Burgess, 2006) plays a role in shaping our sense of self-awareness. Specifically, both the sense of agency and body ownership can be interpreted as arising from the integration of beliefs about one's own self, mapped onto incoming egocentric and allocentric information, ultimately combined to form a cognitive representation of our body in space (Arzy & Schacter, 2019). Accordingly, successful spatial processing entails an integration of 1st and 3rd person perspectives, grounded on the body, which is then integrated with a viewer-independent reference frame. In a recent study, Török and colleagues (2014) asked healthy participants to complete a virtual spatial navigation task entailing different perspectives (1st and 3rd) as well as different reference frames (egocentric and allocentric; Török, Nguyen, Kolozsvári, Buchanan, & Nadasdy, 2014). The authors found that both 1st and 3rd person perspective where preferred when perceived egocentrically on the ground level (i.e. led to better navigational performance), whereas the allocentric frame of reference was preferred when the task was presented in an external, aerial view. Hence, the basis for spatial processing in one's own immediate surroundings may result from an initial egocentric processing: an egocentric representation of the body in space may be a necessary first step to develop an allocentric viewpoint (Filimon, 2015). Accordingly, Serino and Riva (2017) proposed that integrating egocentric and allocentric information is crucial for creating and maintaining awareness of one's own body as well as one's surrounding. Hence, a compromised egocentric frame of reference could lead to impairments in monitoring information regarding the self.

The idea that spatial and mental perspective-taking may play a role in higher-order cognitive functions has been put forward by Besharati and colleagues (2016; see section 6.1. Introduction, Chapter 6). In this study, the authors tested AHP and hemiplegic controls patients and asked them to perform a visuo-spatial task. During the task, patients were instructed to refer to visual stimuli by using either their own perspective or the experimenter's one. Then, they were presented with a mental perspective-taking task, comprising stories taking either the patient or a stranger's point of view. A dissociation between 1st and 3rd person perspective-taking in AHP patients was found in both tasks, with AHP patients performing worse when they were taking a 3rd person perspective rather than a 1st person one. This suggests that AHP patients may be unable to disengage from their own 1st person perspective and adopt an external, 3rd person one. As mentioned above, this could be due to a lack of monitoring abilities regarding the self as experienced egocentrically. Nevertheless, the ability to monitor performance in healthy subjects according to different spatial reference frames has never, to date, been investigated.

Taken together, these findings suggest that the lack of awareness showed by AHP patients may entail an impairment in metacognitive processing and belief updating when adopting an egocentric frame of reference. Such impairment in egocentric metacognitive awareness (i.e. the ability of an observer to correctly use the information available during a given task in order to make confidence judgements on such task; Fleming, 2017; Fleming, Weil, Nagy, Dolan, & Rees, 2010) may underlie AHP patients' judgement of the output of their own actions. However, such possibility of an egocentric bias in metacognitive judgements has never been compared with allocentric processing in the healthy population. Thus, investigating this idea by devising a novel paradigm and testing the hypothesis of an unreliable metacognitive awareness when judgements are made from an egocentric perspective in healthy subjects, would be the first step towards understanding the role of reference frames in metacognition. If allocentric processing depends on a functioning egocentric one, and individuals are biased when judging their own performance when presented with stimuli in an egocentric FoR, this could represent a potential explanation of self-awareness processes both in healthy subjects as well as anosognosic patients. AHP patients may be unable to use allocentric information because their primary FoR, i.e. the egocentric one, is impaired. Hence, given the lack of evidence in metacognitive abilities in egocentric and allocentric FoRs in the healthy population, the last experimental chapter of this thesis (Chapter 7) will test the possibility of a metacognitive egocentric bias underlying perceptual processing in healthy individuals.

1.6. Aims and outline of the thesis

Based on the above, the current thesis had the following main aims: i) to examine the role of the vestibular system in multisensory integration and, specifically, the way in which interoceptive and exteroceptive signals contribute to body ownership and body representation; ii.a) to understand multisensory integration processes leading to body ownership in right-hemisphere stroke patients (with and without disorders of the self) compared with healthy controls ii.b) to explore motor awareness and agency, as well as the relationship between ownership and agency, in anosognosia for hemiplegia; iii) to investigate the extent to which viewing their own body from the 1st or the 3rd person-perspective (as well as their integration) impacts the sense of body ownership and self-awareness in AHP and DSO patients and iv) assess the influence of different frames of reference on metacognition in healthy individuals, specifically testing whether individuals are less metacognitively aware when judging stimuli egocentrically.

The first aim, i.e. to explore the role of the vestibular system in multisensory integration and body representation, was investigated in four neuromodulation studies, reported in Chapters 2-4. Chapter 2 examined the question of whether the vestibular system balances sensory modalities in favour of vision using galvanic vestibular stimulation during a rubber hand experiment that manipulated i) vision and proprioception as well as ii) touch (both affective and neutral) and measured subjective feelings of ownership and proprioceptive drifts (which were also measured in the following studies). Chapter 3 aimed to explore the role of vestibular modulation in different epistemic aspects of touch (i.e. felt vs seen), with a specific focus on affective touch, via an adapted rubber hand illusion paradigm.

Finally, the study reported in Chapter 4 examined specific, possible alternative explanations for the results described in Chapters 2 and 3, by conducting control tasks examining the effects of vestibular modulation on proprioception, visuo-spatial perception and body representation.

The second aim was to extend and expand on previous findings (Martinaud et al., 2017), pointing at a dominance of vision over proprioception in right-hemisphere stroke patients via a bedside version of the RHI as well as exploring motor awareness, agency (and their relationship) in anosognosia for hemiplegia (Chapter 5). Following the task, patients were asked to answer questions related to ownership, motor awareness (following request of a movement) and sense of agency over such movement.

The third aim was to investigate the extent to which different perspective influence motor awareness and body ownership in AHP and DSO patients. This study, reported in Chapter 6, employed a bedside task involving the use of a mirror to manipulate perspective-taking with measures consisting in questions related to patients own' bodily selves (i.e. ownership, awareness and agency).

Finally, the fourth and final aim of this thesis was to assess metacognitive abilities in healthy subjects following presentation of stimuli in different frames of reference (Chapter 7). Specifically, subjects were asked to perform a perceptual judgement and to rate their confidence in such judgements. Accuracy, confidence ratings and prior/posterior beliefs on participants' assumed performance were collected and analysed to investigate subjects' awareness in their own responses following presentation in different reference frames.

Chapter 2

Balancing Body Ownership: Visual Capture of Proprioception and Affectivity During Vestibular Stimulation

2.1. Introduction

As mentioned in the first introductory chapter, the perception of the external world, and our own body, is based on the integration of sensory information conveyed by different modalities (i.e. multisensory integration), each weighted according to their contextual reliability (Fetsch et al., 2011; Stein et al., 2014). For instance, in order to estimate the size of an out-of-reach object, we typically rely upon vision; however, if we are close enough to touch the object, our estimation will result from the integration of visual and tactile information. If there is incongruence between different sensory modalities (e.g. visuo-tactile, Pavani et al., 2000), vision can be weighted more (the so-called 'visual capture' effect, Rock & Victor, 1964), or vice versa depending on the properties of the objects of experience as well as the context in which they are experienced (Ernst & Banks, 2002). For example, the precision (i.e. the certainty about sensory representations; Friston et al., 2012) of proprioceptive information (i.e. regarding the position of our body) can be lowered in favour of vision during conflictual situations (Folegatti et al., 2009) and according to the reference plane in space (i.e. vision is more dominant in the horizontal versus in-depth plane, van Beers et al., 2002).

Interestingly, multisensory integration has been linked to bodily consciousness and, specifically, body ownership (i.e. the feeling that our physical body is our own; Gallagher, 2000). Paradigms that generate conflicts between different sensations have been used extensively to explore the role of multisensory integration in body ownership (Tsakiris et al., 2007; Blanke et al., 2015). In the Rubber Hand Illusion (RHI; Botvinick & Cohen, 1998) for example, participants watch a realistic fake hand being stroked in synchrony with their own (unseen) hand, giving rise to self-reported feelings of rubber hand ownership and a shift in the perceived location of participants' real hand towards the rubber hand (i.e. proprioceptive drift). Initially, these two measures were seen as the subjective and 'objective' measure of the illusion but it is increasingly understood that subjective feelings of ownership and proprioceptive drift dissociate and may reflect different components of the multisensory integration process (Ehrsson et al., 2004; Ehrsson et al., 2005; Makin et al., 2008; Martinaud et al*.,* 2017; Rohde et al., 2011). More generally, there are now hundreds of studies on the RHI, and related psychophysical or virtual reality adaptations (see Kilteni et al., 2015 for a review), indicating that body ownership is mediated by both bottom-up processes of multisensory integration and top–down expectations (Tsakiris, 2010; Apps & Tsakiris, 2014). In line with this, recent predictive coding (Zeller et al., 2015) and Bayesian causal inference (Samad et al., 2015) models suggest that the successful establishment of the illusion relies on the causal attribution of sensory experiences to a common source (in this case, 'my body'), according to prior knowledge and the spatio-temporal congruency of these sensations.

Despite this progress, the contribution of certain modalities, such as the vestibular system and interoception to multisensory integration and body ownership have only recently been studied and hence remain poorly understood. First, although the vestibular system's main role is to contribute to the maintenance of balance and posture (Brandt & Dieterich, 1999), there are some indications that vestibular signals play a role in multisensory integration (Bense et al., 2001). The neuroanatomical basis of the vestibular system remains debated (Fasold et al., 2002; Eulenburg et al., 2012; Lopez et al., 2012b; Lopez, 2016), yet existing evidence suggests an overlap between the cortical areas supporting vestibular sensations (captured by vestibular receptors in the inner ears and conveyed to the central nervous system via the vestibular nerves) and other sensory experiences (such as vision, Brandt et al., 2002; Seemungal et al., 2013; Della-Justina et al., 2015; touch and proprioception, Lackner & DiZio, 2005; Dijkerman & de Haan, 2007), including multimodal areas linked to multisensory integration (e.g. temporoparietal junction, inferior parietal lobule, insula and cingulate cortex, Lopez et al., 2012b; Lopez, 2016). This suggests that vestibular signals may contribute to multisensory integration.

Moreover, recent studies highlight vestibular network contributions to many facets of body representation (Ferrè & Haggard, 2016; Been et al., 2007), from its metric properties (such as shape and size, Lopez et al., 2012c) to body ownership. For example, excitation of the semi-circular canals of the internal ear by insertion of cold or warm water is known to activate contralateral cortical vestibular areas (Caloric vestibular stimulation, CVS) and to modulate spatial cognition (Cappa et al., 1987), bodily awareness (Cappa et al., 1987; Vallar et al., 1993; Bottini et al., 2005) and body ownership (Bisiach et al., 1991) in patients with right hemisphere stroke.

Recently, an easier to control method than CVS (Lopez et al., 2010; Ferrè et al., 2013), namely Galvanic Vestibular Stimulation (GVS), has been used to examine the role of vestibular stimulation on multisensory integration and body ownership. GVS involves a small electrical current applied using two electrodes (one anode and one cathode) positioned on the mastoids (Utz et al., 2011). The change in electrical excitability of the vestibular nerves stimulates the vestibular network of the right hemisphere when the anode is on the left mastoid and the cathode on the right (known as LGVS), while the reverse electrode positioning (RGVS) leads to a bilateral activation (Fink et al., 2003; Utz et al., 2010). Most studies on body ownership have focused on the role of LGVS given the assumed right lateralised activation it causes (in right-handed subjects; Dieterich et al., 2003; Eulenburg et al., 2012) and the link of the latter with body representation disorders (Baier & Karnath, 2008; Bisiach et al., 1991; Moro et al., 2016; Zeller et al., 2011). Specifically, Lopez and colleagues (2010) found that LGVS enhances body ownership during the RHI, and influences multisensory integration by promoting visual dominance over proprioception; however, Ferrè and colleagues (Ferrè et al., 2015), observed a decrease in proprioceptive drift following LGVS, suggesting that LGVS enhances proprioception over vision. Thus, both studies found that stimulation of the right vestibular network influences the balance between proprioceptive and visual information in a hemispheric-specific fashion (Dieterich et al., 2003), but in opposite directions. These conflicting results may be caused by various methodological differences between the two studies (see Discussion for full details); however, taken together, they provide preliminary indications for the role of vestibular signals to the weighting of different sensations during multisensory integration and, hence, to body ownership. The present study aimed to further specify Lopez and colleagues' findings against those of Ferrè and colleagues by testing two further hypotheses regarding visual capture of proprioception and ownership (VoC; Martinaud et al., 2017), as well as interoception, as explained below.

In the current study, galvanic vestibular stimulation was administered during a rubber hand illusion task with the hypothesis that LGVS would increase the RHI, by increasing the weighting of visual signals whilst lowering the precision of proprioceptive ones. During the RHI, the conflict between vision, touch and proprioception is typically solved via a dominance of visual information over proprioceptive one (e.g. see Zeller et al., 2011 and Zeller et al., 2015 for electrophysiological evidence), i.e. what we see can be processed as more reliable than what we feel, resulting in the embodiment of the rubber hand (Folegatti et al, 2009). Hence, when visual information is present and reduces the ambiguity of a conflictual situation, the stimulation of the vestibular system may shift the balance in favour of vision (as in Lopez et al., 2010) rather than proprioception (Ferrè et al., 2015). In order to specifically test this possibility, a mere visual capture condition was devised, during which subjects did not receive any touch on either their hand or the rubber hand but were only required to look at the rubber hand (see Crucianelli et al., 2017). However, even though the current study takes into consideration differences in variance at the group level, it was not possible to directly test whether precision is lowered in favour of vision within each of the different trials in each of our subjects (i.e. at the individual level). In order to do so, multiple trials, or some additional signal strength measure (e.g. see Zeller et al., 2015), would have been needed, which were not possible within the current design; hence, based on previous literature and the current data, it can only be speculated that sensory re-weighting of visual and proprioceptive information, with an increase of the former and a concomitant reduction of the latter, may be the mechanism at play should these predictions be confirmed at the group level (see Discussion section for further details on this point).

Furthermore, the current study aimed to investigate how the combined effects of vestibular stimulation and vision influence body ownership during the RHI when touch is affective rather than neutral. In order to do so, CT-optimal, affective touch and non CT-optimal, neutral touch were administered during both synchronous and asynchronous conditions of the RHI. C-Tactile (CT) afferents are a specialised, unmyelinated class of fibres innervating the hairy skin of the body (McGlone & Reilly, 2010). They are optimally activated by slow, caress-like tactile stimulation at velocities between 1 and 10 cm/s (McGlone et al., 2014). CT-optimal touch is associated with heightened pleasantness (Lӧken et al., 2009; Shaikh et al., 2015; Pawling et al., 2017) and has been identified as a type of affective touch (McGlone *et al.*, 2014). CT-optimal touch activates multimodal areas of converging sensory and affective information regarding the state of the body (including posterior insula Craig, 2002; 2003; Olausson et al., 2002; McGlone et al., 2012 and cingulate cortex, Case et al., 2017). Moreover, the pleasantness associated with CT-optimal touch is not affected by inhibition of the primary and secondary sensory cortices (Case et al., 2016; Case et al., 2017), thus supporting the notion that the CT-system might play a unique role in conveying affective rather than discriminative aspects of touch. CT-afferents are considered as sharing more characteristics with interoceptive (i.e. related to the sense of the physiological condition of one's own body; Ceunen et al., 2016), rather than exteroceptive, modalities (Björnsdotter et al., 2010), in light of their contribution to the maintenance of our sense of self (Crucianelli et al., 2017).

CT-optimal touch has been found to increase embodiment during the RHI (Crucianelli et al., 2013; Crucianelli et al., 2017; Lloyd et al., 2013; van Stralen et al., 2014). For example, Crucianelli and colleagues (2013) found an increase in subjective measures of embodiment during the RHI using synchronous, CT-optimal touch. Nevertheless, the mechanisms behind such enhancement remain unknown. One possibility is that the pleasantness elicited by CT-optimal touch enhances embodiment because interoception is tightly connected with the feelings of body ownership. However, it is also possible that the 'seen' affective touch on the rubber hand, i.e. vicarious affective touch (Morrison et al., 2011), rather than just the felt affectivity of the touch on participant's own arm, contributes to the effect. Both felt and vicarious CT-optimal touch elicit the same response in the posterior insula (Morrison et al., 2011), suggesting that the affectivity conveyed by CT-optimal touch is not exclusively anchored to the felt sensation and may also be influenced by vision. Given that the vestibular system may favour visual information by reducing the precision of proprioceptive signals during conflictual situations (as hypothesised above) and owning to the overlap in neural circuits responsible for interoceptive (see Case et al., 2017) and vestibular (see Lopez et al., 2012b) processing, these two modalities may contribute to the bodily self in a combined fashion. Hence, in the current study, one of the aims was to explore whether vestibular stimulation would shift the balance between vision and interoception by increasing the precision of visual information over signals coming from participant's own body. Specifically, it was hypothesised that stimulation of the vestibular system could enhance the effect of the *seen* affective touch (i.e. vicarious touch) on the rubber hand rather than the felt one on participants' hand, thus further strengthening embodiment of the rubber hand.

In sum, even though existing research suggests that the vestibular system may contribute to body ownership, little is currently known about the direction of such contribution nor the combined effect of the vestibular system and interoceptive modalities (such as affective touch). In the present study galvanic vestibular stimulation (LGVS, RGVS and sham) was applied during a RHI task in which the affectivity of touch (affective, CT-optimal or neutral, non-CT optimal velocity of touch) was manipulated to i) disambiguate previous findings on the role of the vestibular system in balancing vision, touch and proprioception in relation to body ownership and ii) to investigate the combined contribution of vestibular and interoceptive systems in shaping the experience of our own body. A condition where no touch was applied and participants simply looked at the rubber hand for 15 seconds (sufficient to elicit visual capture of the rubber hand, see Martinaud et al., 2017 and Experimental Design below) was also devised to test whether visual information alone, with no tactile stimulation, was enough to elicit ownership of the rubber hand (in line with Samad et al., 2015). LGVS (when compared with RGVS) was expected to stimulate a right vestibular network for bodily awareness leading to a stronger visual capture of the rubber hand during synchronous stroking (as in Lopez et al, 2010) and even in the absence of touch. In agreement with Lopez et al., 2010 and Ferrè et al., 2015 findings, it was hypothesised that the effects observed in the current study would be the result of sensory weighting during multisensory integration, with an increased precision of visual over proprioceptive information: if the effects of GVS during the RHI are due to a separate modulation of vision or proprioception, rather than their integration, a generic decrease or increase in proprioceptive drift regardless of the synchrony of the stroking would be expected. Furthermore, it was predicted that the effects of the visual capture conditions would be comparable to those found in the synchronous conditions (and hence different from the asynchronous ones). Finally, it was predicted that CT-optimal touch would lead to greater RHI effects compared with non-CT optimal touch (see Crucianelli et al., 2013; Lloyd et al., 2013; Van Stralen et al., 2014), and that this effect would be enhanced by LGVS.

2.2. Materials and methods

2.2.1. Participants

Twenty-six right-handed healthy participants (13 females, age range: 18-53, M = 29.8 SD = 9.5 years), were recruited via an institutional subject pool. Participants with psychiatric or neurological history (including vestibular disturbances), pregnancy at the time of testing, or metal implants in their body, were excluded. Participants were asked to refrain from smoking and drinking alcohol during the 24 hours before the experiment. The study was approved by an institutional Ethics Committee and all participants gave informed, written consent.

2.2.2. Experimental design

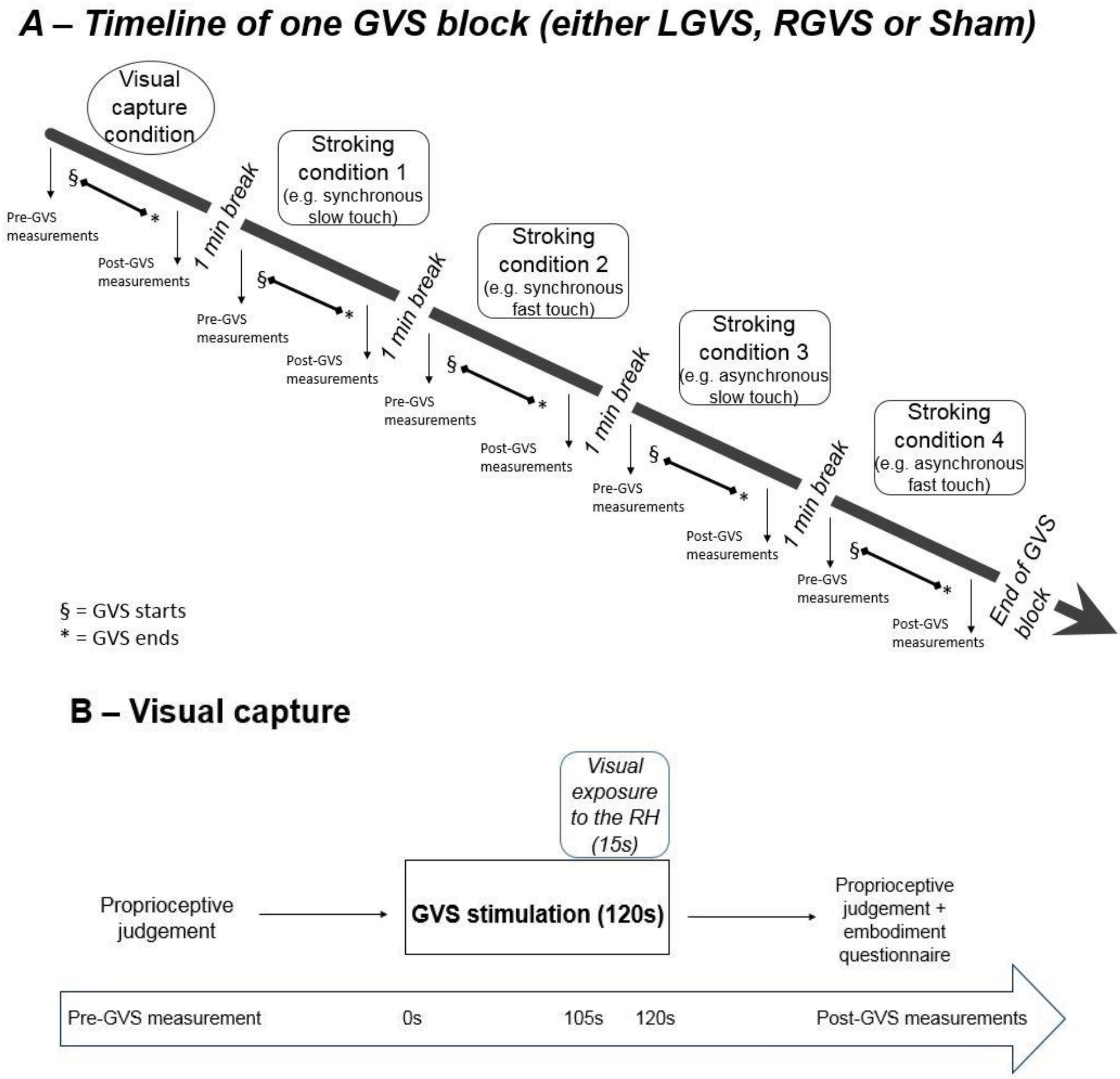
To examine the effect of vestibular activation on visual capture of proprioception, GVS (LGVS, RGVS and sham) was applied during a visual only condition involving observation of the rubber hand for 15 seconds, without touching either the participant's or the rubber hand. Then, to investigate the contribution of vestibular and C-tactile systems' stimulation to body ownership, a rubber hand illusion (RHI) experiment using a 3 (GVS configuration: LGVS, RGVS and sham) x 2 (stroking velocity: slow and fast) x 2 (stroking synchrony: synchronous and asynchronous) within-subjects design was conducted. Stroking velocity was manipulated by administering slow, CT-optimal touch (at 3 cm/s) and fast, non-CT-optimal touch (18 cm/s) (see Crucianelli et al., 2013) for 120 seconds. Stroking synchrony was manipulated by either stroking the participant's hand and the rubber hand simultaneously (i.e. synchronous conditions) or out of synchrony (i.e. asynchronous conditions). The timings of visual capture and stroking conditions were based on previous research indicating the sufficiency of these durations for eliciting ownership as a result of visual capture (Martinaud et al., 2017) and visuo-tactile stimulation (Lopez et al, 2010) respectively.

GVS was performed in a block design (LGVS vs. RGVS vs. sham) with the order of GVS blocks counterbalanced across participants. Each GVS block consisted of one visual capture condition and four different stroking conditions: synchronous slow touch, synchronous fast touch, asynchronous slow touch and asynchronous fast touch. Within each GVS block, the pure visual capture condition was always conducted first, and subsequent stroking conditions were randomised for velocity and synchrony (see Figure 2.1.A). As mentioned in the introduction, previous studies (Crucianelli et al., 2013; Crucianelli et al., 2017; Martinaud et al., 2017; Samad et al., 2015) suggested that a brief visual exposure to the rubber hand can elicit feelings of ownership in right-hemisphere stroke patients as well as in healthy subjects. Thus, one of the aims was to investigate whether healthy participants, when exposed to the rubber hand during right vestibular stimulation, would integrate vision and proprioception in favour of vision, prior to any tactile stimulation (and any related carry-over effects). This decision may have impacted subsequent conditions; however, all following conditions aimed at exploring the 3-way interaction between vision, proprioception and touch, rather than visuo-proprioceptive integration only.

The outcome measures, collected before (Proprioceptive drift) and after each stroking condition (Proprioceptive drift and Embodiment Questionnaire), were as follow:

a) Proprioceptive drift: the perceived shift of the participant's hand towards the rubber hand, measured in centimetres. Proprioceptive drift was calculated by subtracting a post-GVS estimate of the left hand's location from a pre-stimulation estimate (Figure 2.1.A), with positive values meaning that participants perceived their hands as being closer to the rubber hand.

b) Embodiment Questionnaire: a short version of the questionnaire from Longo et al. (2008, see Appendix 1) was used to measure: feelings of *ownership* of the rubber hand, perceived *location* of participants' hand and *affective* aspects of the experience. One of the questions, relating to touch, was administered only in the stroking conditions. The order of the questions was randomised in each condition and responses were given on a 7-point Likert scale, ranging from -3 ('Strongly disagree') to +3 ('Strongly agree'). These ratings were used to obtain a composite embodiment score for each condition by calculating the average score obtained from the ownership and location questions.



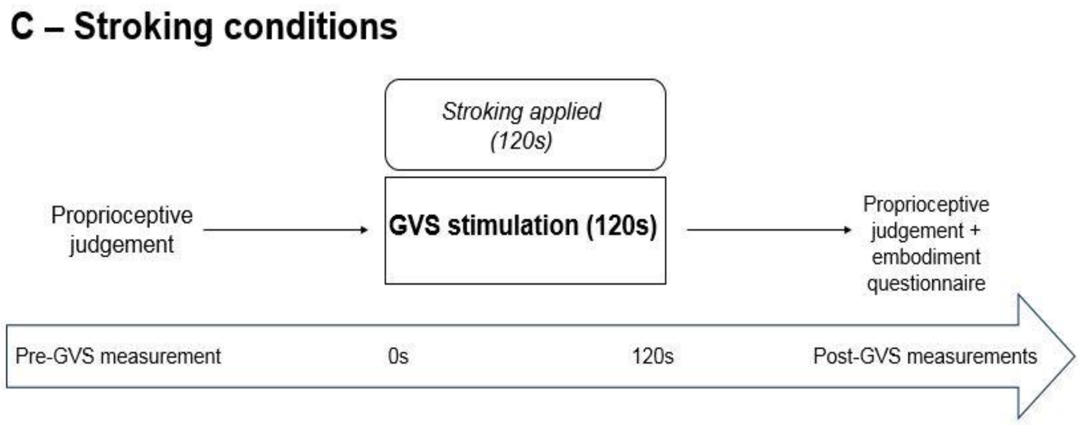


Figure 2.1. A) Timeline of one prototypical GVS block. At the beginning of each of the three GVS blocks (either LGVS, RGVS or Sham), participants undertook the visual capture condition, with measures taken before and after stimulation (see B for details of this condition and its measurements). Subsequently, one of the four stroking conditions (see C for further details) was conducted in a randomised order, with measures again taken before and after stimulation. B) Timeline of the visual capture condition. Before the visual capture condition started participants performed a proprioceptive judgement (pre-GVS measurement). Immediately afterwards, the vestibular or sham stimulation commenced for 2 minutes during which participants sat with their eyes open. During the last 15 seconds of vestibular or sham stimulation, the experimenter opened the box lid and instructed the participant to look at the rubber hand until told otherwise. After 120 seconds (total) stimulation the lid was closed, and participants immediately performed a second proprioceptive judgement and completed the embodiment questionnaire (post-GVS measurements). C) Timeline of the stroking conditions. Each of the four stroking conditions (synchronous slow touch, synchronous fast touch, asynchronous slow touch and asynchronous fast touch) followed the same structure. Participants made an initial (pre-GVS measurement) proprioceptive judgement, followed immediately by vestibular or sham stimulation and concurrent tactile stimulation (i.e. stroking of both the participant and rubber hand's forearm) for 120 seconds, during which participants looked continuously at the rubber hand. A second proprioceptive judgement and embodiment questionnaire was completed immediately following completion of the 120s concurrent vestibular / tactile stimulation (post-GVS measurements).

2.2.3. Experimental setup and materials

Galvanic Vestibular Stimulation

A bipolar stimulation with fixed intensity (1mA) and duration (2 minutes per condition) was applied to all participants using a direct current stimulator (NeuroConn DC-stimulator, neuroCare Group GmbH, München, Germany). The total amount of stimulation per GVS block was 10 minutes, with breaks of 20 minutes between blocks to minimise possible after-effects (Utz et al., 2010). Therefore, the entire experiment involved 30 minutes (including Sham) of non-continuous stimulation.

Two 3x3cm carbon rubber electrodes were inserted into sponges, previously soaked in a saline solution, and then fixed either on the participants' mastoid bones (LGVS and RGVS) or neck (Sham) using a rubber band. During left-anodal/right-cathodal stimulation (i.e. LGVS), the anode was placed on the left mastoid process and the cathode on the right. During left-cathodal/right-anodal GVS (i.e. RGVS), the anode was on the right and the cathode on the left. In the Sham stimulation, both electrodes were placed on the nape (~5 cm below the end of the mastoid processes) with the anode and the cathode randomly positioned either on the left or the right side of the neck.

Rubber Hand Illusion

A black wooden box (62 cm x 43 cm x 26 cm), was positioned on a table 10 cm from the participant's torso. The box was divided in two equal halves by a piece of black cardboard. Two spots were marked on the table with tape, one for the left rubber hand's index finger and one for the participant's left index finger (distance between the rubber hand and the participant's hand=30 cm; Figure 2.2). On the upper side of the box, visible to the experimenter only, there was a measuring tape, used to record proprioceptive drift. In order to reduce the influence of external visual cues, participants wore a black cloth covering their shoulders and arms.

Stroking was administered to the participant's and rubber hand using two identical make-up brushes (Natural hair Blush Brush, N°7, The Boots Company) by an experimenter who was extensively trained to deliver touches in a uniform manner, controlling for speed and pressure (as in Crucianelli et al., 2013 and Krahé et al., 2016; see also Triscoli et al., 2012 for discussions regarding the advantages and limitations of administering pleasant touch using human versus mechanical methods)

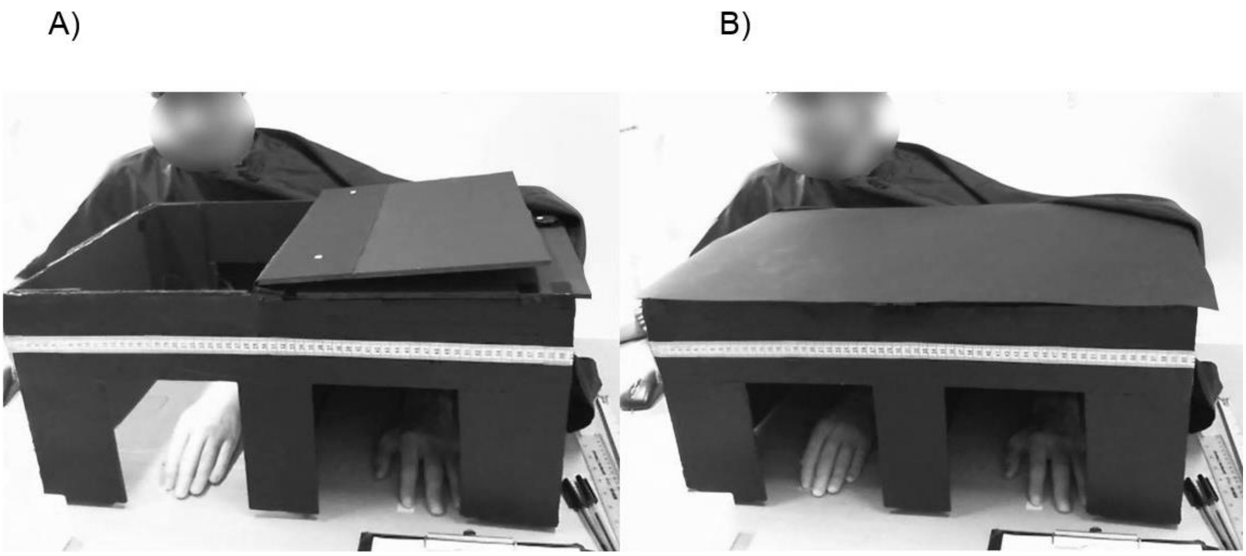


Figure 2.2. Participants sat in front of the table, facing the box, and were asked to insert their left hand into the left compartment of the box, while the rubber hand was positioned in the compartment on the right, aligned with participant's left shoulder. Both the participant's and rubber hand's left index fingers were located on the corresponding marked spots. A) While the box was open, participants were asked to look inside and observe the rubber hand. In particular, during the stroking conditions, participants were instructed to follow the brush while it was stroking the rubber hand's forearm. B) Before and after each condition, with the box closed and covered by a black carton, participants had to perform a proprioceptive judgement (see Experimental procedure).

2.2.4. Experimental Procedure

Main task

After removing any jewellery from the participant's left arm/hand, the experimenter aligned the participant's left shoulder and index finger with the rubber hand, which was hidden from the participant's view inside the box. Participants were instructed to avoid moving their left arm during each condition. The experimenter sat opposite the participant.

Each GVS block consisted of five conditions (Figure 2.1.A), one visual capture and four stroking conditions. Each condition commenced with a proprioceptive judgement (Lloyd et al., 2013): the experimenter passed the tip of a pen along the top of the closed box (~1 cm/s), starting randomly from the left or the right-hand side of the box. Participants were instructed to verbally stop the experimenter when the pen reached the point vertically in line with the perceived position of the participant's left index finger. The experimenter then recorded the actual position and the perceived position, obtaining a pre-GVS measurement of proprioceptive drift (actual finger position minus perceived finger position).

Immediately after the proprioceptive judgement, the experimenter started the GVS. During the first condition (visual capture, Figure 2.1.B), participants were instructed to relax for the first 1 minute and 45 seconds of stimulation, after which the experimenter opened the box, revealing the rubber hand. Participants were then asked to look continuously at the rubber hand for the last 15 seconds of stimulation. Once the stimulation ended, the lid was closed, and the participant performed a second proprioceptive judgement and completed the embodiment questionnaire (post-GVS measurements).

After the visual capture condition, there was a one-minute break, during which participants removed their arm from the box and two adjacent areas, each measuring 9x4cm, were drawn with a washable marker on the participant's left dorsal forearm, in order to control for pressure and habituation by consistently maintaining the brush within the marked area (see Crucianelli et al., 2013) Specifically, given that the amount of spread of the bristles of the brush depends on the amount of pressure applied, pressure can be controlled by keeping the amount of width of the brush within pre-defined parameters (e.g. a wider spread of the brush, extending outside of the marked area, would signal excessive pressure, which needs to be reduced). Subsequently, one of the four stroking conditions commenced. Each stroking condition started with a pre-GVS proprioceptive judgement (Figure 2.1.C), followed by 2 minutes of simultaneous vestibular and tactile stimulation. Touch was always administered proximally to distally and each stroke was followed by a 1 second break. In the synchronous slow, CT-optimal touch condition, the participant's forearm was touched in synchrony with the rubber hand's forearm at 3 cm/s for 2 minutes (i.e. single touch = 3 seconds). In the synchronous fast, non-CT-optimal touch, the stroking was synchronous, at 18 cm/s (i.e. single touch = 0.5 seconds). During the asynchronous touch conditions, the timing of touches delivered to the real and rubber hand was offset, such that while the experimenter was stroking the rubber hand, the participant's forearm was not being touched and vice-versa. During each stroking condition, participants were instructed to continuously look at the rubber hand. After the vestibular-tactile stimulation ended, the post-GVS proprioceptive judgement was obtained and participants answered the embodiment questionnaire (post-GVS measurements). The next stroking condition began after a one-minute break, during which participants were instructed to move their left arm, in order to reduce any discomfort and possible cumulative effects of the illusion.

At the end of the experiment, after having removed the GVS electrodes, participants were asked to report any physical sensation associated with the GVS, in order to identify any noticeable vestibular-induced sensations between conditions. Participants were also asked to guess in which of the three configurations (Sham, LGVS, RGVS) they thought they had received vestibular stimulation to check whether they were aware of the experimental manipulation.

2.2.5. Pleasantness task

As an additional control task, at the end of the 3 GVS blocks (without any vestibular stimulation applied) participants were asked to verbally rate the pleasantness of touches delivered at 3cm/s and 18 cm/s, in order to check that they perceived slow touch as more pleasant than fast touch, in line with the findings reported in previous studies (Löken et al., 2009; Crucianelli et al., 2013; 2017). To do so, a 2 (velocities: slow vs. fast) x 2 (site: forearm vs. palm of the hand) within-subjects task was devised. Touch was delivered either on the forearm (i.e. a CT site) or on the palm of the hand (i.e. non CT site) (Lloyd et al., 2013). There were four different conditions: slow touch on the forearm, slow touch on the palm, fast touch on the forearm and fast touch on the palm.

Two adjacent stroking areas of 6x4 cm each were drawn with a washable marker on the participant's left forearm and palm of the left hand. Participants were instructed to verbally report, with their eyes closed, the pleasantness of the touches received either on the palm or on the forearm, on a 0 ('Not at all pleasant') to 100 ('Extremely pleasant') scale. In total, there were 12 trials: 3 trials per each combination of velocities and sites. All the touches were delivered using the same brush described in section 2.3.1. During the slow touches, each area was stroked for 2 seconds (at a rate of 3 cm/s) with a 1 second interval in between the 2 strokes, whereas during the fast brushes each area was stroked for 0.3 seconds. The order of the trials was randomised and there was a short break in between each trial, during which participants reported their pleasantness ratings.

2.2.6. Data analysis

To examine hemispheric specific effects of GVS on multisensory integration, compared with a generic effect of vestibular stimulation (Ferrè *et al.*, 2015), a planned comparisons of (i) left vs. right vestibular network activation (i.e. LGVS vs. RGVS) was conducted, to test the hypothesis that LGVS is specifically linked with a right-hemisphere network for bodily awareness, and also (ii) this hemispheric-specific hypothesis was compared with a generic arousal due to the stimulation of the vestibular nerves, irrespective of the polarity (i.e. comparing (LGVS+RGSV)/2 vs. Sham). These analyses were conducted using t-tests (visual capture conditions) and repeated measures ANOVA (stroking conditions) on all the outcome measures (proprioceptive drift and embodiment questionnaire). For the stroking conditions, a repeated measures ANOVA was used in order to analyse the possible interactions between type of stimulation, stroking synchrony and stroking velocity, according to our initial hypotheses. Given that the effects of the visual capture conditions were hypothesised to be comparable to those found in the synchronous conditions, the values obtained in slow and fast synchronous and, separately, slow and fast asynchronous stroking conditions, were averaged and compared against visual capture values.

In addition, a trend analysis was run to examine the possibility of a cumulative bias in baseline proprioceptive judgements due to vestibular carry-over effects over time within each GVS blocks. In order to do so, linear trends in pre-stimulation proprioceptive judgements of the stroking conditions in the order they were administered per participant were analysed. These trends were analysed using a repeated measures ANOVA with polynomial contrasts aimed at comparing the trends in each of the three GVS blocks.

Effect sizes for paired sample t-tests were calculated using Cohen's d (pooled SD) to allow maximum comparability between different studies' designs (Field, 2017).

Data were analysed using the IBM Statistical Package for Social Sciences (SPSS) for Windows, version 23 (Armonk, NY) and plotted using the "*ggplot2*" package for R (Wickham, 2016).

2.3. Results

Three participants were excluded from the analyses: one was excluded because he failed to follow instructions and another participant was more than 2.5 SD away from the group mean in proprioceptive measures across most LGVS and Sham conditions (8/10). Additionally, in order to create a homogeneous sample in terms of pleasantness ratings of touch, another participant who was more than 2.5 SD away from the group mean in the pleasantness ratings task (when rating the 3cm/s velocity on both palm and forearm) was excluded.

Hence, the final sample consisted of 23 participants (12 females; age range = 18-53 years, mean = 30.04, SD = 9.77). The majority of the proprioceptive drifts and embodiment questionnaire distributions were normal and hence parametric analyses were employed. However, non-parametric ones were also run to confirm the parametric results. The non-parametric analyses have not been reported here for brevity but they can be found in Appendix 2, alongside other additional analyses aimed at further exploring embodiment.

2.3.1. Proprioceptive drift

Hemispheric specific effects

Visual capture conditions

A paired sample *t*-test was used to compare proprioceptive drift after observation of the rubber hand without tactile stimulation following LGVS versus RGVS. As predicted, LGVS led to greater proprioceptive drift than RGVS (LGVS: M=2.60 cm, SD=2.50; RGVS: M=0.17 cm, SD=2.30; t_{22}=3.601, p=.002, d=1.08) after visual exposure to the rubber hand (see Figure 2.3.A below).

Stroking conditions

A 2 (stimulation: LGVS and RGVS) x 2 (stroking synchrony: synchronous and asynchronous) x 2 (stroking velocities: slow and fast) repeated measures ANOVA revealed a main effect of Synchrony ($F_{(1,22)}$=19.426, p<.001, η_p^2=.469), but no main effect of Stimulation ($F_{(1,22)}$=.271, p=.608 , η_p^2=.012) or Velocity ($F_{(1,22)}$=2.688, p=.115, η_p^2=.109). As hypothesised, synchronous stroking led to greater proprioceptive drifts. The interaction between Stimulation and Synchrony was significant ($F_{(1,22)}$=9.149, p=.006, η_p^2=.294), as was the 3-way interaction between Stimulation, Synchrony and Velocity of stroking ($F_{(1,22)}$=5.260, p=.032, η_p^2=.193). No other interactions were significant (Stimulation*Velocity, $F_{(1,22)}$=.663, p=.424, η_p^2=.029; Synchrony*Velocity, $F_{(1,22)}$=3.254, p=.085, η_p^2=.129) (Figure 2.4.A).

To explore the nature of the above, significant, interactions, two additional 2 (stroking synchrony) x 2 (stroking velocity), repeated-measures ANOVAs were conducted on LGVS and RGVS separately. For LGVS, a main effect of Synchrony ($F_{(1,22)}$=23.345, p<.001, η_p^2=.515) indicated that synchronous conditions resulted in an increase in proprioceptive drift. There was no main effect of Velocity ($F_{(1,22)}$=3.467, p=.076, η_p^2=.136), but there was a significant Synchrony*Velocity interaction ($F_{(1,22)}$=10.052, p=.004, η_p^2=.314). This was further analysed using post-hoc paired sample *t*-tests (Bonferroni corrected, α = 0.025), to compare slow and fast touch during synchronous conditions, and separately, during asynchronous conditions. As expected, synchronous slow touch led to significantly higher proprioceptive drift than synchronous fast touch (synchronous slow touch: M=3.57 cm, SD=2.70; synchronous fast touch: M=2.16cm, SD=2.42; t_{22}=3.131, p=.005, *d*=0.94), while the difference between the two asynchronous conditions was not significant (asynchronous slow touch: M=.40 cm, SD=1.64; asynchronous fast touch: M=.68 cm, SD=2.12; t_{22}=-.807, p=.428, *d*=0.24).

Conversely, for RGVS there were no main effects or interactions (Synchrony: $F_{(1,22)}$=2.327, p=.141, η_p^2=.096; Velocity: $F_{(1,22)}$=.335, p=.569, η_p^2=.015; Synchrony*Velocity: $F_{(1,22)}$=.087, p=.770, η_p^2=.004).

Non-hemispheric specific effects

Visual capture conditions

As expected, no generic effect of GVS was found on proprioceptive drift after visual exposure to the rubber hand; a paired sample t-test comparing the overall effect of stimulation (LGVS+RGVS/2) with Sham was not significant (LGVS+RGVS/2: M=1.39cm, SD=1.78; Sham: M=.92cm, SD=2.58; t_{22}=.749, p= .462, *d*=0.22; Figure 2.3.B).

Stroking conditions

A 2 (stimulation: (LGVS+RGVS/2) and Sham) x 2 (stroking synchrony: synchronous and asynchronous) x 2 (stroking velocities: slow and fast) repeated measures ANOVA revealed a main effect of Stimulation ($F_{(1,22)}$=4.862, p=.038, η_p^2=.181) and main effect of Synchrony ($F_{(1,22)}$=16.744, p<.001, η_p^2=.432), indicating that the average of the two GVS stimulations, as well as synchronous conditions, increased proprioceptive drift. The main effect of Velocity was also approaching significance ($F_{(1,22)}$=4.183, p=.053, η_p^2=.160), with slow touch leading to marginally greater proprioceptive drift than fast touch. None of the interactions were significant (Stimulation*Synchrony, $F_{(1,22)}$=.438 p=.515, η_p^2=.020; Stimulation*Velocity ($F_{(1,22)}$=.058, p=.812, η_p^2=.003; Synchrony*Velocity, $F_{(1,22)}$=.296, p=.592, η_p^2=.013; Stimulation*Synchrony*Velocity, $F_{(1,22)}$=.931, p=.345, η_p^2=.041) (Figure 2.4.B).

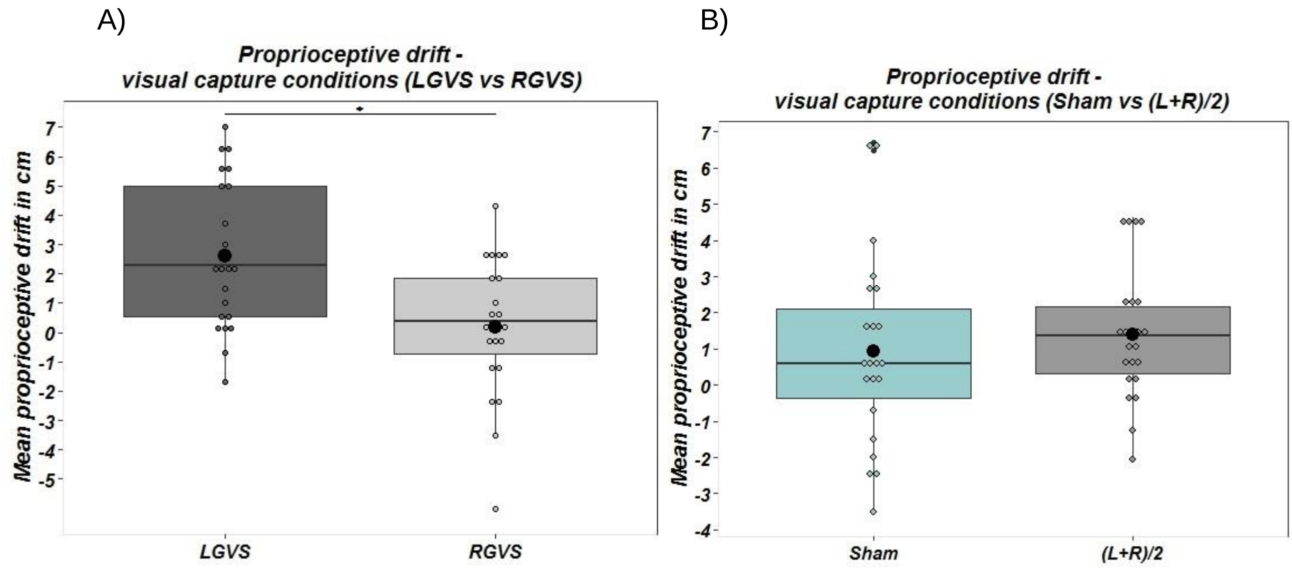


Figure 2.3. GVS effects during Visual Capture on Proprioceptive drift. A) Mean values of the proprioceptive drift measured in cm in the LGVS and in the RGVS; B) Mean values of the proprioceptive drift measured in cm in (LGVS+RGVS)/2 and Sham obtained during visual capture conditions. *= p<0.01; Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR).

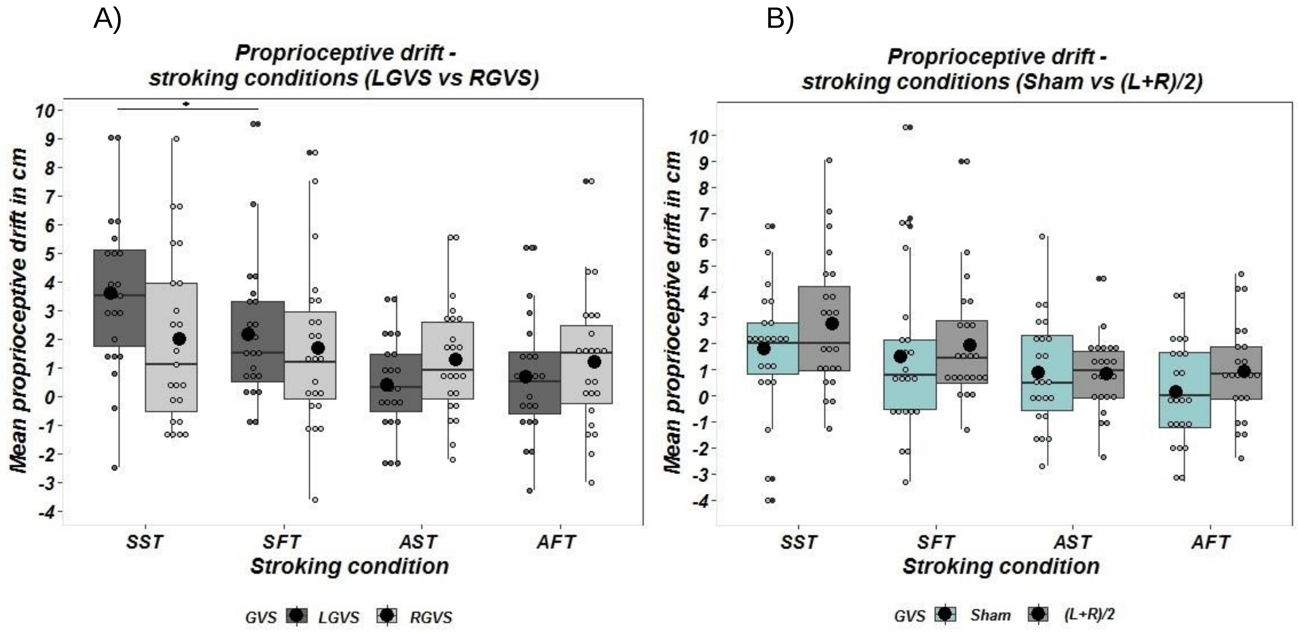


Figure 2.4. A) Mean values of the proprioceptive drift measured in cm in the LGVS and in the RGVS; B) Mean values of the proprioceptive drift measured in cm in (LGVS+RGVS)/2 and Sham obtained during the stroking conditions of the rubber hand illusion. SST= synchronous slow touch; SFT= synchronous fast touch; AST= asynchronous slow touch; AFT= asynchronous fast touch. *= p<0.01; Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR).

2.3.2. Embodiment questionnaire

Hemispheric specific effects

Visual capture conditions

A paired sample t-test comparing LGVS and RGVS did not indicate a significant difference between the two vestibular stimulations in subjective aspects of embodiment following mere visual exposure to the rubber hand (t_{22}=-.064, p=.950, *d*=.01) (Table 2.1).

Stroking conditions

A 2 (stimulation: LGVS and RGVS) x 2 (stroking synchrony: synchronous and asynchronous) x 2 (stroking velocities: slow and fast) repeated measures ANOVA revealed a main effect of Synchrony ($F_{(1,22)}$=30.502, p<.001, η_p^2=.581), indicating that synchronous conditions led to greater embodiment. There was no main effect of Stimulation ($F_{(1,22)}$=1.787, p=.195, η_p^2=.075) or Velocity of stroking

($F_{(1,22)}$=2.851, p=.105, η_p^2=.115) and none of the interactions were significant (Stimulation*Synchrony, $F_{(1,22)}$=.970 p=.335, η_p^2=.042; Stimulation*Velocity, $F_{(1,22)}$=1.422, p=.246, η_p^2=.061; Synchrony*Velocity, $F_{(1,22)}$=1.524, p=.230, η_p^2=.065; Stimulation*Synchrony*Velocity, $F_{(1,22)}$=.119, p=.734, η_p^2=.005).

Non-hemispheric specific effects

Visual capture conditions

A paired sample t-test comparing the average of the two stimulations ((LGVS+RGVS)/2) with Sham was not significant (t_{22}=-.714, p= .483, *d*=-.21); hence, no generic arousal effects due to GVS on subjective embodiment were found following visual exposure to the rubber hand.

Stroking conditions

A 2 (stimulation: (LGVS+RGVS)/2 and Sham) x 2 (stroking synchrony: synchronous and asynchronous) x 2 (stroking velocities: slow and fast) repeated measures ANOVA revealed main effects of Synchrony ($F_{(1,22)}$=26.753, p<.001, η_p^2=.549), Stimulation ($F_{(1,22)}$=6.296, p=.020, η_p^2=.223) and Velocity ($F_{(1,22)}$=4.581, p=.044, η_p^2=.172). No significant interactions were found (Stimulation*Synchrony, $F_{(1,22)}$=.007 p=.935, η_p^2=.000; Stimulation*Velocity, $F_{(1,22)}$=.031, p=.863, η_p^2=.001; Synchrony*Velocity, $F_{(1,22)}$=.065, p=.801, η_p^2=.003; Stimulation*Synchrony*Velocity, $F_{(1,22)}$=2.103, p=.161, η_p^2=.087). This analysis suggested that each of the factors independently contributed to a higher level of subjective embodiment (see Table 2.1 below). As expected, synchronous conditions significantly increased the subjective experience of the rubber hand illusion. Furthermore, the overall level of embodiment was higher during Sham stimulation, indicating that GVS decreased participants' subjective feelings of ownership towards the rubber hand. Finally, fast touch led to a slightly higher subjective embodiment than slow touch.

Table 2.1. Descriptive statistics of embodiment questionnaire's average values in the different conditions.

Conditions	LGVS	RGVS	Sham	(L+R)/2
	Mean *(SD)*	Mean *(SD)*	Mean *(SD)*	Mean *(SD)*
Visual Capture	-0.61 *(1.60)*	-0.60 *(1.54)*	-0.45 *(1.65)*	-0.60 *(1.46)*
Synchronous Slow Touch	*0.59 (1.40)*	0.38 *(1.45)*	0.85 *(1.35)*	0.48 *(1.33)*
Synchronous Fast Touch	0.94 *(1.38)*	0.59 *(1.42)*	0.90 *(1.37)*	0.76 *(1.36)*
Asynchronous Slow Touch	-0.63 *(1.46)*	-0.65 *(1.38)*	-0.46 *(1.71)*	-0.64 *(1.35)*
Asynchronous Fast Touch	-0.40 *(1.49)*	-0.65 *(1.35)*	-0.17 *(1.47)*	0.53 *(1.30)*

2.3.3. Visual capture versus stroking conditions

In order to exploratorily compare the effects of the visual capture conditions with the stroking conditions, two separate 2 (GVS: LGVS vs RGVS / Sham vs L+R/2) x 3 (Stroking applied: no stroking, synchronous stroking, asynchronous stroking) repeated measures ANOVA on LGVS vs RGVS and on Sham vs the average of the two vestibular stimulations on both proprioceptive drift values and questionnaire scores were conducted. Given that the aim was to investigate whether the effects of the visual capture conditions were comparable to those found in the synchronous conditions and statistically different from the asynchronous ones, the values obtained in slow and fast synchronous and, separately, slow and fast asynchronous stroking conditions, were averaged.

Proprioceptive drift - LGVS vs RGVS

A 2 (GVS: LGVS vs RGVS) x 3 (stroking: no stroking vs synchronous stroking vs asynchronous stroking) repeated measures ANOVA revealed a main effect of stimulation ($F_{(1,22)}$=8.009, p=0.01, ηp^2=.267), with LGVS leading to greater proprioceptive drift in comparison with RGVS, a main effect of stroking ($F_{(2,44)}$=5.737, p<0.01, ηp^2=.207) and a significant interaction between stimulation and stroking type ($F_{(2,44)}$=9.096, p<0.01, ηp^2=.293).

To further investigate the significant main effect of stroking as well as the interaction between stimulation and stroking, three paired sample t-test (Bonferroni corrected, α=0.016) were conducted within each GVS block between no stroking and synchronous conditions, no stroking and asynchronous conditions and synchronous and asynchronous conditions. This set of comparisons revealed a significant difference between synchronous and asynchronous conditions in LGVS, with synchronous conditions leading to greater proprioceptive drifts (synchronous stroking: M= 2.87 cm, SD=2.33; asynchronous stroking: M=0.55, SD=1.70; t_{22}=4.832, p<0.01, d=1.456) as well as a significant difference between the no stroking condition and the asynchronous conditions, with the no stroking condition leading to greater proprioceptive displacement (no stroking: M=2.61cm, SD=2.51; t_{22}=3.511, p<0.01, d=1.059). There was no significant difference between the no stroking condition and synchronous conditions (t_{22}=-.480, p=0.636, d=0.145). No comparison within the RGVS block was significant (synchronous stroking: M=1.82 cm, SD=2.64; asynchronous stroking: M=1.23cm, SD=1.95; t_{22}=1.525, p=0.141, d=0.460; no stroking: M=0.18 cm, SD=2.30; t_{22}=-1.767, p=0.91, d=-0.533; no stroking vs synchronous stroking: t_{22}=-2.174, p=0.041, d=-0.655). This analysis suggests that, in LGVS only and in agreement with the results reported above, the visual capture condition is indeed eliciting an effect on the proprioceptive drift that is comparable to the one found in the synchronous conditions and that is statistically greater than in the asynchronous conditions.

Proprioceptive drift - Sham vs L+R/2

A 2 (GVS: Sham vs L+R/2) x 3 (stroking: no stroking vs synchronous stroking vs asynchronous stroking) revealed a main effect of stroking ($F_{(2,44)}$=9.757, p<0.01, ηp^2=.307), a main effect of stimulation approaching significance ($F_{(1,22)}$=4.063, p=.056, ηp^2=.156), with the average of the 2 GVS stimulation leading to greater proprioceptive drift in comparison with Sham, but no interaction between stimulation and stroking type ($F_{(2,44)}$=1.778, p=.181, ηp^2=.075).

Three paired sample t-test (Bonferroni corrected, α=0.016), run within each GVS block between no stroking and synchronous conditions, no stroking and asynchronous conditions and synchronous and asynchronous conditions, revealed a significant difference between synchronous and asynchronous conditions in L+R/2 (synchronous stroking: M=2.35 cm, SD=2.25; asynchronous stroking: M=0.89 cm, SD=1.47; t_{22}=4.407, p<0.01, d=1.329), with synchronous conditions leading to greater proprioceptive drifts. No other comparison was significant (Sham: synchronous stroking: M=1.63 cm, SD=1.94; asynchronous stroking: M=0.52 cm, SD=1.65; t_{22}=2.350, p=0.028, d=0.708; no stroking: M=0.93 cm, SD=2.59; t_{22}=-1.379, p=0.182, d=-0.416; no stroking vs asynchronous stroking: t_{22}=0.739, p=0.468, d=0.223; L+R/2: no stroking: M=1.39 cm, SD=1.78; t_{22}=-1.783, p=0.088, d=-0.537; no stroking vs asynchronous stroking: t_{22}=1.196, p=0.244, d=0.360).

Embodiment questionnaire - LGVS vs RGVS

A 2 (GVS: LGVS vs RGVS) x 3 (stroking: no stroking vs synchronous stroking vs asynchronous stroking) revealed a main effect of stroking ($F_{(2,44)}$=22.088, p<0.01, ηp^2=.501), but no main effect of stimulation ($F_{(1,22)}$=0.683, p=.417, ηp^2=.030), and no interaction between stimulation and stroking type ($F_{(2,44)}$=1.146, p=.327, ηp^2=.050).

Three paired sample t-test (Bonferroni corrected, α=0.016) were conducted within each GVS block between no stroking and synchronous conditions, no stroking and asynchronous conditions and synchronous and asynchronous conditions. These comparisons revealed a significant difference between synchronous and asynchronous conditions in LGVS (synchronous stroking: M=0.77, SD=1.35; asynchronous stroking: M=-0.52, SD=1.43; t_{22}=4.850, p<0.001, d=1.462) and RGVS (synchronous stroking: M=0.47, SD=1.37; asynchronous stroking: M=-0.66, SD=1.31; t_{22}=5.939, p<0.001, d=1.790), with synchronous conditions leading to greater embodiment. Moreover, a significant difference between the no stroking conditions and the synchronous conditions in both LGVS (no stroking: M=-0.62, SD=1.61; t_{22}=-4.805, p<0.001, d=-1.448) and RGVS (no stroking: M=-0.60, SD=1.54; t_{22}=-4.764, p<0.001, d=-1.436) was found, thus suggesting that the no stroking condition (i.e. visual capture) did not lead to greater embodiment in neither of the vestibular stimulations. No other comparison was significant (LGVS: no stroking vs asynchronous stroking: t_{22}=-0.440, p=0.664, d=-0.132; RGVS: no stroking vs asynchronous stroking: t_{22}=0.289, p=0.775, d=0.087).

Embodiment questionnaire - Sham vs L+R/2

A 2 (GVS: Sham vs L+R/2) x 3 (stroking: no stroking vs synchronous stroking vs asynchronous stroking) revealed a main effect of stroking ($F_{(2,44)}$=22.932, p<0.001, ηp^2=0.510), a main effect of stimulation approaching significance ($F_{(1,22)}$=4.221, p=0.052, ηp^2=0.161), with Sham leading to overall higher levels of embodiment, and no interaction between stimulation and stroking type ($F_{(2,44)}$=0.191, p=0.827, ηp^2=0.009).

Three paired sample t-test (Bonferroni corrected, α=0.016) were subsequently run within each GVS block between no stroking and synchronous conditions, no stroking and asynchronous conditions and synchronous and asynchronous conditions, revealing a significant difference between synchronous and asynchronous conditions in Sham (synchronous stroking: M=0.88, SD=1.65; asynchronous stroking: M=-0.32, SD=1.52; t_{22}=4.489, p<0.001, d=1.353) as well as in the average of the other two vestibular stimulation (synchronous stroking: M=0.63, SD=1.31; asynchronous stroking: M=-0.59, SD=1.29; t_{22}=5.523, p<0.001, d=1.665), with synchronous conditions leading to greater embodiment. In line with the comparison between LGVS and RGVS reported above, a significant difference between the no stroking conditions and the synchronous conditions in both Sham (no stroking: M=-0.46, SD=1.65; t_{22}=-5.417, p<0.001, d=-1.633) and L+R/2 (no stroking: M=-0.61, SD=1.46; t_{22}=-5.240, p<0.001, d=-1.579) was found, suggesting that the no stroking condition did not lead to greater embodiment in neither Sham or the average of the two vestibular stimulations. No other comparison was significant (Sham: no stroking vs asynchronous stroking: t_{22}=-0.523, p=0.606, d=-0.157; L+R/2: no stroking vs asynchronous stroking: t_{22}=-0.110, p=0.914, d=-0.033).

2.3.4. Control analysis and manipulation checks

Pleasantness task

Pleasantness ratings were analysed using a 2 (velocity: slow, CT-optimal vs. fast, non CT-optimal) x 2 (site: forearm vs. palm of the hand) repeated measures ANOVA. The results revealed a main effect of Velocity ($F_{(1,22)}$=18.962, p=.000 , η_p^2=.463) but not of Site ($F_{(1,22)}$=.753, p=.395, η_p^2=.033), indicating that slow, CT-optimal stroking is indeed perceived as more pleasant that fast, non CT-optimal touch (Figure 2.5). The interaction between velocity and site was not significant ($F_{(1,22)}$=1.457, p=.240, η_p^2=.062), indicating that slow touch is perceived as more pleasant even if it is administered in a site that does not contain CT-afferents.

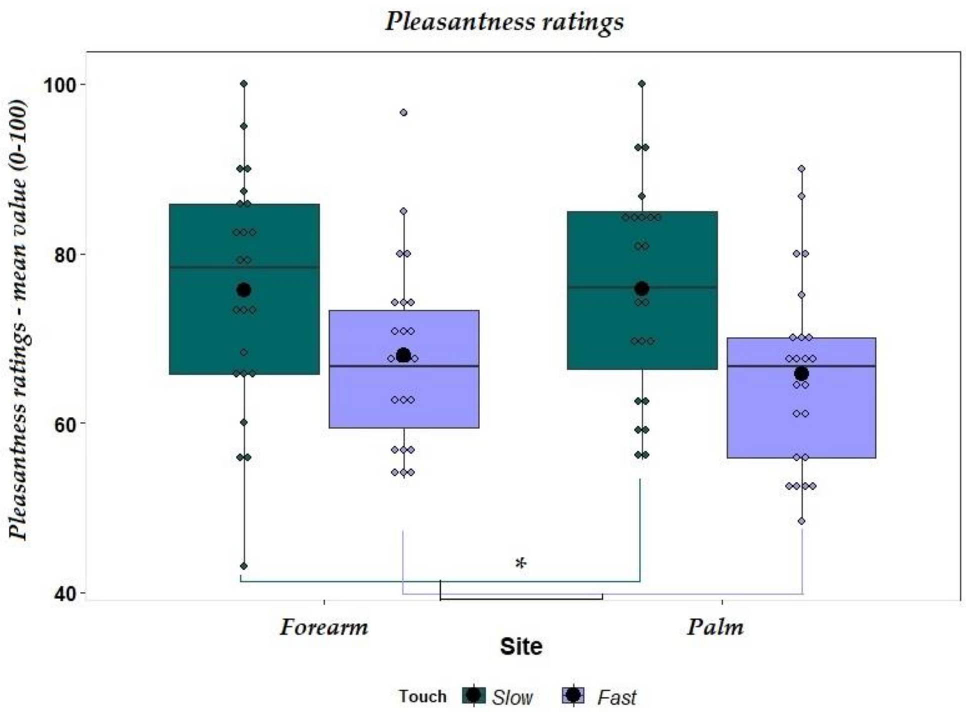


Figure 2.5. Mean values of the pleasantness ratings on a scale from 0 (not at all pleasant) to 100 (extremely pleasant). *= p<0.01; Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR).

Cumulative effects of GVS

In this additional control analysis, the aim was to explore whether vestibular stimulation had any cumulative, carry over effects on proprioception, over and above any effects of rubber hand manipulations. In order to do so, the proprioceptive judgements taken before each of the stroking conditions were analysed and their trend in each of the three GVS blocks (Sham, LGVS, RGVS) was investigated and compared across the blocks. A 3 (stimulation: LGVS, RGVS and Sham) x 4 (time: 1st Proprioceptive judgement, 2nd proprioceptive Judgement, 3rd Proprioceptive Judgement, 4th Proprioceptive judgement) repeated measures ANOVA was conducted, revealing a main effect of Time ($F_{(3, 66)}$=3.868, p=0.013, ηp^2=.150), indicating a progressive increase in proprioceptive displacement during each block, but no main effect of Stimulation ($F_{(2, 44)}$=.383, p=.684, ηp^2=.017) nor significant interaction between Stimulation and Time ($F_{(6, 132)}$=1.401, p=0.219, ηp^2=.060). Accordingly, the polynomial contrasts indicated a significant linear trend over time ($F_{(1, 22)}$=7.193, p=0.014, ηp^2=.246), suggesting that regardless of the type of stimulation involved, participants' proprioceptive judgements were increasingly less accurate. This analysis suggests that the abovementioned findings concerning the proprioceptive drifts (i.e. the differentials between post-RH and pre-RH proprioceptive judgements, see Figure 2.1.A) were not biased by a cumulative carry-over effect of vestibular stimulation on baseline proprioceptive judgements.

Vestibular sensations

At the end of the main experiment, participants were asked to report any physical sensation associated with the stimulation in order to identify any noticeable vestibular-induced sensations between conditions. All of them reported tingling and itching on the skin's surface below the electrodes and none of the participants described the stimulation as painful. When asked about vestibular-related feelings, 15/23 reported dizziness, vertigo or loss of balance, whereas 8 participants did not. This suggests that a 1mA stimulation has been able to trigger distinctive vestibular sensations in two thirds of the sample.

In order to control for the role of Sham stimulation as a placebo-like intervention, participants were asked to guess in which of the 3 GVS configurations they thought to have received a vestibular system's stimulation, specifying that the answer might have been all of them, 2 or 1. The majority of them guessed correctly about LGVS and RGVS (19/23 and 20/23, respectively), whereas approximately one third of the sample reported Sham as a vestibular stimulation (15/23 guessed that Sham was not inducing vestibular sensations, when directly invited to compare it with the other 2 GVS configurations). No significant difference between these frequencies was found using a Likelihood Ratio Chi-square analysis ($\chi^2_{(2)}$ = 3.469, p=0.167; ϕ_c = .167).

2.4. Discussion

GVS was administered to healthy participants during a rubber hand illusion task, in order to explore the influence of vestibular stimulation on body ownership during multisensory integration. Participants showed a significantly greater perceived hand displacement towards the rubber hand during LGVS, but not RGVS, even in the absence of any tactile stimulus (i.e. during pure 'visual capture') and beyond any general (i.e. not lateralised) GVS effect. Furthermore, when participants' forearms were stroked synchronously with the rubber hand, proprioceptive drifts were greater during LGVS in comparison with RGVS conditions. Lastly, during LGVS synchronous conditions only, slow, CT-optimal touch led to greater proprioceptive drifts in comparison to fast, non-CT-optimal touch.

These findings corroborate the hypothesis that the vestibular system plays a modulatory role in multisensory integration: when there is a conflict between proprioception and vision, the right vestibular network may solve the ambiguity by increasing the relative weighting of visual signals over proprioceptive ones. This interpretation is consistent with the idea that the vestibular system actively contributes to the formation of an updated representation of our body in space according to bodily and environmental changes (Pfeiffer et al., 2014). It has been showed that LGVS induces a disruption of the normal egocentric (i.e. based on the perceiver) reference frame when performing an allocentric (i.e. based on the external environment) judgement (Fink et al., 2003). A recent study (Harris & Hoover, 2015) found that GVS disrupted the natural self-advantage (i.e. greater accuracy in 1st person perspective) when detecting delays in virtually reproduced self-generated fingers movements, with no difference in participants' performance when the stimuli were presented from a 3rd person perspective. The results of the current study could be due to a vestibular-induced disruption of the normal body representation, based on an egocentric reference frame: a perturbation of body-centred multisensory processing might lead to an increased weighting of visual cues with a concomitant reduction of proprioceptive ones, thus favouring a proprioceptive displacement towards an external object (i.e. the rubber hand). Within a predictive coding framework, Zeller and colleagues (2015) suggested that the occurrence of the RHI may be the result of lowering the precision (i.e. the certainty about sensory representations) of somatosensory signals to allow a top-down resolution of sensory ambiguity. In the current study, this may have translated into an increased 'visual capture' of the rubber hand, in absence of any tactile stimulation (in line with the findings reported by Samad et al., 2015 2015 and Longo, Cardozo and Haggard, 2008 in healthy subjects and Martinaud et al., 2017 in right-hemisphere stroke patients), as well as of the touch delivered to the rubber hand, during synchronous conditions only (conversely to what has been found in patients affected by eating disorders, whereby visual capture effects are enhanced regardless of synchrony; Eshkevari et al., 2012). Nevertheless, as mentioned in the introduction, the design employed in this study did not allow for directly testing changes in variances associated with the proprioceptive drifts at the individual level but only at the group one. Hence, it can only be speculated that this may be the mechanism at play here. Further studies are needed in order to clearly define the degree to which the increased weighting of visual information is accompanied by a decrease in precision of proprioceptive one (e.g. as suggested by Zeller et al., 2015). Importantly, the enhanced visual capture of the seen touch observed in the present study occurs solely when there is temporal congruency (synchronous stroking conditions), a factor deemed necessary to allow multisensory integration and ownership (Constantini et al., 2016). Moreover, the trend analysis of proprioceptive judgements demonstrates that these effects are observed over and above a generic, vestibular-induced progressive bias in participants' proprioceptive ability over time. Thus, these findings corroborate the hypothesis that the vestibular system acts on multisensory integration rather than at the unimodal level (as suggested by Ferrè et al., 2015).

This 'visual capture' of proprioception and touch is also consistent with the observed increase in proprioceptive drifts following synchronous slow, CT-optimal touch compared to fast touch (with no difference between asynchronous conditions) during LGVS conditions only. That is, the proprioceptive displacement towards a rubber hand was enhanced by synchronous, affective touch only during a right vestibular network stimulation. The specific contribution of the CT-system in our study may hence relate to the affectivity conveyed by the touch seen on the rubber hand, rather than only by the one felt. Observing the administration of CT-optimal touch on another person's skin leads to the activation of cortical areas involved in affective processing ("vicarious touch", Morrison et al., 2011a). In addition, two recent studies found that inhibition of the somatosensory cortices does not influence the perceived pleasantness of CT-optimal touch, highlighting the possible anatomical and cognitive dissociation between affective and discriminative aspects of CT-optimal touch (Case et al., 2016; Case et al., 2017). In the current study, the stimulation of the right vestibular network, may have promoted a visual capture of the seen affective touch, by rebalancing multisensory weighting in favour of vision while lowering the precision of felt sensations, in line with the hypothesised top-down modulation discussed above. Future studies are needed to shed light on the role of vicarious affective touch in multisensory integration as well as on the precise contribution of each sensory modality, with paradigms investigating changes in variances at the individual level. This possibility will be investigated in the following chapter.

It might be argued that these results could be explained in terms of a generic, vestibular-dependent shift in space towards the left side. It has been shown that LGVS induces a leftward shift on the lateral plane in right hemisphere stroke patients (Utz et al., 2011; Wilkinson et al., 2014) and healthy subjects (Ferrè et al., 2013). Accordingly, during rotational vestibular stimulation, peri-personal space is remapped in a direction-specific fashion and sensory congruency further expands the boundaries of subjects' peri-personal space (Pfeiffer et al., 2018). However, in a separate control condition devised within a follow-up experiment (see Chapter 4), it has been showed that galvanic vestibular stimulation did not induce shifts on the lateral plane per se (i.e. when no rubber hand is present). Differences in the types of stimulation used (rotational vs galvanic) as well as duration of stimulation (as further discussed below in relation to Ferrè and colleagues' findings) may partially account for the conflicting results. However, further research should investigate the effects of GVS on multisensory integration when there is a stimulus in view (e.g. a rubber hand) but such stimulus is displaced in depth rather than laterally.

The present findings also corroborate the hypothesis of a hemispheric specific vestibular network for bodily awareness (see also Ferrè et al., 2015). However, since LGVS stimulates mainly areas in the right-hemisphere, it is possible that the mechanisms observed in the current study are limited to the left hand, and may not represent a generalised effect on bodily awareness. On the other hand, given that the right hemisphere is dominant for vestibular processing (Dieterich et al., 2003; Eulenburg et al., 2012) and generally considered crucial for body representation in both healthy subjects and clinical population (Cappa et al., 1987; Bisiach et al., 1991; Naito et al., 2005; Tsakiris et al., 2007; Tsakiris, 2010), it is reasonable to assume that if the hand used for the illusion was the right rather than the left, the results would point in the same direction. Accordingly, previous studies showed that when the RHI is performed on the right hand, areas of the fronto-parietal network are activated bilaterally, i.e. the activation occurs in the right as well as the left hemisphere (Ehrsson et al. 2004; Gentile et al., 2013). Furthermore, evidence from anosognosia for hemiplegia suggests that lesions in the right fronto-parietal network may lead to a generalised bodily awareness impairment, affecting the paralysed as well as the healthy limb (Preston et al., 2010). Further studies should investigate this specific hypothesis regarding laterality.

While the role of proprioception, vision and touch in processing information coming from different body parts is well established, the same is not necessarily true for the vestibular system, which has been predominantly considered responsible for the perception of our body as a whole in space. However, as suggested by Ferrè and Haggard (2016), the vestibular system contributes to processing of bodily signals at different hierarchical levels (i.e. somatosensation, somatoperception and somatorepresentation), including processing of different body parts in space (somatoperception) as well as their attribution to the self (somatorepresentation). Hence, as for every other sensory modality, the vestibular system appears to influence body representation at different levels of the hierarchical multisensory processing, including the ones related to specific body parts (e.g. hand's shape and size, Lopez et al., 2012). However, no study to date has investigated whether the re-weighting of visual and proprioceptive information following vestibular stimulation and observed in the current and previous studies in relation to specific body parts, also extends to whole-body illusions. Future studies could address this question.

The comparison between sham and the average of LGVS and RGVS indicated a generic, non-task specific effect of stimulation on proprioceptive drift, during stroking conditions, suggesting that, beyond the polarity specific effects, GVS might also induce a generic decrease in participants' proprioceptive ability. As suggested by Schmidt and colleagues (2013), GVS might lead to a decrease in participants' proprioceptive ability during an arm positioning task. Hence, vestibular stimulation might have an additional effect on multisensory integration by modulating proprioceptive displacement of participants' hand in relation to the rubber hand (determined as a differential between pre and post proprioceptive judgements) on the top of the rebalancing suggested above. Further research should disentangle the differential effects of vestibular stimulation on basic proprioception and multisensory integration.

By contrast, vestibular manipulations did not reveal any specific effects on subjective ratings of body ownership. The dissociation between subjective and behavioural measures of the RHI has been confirmed by previous studies (Abdulkarim & Ehrsson, 2016; Makin et al., 2008; Rohde et al., 2011). In this case, the change in proprioceptive drift was not accompanied by a similar change in felt ownership. This was true also for the visual capture conditions: additional analyses on questionnaire values revealed that visual capture conditions did not differ significantly from asynchronous conditions and were significantly lower than the synchronous conditions in all the different GVS configurations

(LGVS, RGVS, Sham and L+R/2), thus suggesting that this condition did not lead to the embodiment of the rubber hand. These findings on visual capture are different than similar ones reported by Samad and colleagues (2015): in their study, participants felt ownership of the rubber hand after visual exposure (in absence of stroking) as measured via questionnaires as well as changes in skin conductance. On the contrary, Rohde et al. (2011), reported a significant proprioceptive drift following a no stroking condition in absence of feelings of ownership of the rubber hand (it has to be noted, however, that they did not use a standardised questionnaire but only recorded, anecdotally, differences in ownership following no stroking, synchronous and asynchronous conditions). These differences between the studies will need to be explored in future research, ideally with larger samples to examine whether they relate to individual differences or differences between the experimental designs or set-up of the studies. One such difference may relate to the distance between the real and the rubber hand. Specifically, as discussed in detail below, the distance between real and rubber hand has been shown to play different roles in embodiment and in proprioceptive displacement: whilst greater distances may favour proprioceptive displacement (Preston, 2013), the same may not be true for felt ownership (Samad et al., 2015). Samad and colleagues' computational model predicts that feelings of ownership during the RHI should fail to occur when the rubber and real hands are further than 30 cm apart. Even though feelings of ownership still occur following synchronous stroking when the real hand and the rubber hand are positioned 35 cm apart (Preston, 2013), the same may not be true when tactile stimulation is absent and does not contribute to multisensory processing. Thus, it may be possible that increasing the distance between real and rubber hand during a mere visual exposure to the latter is enough to abolish the occurrence of feelings of ownership. Further studies should specifically address this possibility.

Furthermore, it is possible that the aforementioned disruption of the egocentric reference frame induced by LGVS did not translate into corresponding feelings of embodiment towards an external object in our setup. This might be due to the fact that the proprioceptive drift is a measure of perceived position in space and it is hence influenced by the relative weighting of vision and proprioception induced by the vestibular activation. On the other hand, as mentioned above, feelings of embodiment might involve additional, higher-order processes that are not affected by the stimulation (Tsakiris, 2010; Martinaud et al., 2017). In the current study, the comparison between sham and the average of the other two GVS configurations indicated that feelings of ownership of the rubber hand were higher during sham, suggesting that GVS possibly reduces subjective (explicit) experiences of body ownership as measured via self-report questionnaires. These findings contrast with Lopez and colleagues (2010), who found that LGVS increased felt ownership towards the rubber hand. In the current study, fast touch led to greater subjective embodiment overall, compared with slow touch, irrespective of the synchrony and type of stimulation (in contrast with Crucianelli et al., 2013 and Lloyd et al., 2013). However, fast stroking did not itself lead to particularly strong embodiment, with scores not above 1 on average (see Ehrsson et al., 2004; Petkova and Ehrsson, 2009; Kalckert and Ehrsson, 2012 for discussions regarding the use of a minimum score for embodiment). These unexpected findings may be explained, at least in part, by variability between studies in the measures (i.e. embodiment questions) used to assess the illusion, and further research is needed to examine these effects on subjective embodiment.

Methodological differences between the current set-up and previous studies may also account for the negative finding on enhancement of the proprioceptive displacement by slow, CT-optimal touch during Sham conditions. In van Stralen and colleagues (2014) the velocities used to administer the stroking were 0.3 cm/s (non-CT-optimal), 3 cm/s (CT-optimal) and 30 cm/s (CT-optimal). It may be possible that using markedly different velocities as control conditions (30 cm/s rather than 18 cm/s) would result in differences in behavioural and subjective measures of the RHI. However, the same velocities (3 cm/s and 30 cm/s) have been implemented in Lloyd et al., 2014, but without replication of van Stralen’s findings. The results of the current study are in line with the negative findings reported by Crucianelli et al., 2013 as well as Lloyd et al., 2014, i.e. that CT-optimal touch does not enhance proprioceptive displacement (in the absence of vestibular stimulation). However, as mentioned above, their positive finding on enhancement of feelings of embodiment following slow, CT-optimal stroking was not replicated. In the current study, the same velocities (3 cm/s and 18 cm/s) used in previous studies were used (Crucianelli et al., 2013; 2017); however, the paradigm in recording embodiment was not exactly the same, i.e. there was no pre-measurement of embodiment following visual capture as a baseline for each condition. In addition, all these studies involve manual touch and it is possible that there are some experimenter effects, either due to the way the touch is administered or due to other factors such as gender (Gazzola et al., 2012) or attractiveness (unpublished data from our group). Future or meta-analytic studies should investigate the influence of such factors on the various measures of body ownership.

The current findings are in line with the positive trend for LGVS to increase proprioceptive drift reported by Lopez et al. (2010) but contradict findings by Ferrè and colleagues (2015). One possible explanation for the variability in findings is a difference in the GVS protocols used across studies. While Ferrè and colleagues used brief GVS pulses (around 4.5 seconds), both Lopez et al. and our study implemented longer stimulation windows (1 minute in Lopez et al. and 2 minutes in the current study). Interestingly, fMRI studies (Bense et al., 2001; Della-Justina et al., 2015) have shown that longer GVS pulses (of 27.5 and 21 seconds respectively) caused a decrease in activation of somatosensory areas, thus suggesting a possible inhibition of proprioceptive processing during vestibular stimulation. Stimulation periods of 4.5 seconds may hence fail to elicit the somatosensory inhibition mentioned above, which might be responsible for the dominance of visual aspects of multisensory processing over proprioceptive ones during longer stimulation windows. This possibility was not directly addressed in the current study, and further research is needed.

Finally, several studies have also examined the effects of hand position on body ownership during the RHI (Zopf et al., 2010; Preston, 2013; Kalckert and Ehrsson, 2014). In Ferrè and colleagues, the distance between the rubber and real hands was approximately 20cm, whereas in Lopez and colleagues the hands were 24.5cm apart. In the current study, the rubber hand and the real hand were positioned approximately 30cm apart, both on the left of the participant's midline. Preston (2013) found that similar spatial arrangements (i.e. rubber hand and real hand at approximately 35cm distance) to our own produced greater differences in proprioceptive drift in synchronous relative to asynchronous conditions of the RHI when compared against other spatial configurations. Existing studies in healthy and clinical populations suggest that GVS affects spatial cognition (see Utz et al., 2010 for a review).

Thus, it may be that right-hemisphere vestibular stimulation is especially effective in modulating multisensory integration when the hands are further apart, and closer to left extra-personal space, where the fake hand is less readily incorporated into the body representation. Future research could investigate this possibility.

The present study confirmed the suggestion that visual dominance over proprioception is the preferred way through which visuo-proprioceptive multisensory conflict is resolved in ambiguous situations. Furthermore, the specificity of a right vestibular network for bodily awareness was highlighted: these findings support the hypothesis of a lateralisation of bodily-related stimuli processing. It was also showed that right vestibular stimulation during synchronous tactile stroking modulates multisensory integration such that synchronous touch is more ‘captured’ by vision. Lastly, the current findings suggest the importance of affective processing in multisensory integration during sensory conflicting situations: slow, affective touch may reduce sensory ambiguity by promoting a visual capture of the seen affective touch.

As discussed above, several possibilities for future research remain open. As such, in Chapter 3, the possibility of a differential modulation of felt and seen components of touch (and, specifically affective touch) by the vestibular system will be investigated, shedding light on the role of vicarious aspects of affective touch in multisensory integration. In Chapter 4, potential alternative mechanisms explaining the effect of vestibular stimulation observed in the current chapter will be explored.

Chapter 3

Vestibular Modulation of Multisensory Integration During Actual and Vicarious Tactile Stimulation

3.1. Introduction

As mentioned in the previous two Chapters, during multisensory integration, signals from different sensory modalities are weighted according to their contextual reliability and combined to produce a unitary perceptual experience of the world (Ernst & Banks, 2002; Fetsch et al., 2011; Stein et al., 2014). Such experience includes our own body and the sense that our body belongs to us (body ownership; Gallagher, 2000). Body ownership has been extensively studied using the Rubber Hand Illusion (i.e. RHI; Botvinick & Cohen, 1998), during which participants watch a fake hand being touched in- or out-of-synchrony with their own unseen hand. As a result of synchronous stroking of the rubber hand and participant's hand, individuals may feel subjective feelings of ownership of the rubber hand, and/or a shift in the perceived location of their own real hand towards the position of the rubber hand (i.e. proprioceptive drift). The amount of shift resulting from the experimental condition is obtained by asking participants, before and after the stroking, to report where they feel their own index finger to be. Then, the difference between post vs pre-measurements is calculated to obtain the proprioceptive drift.

The RHI has provided significant insight into how conflict between vision of a synchronously touched rubber hand and proprioception of the real hand's location is resolved by information from one modality (vision) dominating over the others (proprioception and touch; Folegatti, de Vignemont, Pavani, Rossetti, & Farne, 2009; Pavani, Spence, & Driver, 2000; van Beers, Wolpert, & Haggard, 2002). This "visual capture" effect, characterised by a dominance of visual cues over other modalities (Rock & Victor, 1964) occurs, in particular, when vision is deemed contextually most reliable (e.g. when we process visuo-proprioceptive signals in the horizontal plane; van Beers et al., 2002). However, not all sensory conflictual situations are solved with a dominance of vision over proprioception. For example, an illusory feeling of movement is often experienced whilst sitting on a stationary train and observing an adjacent train beginning to move past. In such instances, the vestibular system, primarily involved in regulating balance and coordination during self-motion, also contributes to multisensory integration, providing information signalling an unresolved conflict between vision (i.e. “I see motion”) and proprioception (i.e. “I feel I am *not* moving”), which often results in motion sickness (Bertolini & Straumann, 2016).

An increasing number of studies suggests that the functional role of the vestibular system extends beyond the regulation of posture and balance (Blini et al., 2018; Brandt & Dieterich, 1999; Lopez & Elzière, 2018). Neuroanatomical evidence (Fasold et al., 2002; zu Eulenburg, Caspers, Roski, & Eickhoff, 2012) indicates shared neural mechanisms for vestibular processes and other sensory modalities, such as vision (Brandt et al., 2002; Seemungal et al., 2013; Della-Justina et al., 2015), touch and proprioception (Dijkerman & de Haan, 2007; Lackner & DiZio, 2005). A partial overlap between the vestibular network and brain regions linked to multisensory integration has also been identified, with activations in the temporoparietal junction, inferior parietal lobule, insula and cingulate cortex (Lopez et al., 2012; Lopez, 2016). In order to test the influence of vestibular signals on body ownership, several studies implemented artificial vestibular stimulation to activate the peripheral vestibular organs (such as Galvanic Vestibular Stimulation, i.e. GVS; see Utz, Dimova, Oppenländer, & Kerkhoff, 2010). Neuroimaging findings showed that such peripheral stimulation leads to the activation of the right vestibular network when the anode is positioned on the left vestibular nerve and the cathode on the right (i.e. LGVS). The opposite configuration leads to bilateral activation of both vestibular networks (i.e. RGVS; Fink et al., 2003; Utz et al., 2010). However, results from studies employing GVS to investigate the influence of vestibular activation on body ownership have not been always consistent. Different studies suggest a differential mechanism underlying right-hemisphere vestibular effects on body ownership: while some authors suggest that vestibular stimulation increases the weight of proprioception (Ferre, Berlot, & Haggard, 2015), others posit the opposite (Lopez, Lenggenhager, & Blanke, 2010).

A previous study, reported in Chapter 2 (Ponzo, Kirsch, Fotopoulou, & Jenkinson, 2018), aimed to clarify these conflicting findings, whilst assessing how vestibular and interoceptive signals (i.e. feelings about the physiological condition of one's own body; Ceunen, Vlaeyen, & Van Diest, 2016; Craig, 2002) interact to shape body ownership. Recent research indicates that body ownership is modulated by interoceptive signals (Suzuki et al., 2013; Tsakiris, Jimenez, & Costantini, 2011), and can be enhanced by applying gentle touch at slow velocities that activate specialised nerve fibres (CT afferents), which provide interoceptive information in the form of tactile pleasure (Crucianelli, Metcalf, Fotopoulou, & Jenkinson, 2013; Crucianelli, Krahé, Jenkinson, & Fotopoulou, 2018; Lloyd, Gillis, Lewis, Farrell, & Morrison, 2013; Loken, Wessberg, Morrison, McGlone, & Olausson, 2009; van Stralen et al., 2014). In the study presented in Chapter 2, GVS was administered during a RHI procedure using slow, affective, CT-optimal or fast, emotionally neutral, CT- sub-optimal touch. Findings revealed that right-hemisphere vestibular stimulation increased proprioceptive drift during “vision only conditions” and synchronous visuo-tactile conditions. However, no observable effect on subjective embodiment was found. Moreover, the enhancement of proprioceptive drift during right vestibular stimulation was greater following affective compared with neutral touch conditions. These findings were interpreted as a right-hemisphere stimulation-induced enhancement of vision over proprioception (see also Martinaud, Besharati, Jenkinson, & Fotopoulou, 2017; Samad, Chung, & Shams, 2015). However, the specific mechanism by which touch enhances body ownership during LGVS remains unclear. Affective touch has been shown to elicit comparable feelings of pleasure, and neural activation in the posterior insula, when experienced directly on one’s own skin as well as when observed on someone else’s skin, i.e. vicarious affective touch (Morrison, Bjornsdotter, & Olausson, 2011; Morrison et al., 2011). Hence, the contribution of affective touch to body ownership may not only depend on its felt components but also on its *seen*, vicarious aspects. Thus, the vestibular system may differentially modulate such contribution according to the way touch is perceived.

The current work sought to address this outstanding ambiguity, by dissociating felt and seen touch during two RHI experiments with concurrent GVS. Conditions during which slow (affective) or fast (neutral) touch was applied only to the real hand without concurrent touch on the rubber hand (Experiment 1), and vice-versa (Experiment 2) were included. This was done to determine whether the enhancement of proprioceptive drift was driven by the *seen* or the felt component of affective touch.

Firstly, the aim was to replicate the effect presented in Chapter 2, showing that vision of a rubber hand during right-hemisphere vestibular stimulation leads to increased proprioceptive drifts towards the rubber hand, even without touch (“visual capture of proprioception”). Secondly, the aim was to explore whether vestibular stimulation would favour proprioception over vision when touch is felt but not seen, but favour vision over proprioception when touch is seen but not felt. It was hypothesised that administering affective touch only on participant’s own hand during LGVS would lead to smaller proprioceptive drifts (i.e. disruption of a previously induced “visual capture”), compared with neutral, fast touch, whilst affective touch on the rubber hand only would have opposite effects (i.e. enhancement of “visual capture”) due to the vicarious properties of affective touch. No changes in embodiment questionnaire scores were expected, since all touch conditions in the current study involved visuo-tactile asynchrony, consistently found not to elicit increased embodiment feelings (Costantini et al., 2016; Rohde, Di Luca, & Ernst, 2011).

3.2. Materials and methods

3.2.1. <u>Participants</u>

In Experiment 1, thirty-six, right-handed, healthy participants (23 females, age range=18-48 years, M=24.39; SD=6.01), were recruited via an institutional subject pool. Two participants were excluded from the analysis (they scored more than 2.5 SD away from the mean in more than 2 levels of the examined dependent variables). The final sample consisted of 34 participants (22 females; age range=18-48 years, M=24.24, SD=5.90). Thirty-seven new healthy participants (24 females, age range: 18-44, M=22.27; SD=5.35 years), partook in Experiment 2. Two participants were excluded (see above for criteria), with a final sample of 35 participants (22 females; age range=18-44, M=22.26; SD=5.44).

Exclusion criteria included psychiatric/neurological history, vestibular disturbances, pregnancy or metal plates in participants’ body and previous participation in GVS studies (due to the necessary deception involved in sham conditions). Both studies were approved by an institutional Ethics Committee and all participants gave written consent.

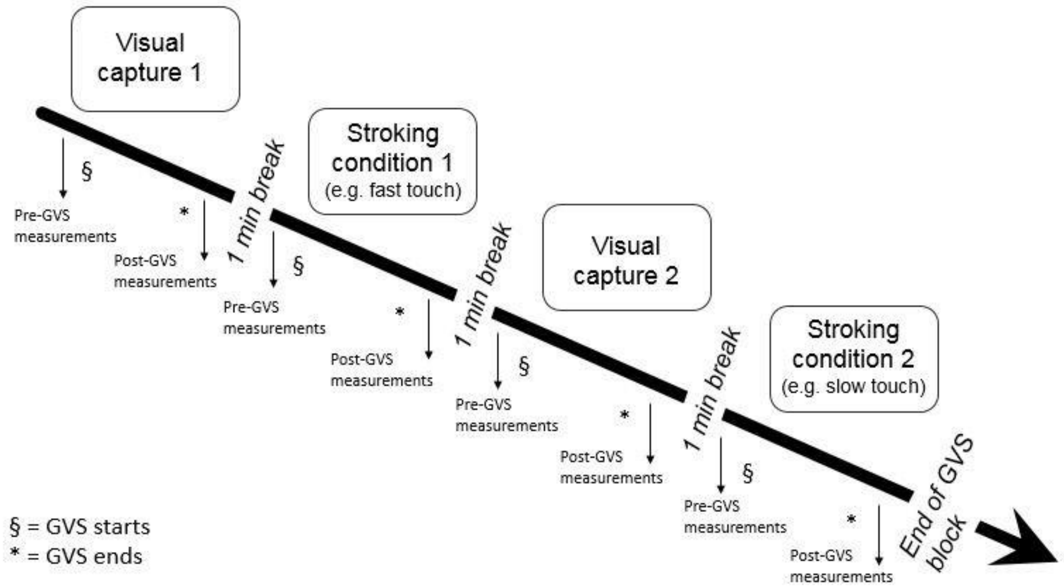
3.2.2. Experimental design

GVS (LGVS, RGVS, Sham) was applied during a RHI task in a within-subjects, block design, with the order of the three GVS blocks counterbalanced across the sample. Each of the 3 GVS blocks comprised two stroking conditions (slow, affective at 3 cm/s or fast, neutral at 18 cm/s touch; Crucianelli et al., 2013), administered in a counterbalanced order across participants), each preceded by a visual only condition (pure “visual capture”) (see Figure 3.1A and 3.1B). Stroking conditions (Figure 3.1C) were administered to explore whether touch on participant’s hand only during LGVS would reduce a previously induced visual capture, with the prediction that affective touch would have a further disrupting effect than neutral touch.

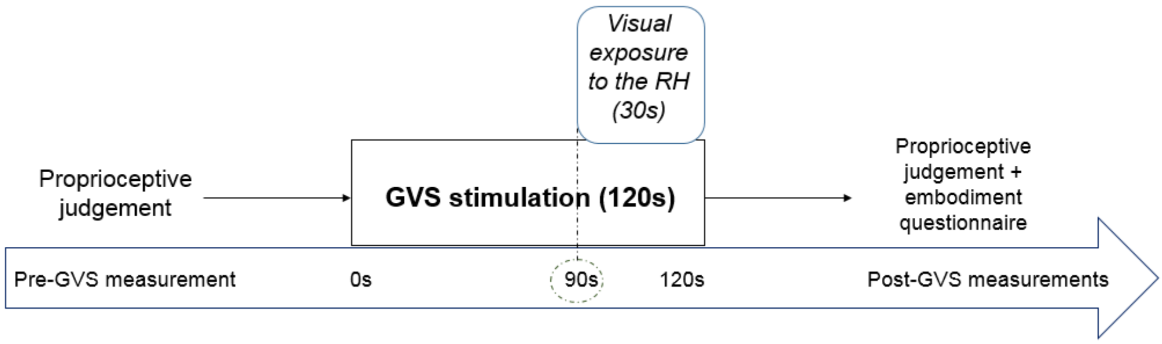
Two outcome measures were collected: proprioceptive drift (i.e. the perceived shift of the participant's hand towards the rubber hand, in centimetres) and an Embodiment Questionnaire. Proprioceptive drift was assessed pre-GVS and post-GVS for each condition and calculated by subtracting the post-GVS estimate of the left hand's location from the pre-GVS one (Fig. 3.1A and section 2.2. Materials and methods, Chapter 2 for a detailed description of the proprioceptive drift procedure). At the end of each condition, participants completed the Embodiment Questionnaire (Longo, Schuur, Kammers, Tsakiris, & Haggard, 2008), presented on a computer in a randomised order (see Appendix 1). The answers to each question were averaged in order to obtain an overall embodiment score per condition.

The design and procedure for Experiment 2 were identical to Experiment 1 except for the fact that touch was applied on the Rubber Hand only (instead of participant’s own hand) and that an enhancement, rather than a disruption of visual capture effects, was predicted.

A – Timeline of one GVS block (either LGVS, RGVS or Sham)



B – Visual capture (baseline)



C – Stroking conditions

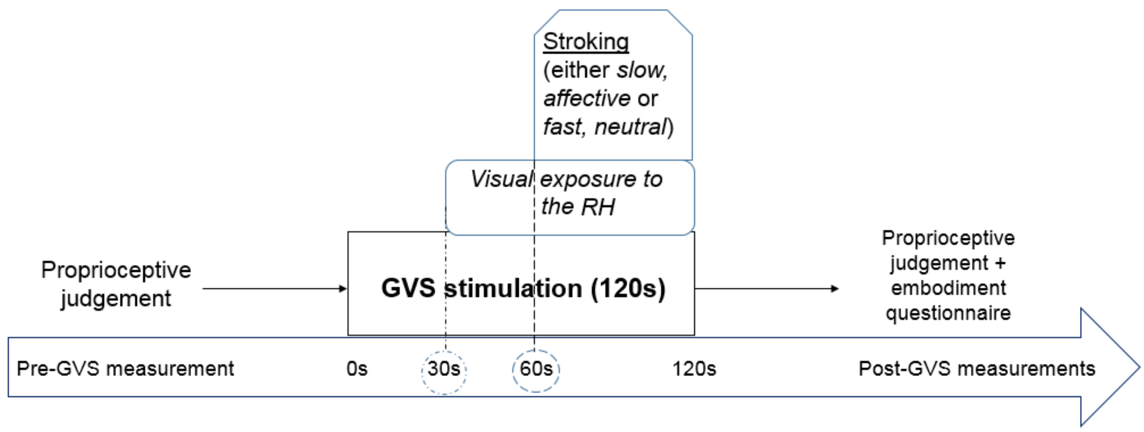


Figure 3.1. A) *Timeline of one prototypical GVS block.* At the beginning of each of the three GVS blocks (either LGVS, RGVS or Sham), participants undertook the first visual capture baseline, with measures taken before and after stimulation (see B for details). Subsequently, one of the two stroking conditions (see C for further details) was conducted in a counterbalanced order, with measures taken before and after stimulation. B) *Timeline of the visual capture baselines*. Before the visual capture condition started, participants performed a proprioceptive judgement (pre-GVS measurement). Immediately afterwards, the vestibular or sham stimulation commenced, lasting for 2 minutes, during which participants sat with their eyes open. During the last 30 seconds of vestibular or sham stimulation, the experimenter opened the box lid and instructed the participant to look at the rubber hand until told otherwise. After 120 seconds (total) stimulation the lid was closed, and participants immediately performed a second proprioceptive judgement and completed the embodiment questionnaire (post-GVS measurements). C) *Timeline of the stroking conditions*. Both stroking conditions (slow, affective or fast, neutral touch) followed the same structure. Participants made an initial (pre-GVS measurement) proprioceptive judgement, followed immediately by vestibular or sham stimulation lasting for 120 seconds. After 30 seconds of vestibular stimulation, the rubber hand was revealed by the experimenter and participants were asked to continuously look at it for 30 seconds. Then, the experimenter started stroking participants (experiment 1) or rubber hand's (experiment 2) forearm slowly or fast for 60 seconds, while the participant was asked to keep looking at the rubber hand. At the end of the 2 minutes, both tactile and vestibular stimulation ended, and participants were asked to perform a second proprioceptive judgement and answer the embodiment questionnaire (post-GVS measurements).

3.2.3. Experimental set-up and materials

Galvanic Vestibular Stimulation

A bipolar stimulation with fixed intensity (1mA) and duration (2 minutes per condition), delivered via a direct current stimulator (NeuroConn DC-stimulator, neuroCare Group GmbH, München, Germany), was implemented. The total amount of stimulation per GVS block was 8 minutes, with each experiment involving 24 minutes (including Sham) of non-continuous stimulation. Each GVS block was followed by a 20-minute break in order to minimise possible stimulation after-effects (Utz et al., 2010).

As described in Chapter 2, GVS was delivered via two 3x3cm carbon rubber electrodes fixed either on the participants' mastoid bones (LGVS and RGVS) or neck (Sham) using a rubber band. During LGVS (i.e. left-anodal/right-cathodal stimulation, affecting the right-hemisphere vestibular network), the anode was on the left mastoid process and the cathode on the right. During RGVS (i.e. left-cathodal/right-anodal, affecting both vestibular networks), the inverse configuration was used. During Sham, the electrodes were placed on the nape (~5 cm below the end of the mastoid processes).

Rubber Hand Illusion

The apparatus was the same as detailed in Chapter 2, with the exception of the distance between the rubber and participant's hand (see Figure 3.2). A black wooden box (62 cm x 43 cm x 26 cm), was positioned on a table 10 cm from the participant's torso. The box was divided in two equal halves by a black cardboard. Two spots were marked on the table with tape, one for the left rubber hand's index finger and one for the participant's left index finger. On the upper side of the box, there was a measuring tape, used to record proprioceptive drift and visible to the experimenter only. Participants wore a black cloth covering their shoulders and arms throughout the experiment in order to minimise the influence of external visual cues. Stroking was delivered on participant's forearm or on the rubber hand using a make-up brush (Natural hair Blush Brush, N°7, The Boots Company) by trained experimenters, expert in controlling for speed, pressure and uniformity of the applied touch (Crucianelli et al., 2013 and Krahé, Drabek, Paloyelis & Fotopoulou, 2016; Triscoli, Olausson, Sailer, Ignell, & Croy, 2013).

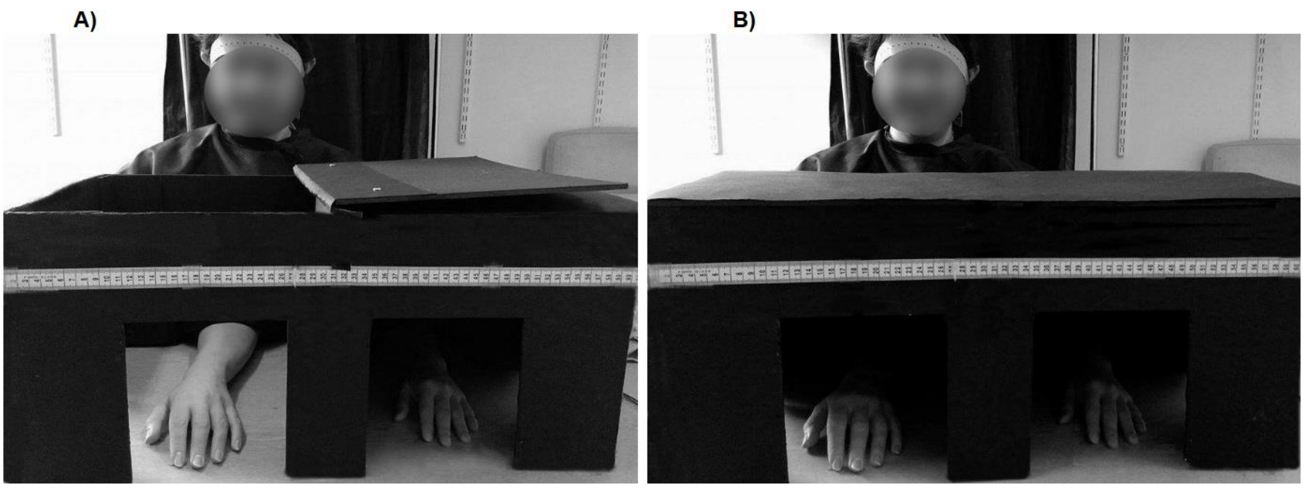


Figure 3.2. Participants were asked to place their left hand into the left half of the box, while the rubber hand was positioned in the right half, in line with the centre of participant's torso (distance between the rubber hand and the participant's hand=27.5 cm). Both the participant's and rubber hand's left index fingers were located on the marked spots. A) While the box was open, participants were asked to look inside and observe the rubber hand. B) Before and after each condition, with the box closed and covered by a black carton, participants had to perform a proprioceptive judgement (see Experimental procedure).

3.2.4. Experimental procedure

Participants positioned their left forearm in the box and the experimenter aligned their index finger with the rubber hand (hidden from participant's view). Each condition started with a proprioceptive judgement (pre-GVS measurement; see section 2.2. Materials and methods, Chapter 2), followed by GVS stimulation. Each proprioceptive judgement was obtained with the same procedure described in the previous chapter (as in Lloyd et al., 2013): the experimenter continuously moved the tip of a pen along the top of the closed box (~1 cm/s), starting either from the left or the right-hand side of the box. Participants were asked to verbally stop the experimenter when the pen reached the point vertically in line with the perceived position of the participant's left index finger. The experimenter recorded the actual position of participant's finger and the perceived position (pre-GVS measurement of proprioceptive drift: actual finger position minus perceived finger position). During the first condition (visual capture, Figure 3.1B), the rubber hand was only revealed after 1 minute and 30 seconds of stimulation and participants were asked to continuously look at the rubber hand for the last 30s. Participants then performed a second proprioceptive judgement with the box closed and completed the embodiment questionnaire (post-GVS measurements).

After the first visual capture condition, there was a one-minute break, during which participants were asked to move their left arm to reduce any cumulative effects. During the break (in Experiment 1 only), two adjacent 9x4cm areas were drawn with a washable marker on the participant's left forearm, to control for stroking pressure (i.e. by maintaining the brush within the marked borders) and habituation (i.e. by alternating between the two areas following each stroke) (Crucianelli et al., 2013). Subsequently, one of the two stroking conditions began (slow or fast velocity), with a pre-GVS proprioceptive judgement (Figure 3.1C). Immediately afterwards, the vestibular stimulation started and for the first 30s participants sat without performing any task. Then, the experimenter opened the lid and asked participants to focus on the rubber hand. After 30s of visual only exposure to the rubber hand, the experimenter started stroking the participants' forearm (Experiment 1) or the Rubber Hand (Experiment 2), either slowly at 3 cm/s (i.e. single touch=3s) or fast at 18 cm/s (i.e. single touch=0.5s) for 60s. Touch was always administered proximally to distally and each stroke was followed by a 1s pause. Participants were instructed to maintain their gaze on the rubber hand. After 120s, the vestibular-tactile stimulation ended, the post-GVS proprioceptive judgement was obtained and participants answered the embodiment questionnaire (post-GVS measurements). The second visual capture and stroking conditions of the block began after a one-minute break.

3.2.5. Manipulation checks

At the end of the experiment, with no vestibular stimulation applied, participants were asked to rate the pleasantness of two sets of stroking (at 3cm/s and 18cm/s) to ensure that they perceived slow touch as more pleasant than fast touch (Crucianelli et al., 2013; Crucianelli et al., 2018; Löken et al., 2009; Ponzo et al., 2018) as detailed in section 2.2. Materials and methods, Chapter 2.

In Experiment 2, an extra block of 6 trials (3 of which included administration of 2 slow, affective consecutive strokes and 3 entailing 2 fast, neutral strokes) was included in which participants were asked to rate pleasantness of strokes observed on the rubber hand only (the vicarious and actual stroking block were counterbalanced), to check whether they would rate the seen affective touch as more pleasant than the seen neutral touch (on the same 0-100 rating scale described above). This block of vicarious pleasantness ratings was counterbalanced across participants (i.e. half the participants did the vicarious rubber hand block first whilst the other half started with the actual touch block), in order to avoid the influence of perceiving touch on participants' own skin on vicarious ratings.

Finally, before debriefing, participants were asked to report any physical sensation associated with the vestibular stimulation and guess in which of the three configurations they thought they had received vestibular stimulation (as in the previous study – see Chapter 2).

3.2.6. Data analysis

As several of the proprioceptive drifts distributions were non normal in Experiment 1 and in Experiment 2, non-parametric analyses were run on the distributions of interest. When distributions were normal, repeated measures ANOVA, followed up by paired-samples t-tests (with Bonferroni corrections for multiple comparisons), was used. When data were not normally distributed, main effects were calculated by averaging the values of the proprioceptive drifts across one factor. Then, these values were compared using Friedman's ANOVA when the factor had three levels, followed up by Bonferroni-corrected (α=0.025) Wilcoxon signed rank tests and Wilcoxon signed rank test when the factor had only two levels. 2-way interactions were obtained by subtracting one level of the factor of interest from the other one and then analysing these with Friedman's ANOVA and Wilcoxon signed rank tests. In both experiments, to investigate subjective feelings of embodiment, the same analyses detailed above were run on the embodiment questionnaire scores.

In all the parametric analysis reported below, Greenhouse–Geisser corrections for repeated measures designs were used (in accordance with the guidelines outlined in Jennings, 1987) and the p values and effect sizes are reported accordingly. Cohen's d was used to compute effect sizes for paired-samples t-tests (see section 2.2.6.).

Data were analysed using the IBM Statistical Package for Social Sciences (SPSS) for Windows, version 25 (Armonk, NY) and plotted using the "*ggplot2*" package for R (Wickham, 2016).

3.3. Results

3.3.1. Experiment 1

Proprioceptive drifts

Visual capture

The first aim was to replicate previous findings of increased visual capture following LGVS (Chapter 2), with the hypothesis of a right-hemisphere-specific effect of vestibular stimulation on visual capture. To do so, a one-way repeated-measures ANOVA was run on the averages of the two visual capture conditions in the three GVS configurations to explore main effects of stimulation and a Wilcoxon signed-rank test to explore main effects of order (owing to lack of normality in one of the distributions). A significant main effect of stimulation ($F_{(2,66)}$= 6.110, p=0.004, η_p^2 =0.156, ε=.987), but no main effect of order (Z= 0.222, p=0.824, *r*=0.027), was found (Figure 3.3A). A Friedman's ANOVA was run to investigate the interaction between the two factors, which was not significant ($\chi^2_{(2)}$= .993, p=.609). Given that the averages of the two visual capture conditions were normal, planned contrasts paired sample t-tests (Bonferroni-corrected, α=0.025) were employed as a follow-up, revealing significantly greater proprioceptive drift following LGVS compared to Sham (LGVS: M=1.75 cm, SD=2.62; Sham: M=0.15 cm, SD=2.16; LGVS vs Sham: $t_{(33)}$=3.410 p=.002 *d*=0.59) and RGVS (RGVS: M=0.50 cm, SD=2.10; LGVS vs RGVS: $t_{(33)}$= 2.459 p=.019 d=0.42) (Figure 3.3B).

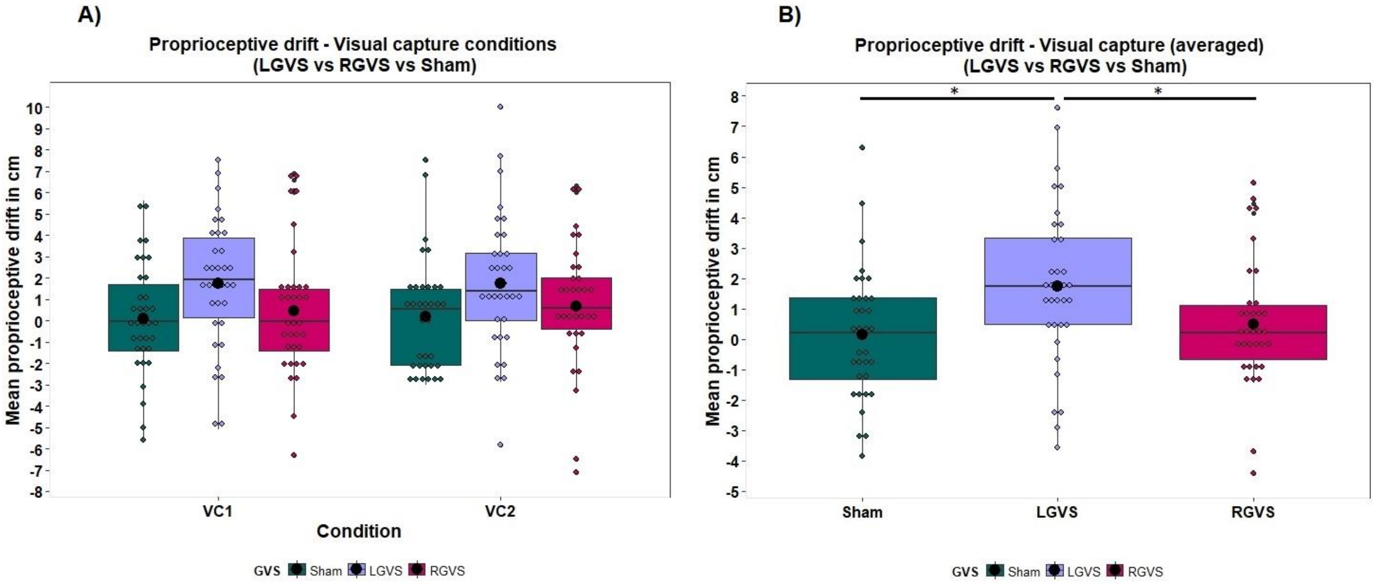


Figure 3.3. Mean values of the proprioceptive drift measured in cm in Sham, LGVS and RGVS. A) Visual capture conditions 1 and 2 as performed by the participants during the block; B) visual capture baselines averaged. *= p<0.05; Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR).

Stroking conditions – raw proprioceptive drifts

In order to examine the effects of vestibular stimulation on proprioceptive drifts following stroking, a Friedman's ANOVA on the averaged values of the two stroking conditions was run, which did not show any difference between the three GVS configurations ($\chi^2_{(2)}$ =3.173, p=0.205). Then, proprioceptive drift values across the different GVS configurations were averaged and a Wilcoxon signed-rank test was used in order to check for differences due to the stroking conditions, which did not yield significant results (Z=1.402, p=0.161, *r*=0.17). The interaction between the two factors was tested by subtracting the values of fast touch from the slow touch ones within each GVS configuration and then comparing the differentials via a Friedman's ANOVA, which did not reveal a difference between the conditions ($\chi^2_{(2)}$ =1.111, p=0.574; Figure 3.4).

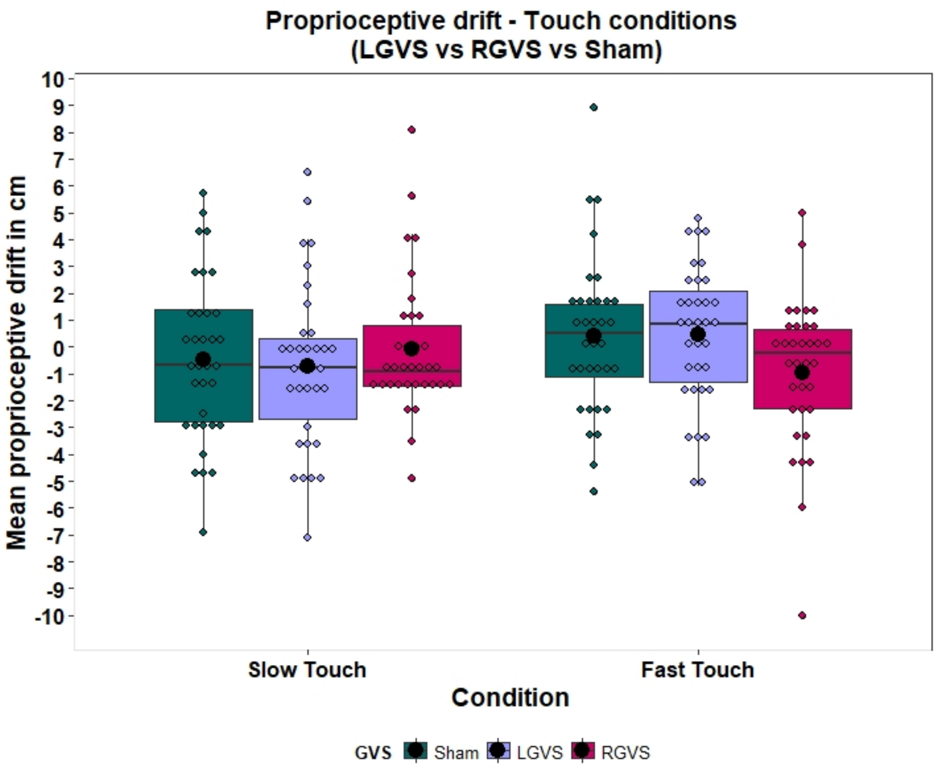


Figure 3.4. Mean values of the proprioceptive drifts in the different stroking conditions (slow, affective touch and fast, neutral touch) measured in cm and in the three different vestibular configurations (Sham, LGVS and RGVS). Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR).

Disruption of Visual Capture – differential scores

To examine the effects of touch in disrupting a previously induced visual capture, differential scores were calculated by subtracting the proprioceptive drift score obtained during the stroking condition from its immediately preceding visual capture baseline and analysed via a repeated measures ANOVA (followed by Bonferroni corrected paired samples t-tests). A 3 x 2 repeated measures ANOVA on the differential scores revealed a main effect of Stimulation ($F_{(2,66)}$=5.054, p=.011, η_p^2=.133, ε=.926), but no main effect of Velocity ($F_{(1,33)}$=.199, p=.659, η_p^2=.006) and no significant two-way interactions (Figure 3.5); Vestibular Simulation*Velocity ($F_{(2,66)}$=2.167, p=.128, η_p^2=.062, ε=.904). Post-hoc paired samples t-tests comparing each type of GVS regardless of touch velocity (Bonferroni-corrected, α=0.0167) indicated that LGVS led to significantly greater disruption of visual capture (i.e. smaller proprioceptive drifts) in comparison with Sham (LGVS: M=-1.90 cm, SD=2.45; Sham: M=-0.18 cm, SD=2.02; $t_{(33)}$=3.591 p=.001 *d*=0.62) but not RGVS (RGVS: M=-1.02 cm, SD=2.75; $t_{(33)}$=-1.453 p=.156 *d*=0.25), with no difference between RGVS and Sham ($t_{(33)}$=-1.583 p=.123 *d*=0.27).

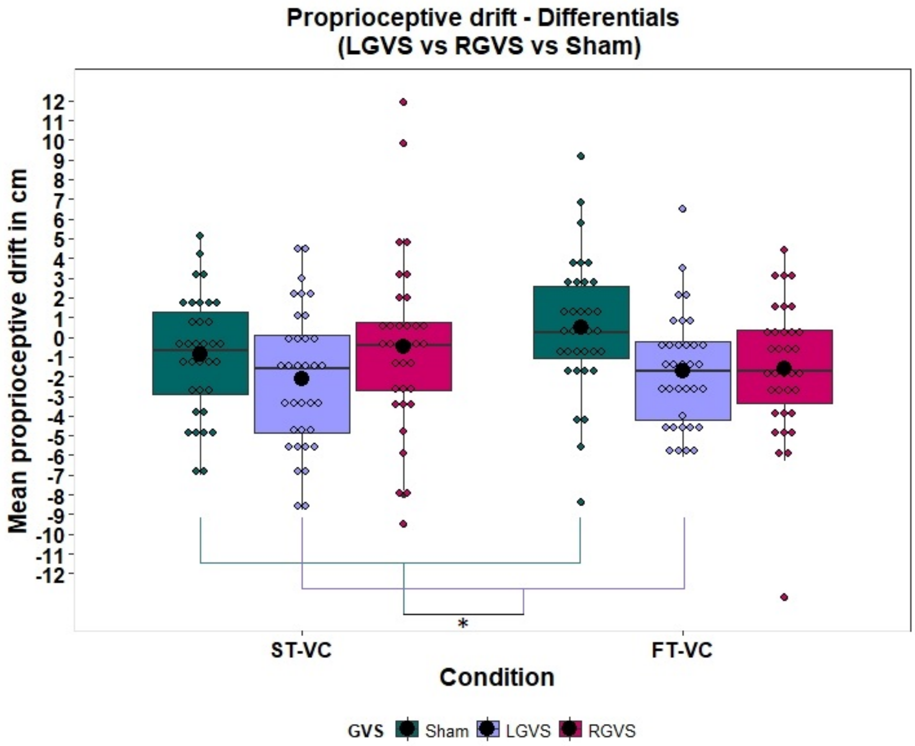


Figure 3.5. Mean values of the differential scores obtained from the subtraction of the proprioceptive drift values of the visual capture baselines from the stroking conditions' ones measured in cm and in the three different vestibular configurations (Sham, LGVS and RGVS). ST= slow, affective touch; FT= Fast, neutral touch. *= p<0.05; Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR).

Embodiment questionnaire values

Visual capture

As for the proprioceptive drift values, to investigate the effects of vestibular stimulation on embodiment, a 3 (GVS: Sham vs LGVS vs RGVS) x 2 (Order: Visual Capture First vs Visual Capture Second) repeated measures ANOVA was conducted on the questionnaire values of the two visual capture conditions. None of the main effects or interactions were significant (stimulation: $F_{(2,66)} = 2.196$, $p = .119$, $\eta p^2 = .062$, $\varepsilon = .777$; order: $F_{(1,33)} = .011$, $p = .918$, $\eta p^2 = .000$; Stimulation*Order: $F_{(2,66)} = 2.002$, $p = .143$, $\eta p^2 = .057$, $\varepsilon = .789$).

Stroking conditions – raw values

To explore the effects of vestibular stimulation on embodiment following slow, affective touch and fast, neutral touch, a 3 (GVS: Sham vs LGVS vs RGVS) x 2 (Velocity: Slow touch vs Fast touch) repeated measures ANOVA was run on the questionnaire values of the two stroking conditions. None of the main effects or interactions were significant (stimulation: $F_{(2,66)}=1.929$, $p=.153$, $\eta p^2=.055$, $\varepsilon =.999$; velocity: $F_{(1,33)}=.515$, $p =.478$, $\eta p^2 =.015$; Stimulation*Velocity: $F_{(2,66)}=.179$, $p =.874$, $\eta p^2 =.005$, $\varepsilon = .935$).

Disruption of Visual Capture – differential scores

To investigate the effects of vestibular stimulation and touch in disrupting visual capture, a differential value was calculated by subtracting the scores obtained following each visual capture condition from the ones obtained after the subsequent stroking condition. A 3 (GVS: LGVS vs RGVS vs Sham) x 2 (velocity: slow touch vs fast touch) repeated measures ANOVA was run on these values, revealing no main effect or interaction (stimulation: $F_{(2,66)} =1.073$, $p =.348$, $\eta p^2 = .031$, $\varepsilon = .866$; velocity: $F_{(1,33)} = 2.099$, $p = .157$, $\eta p^2 = .060$; Stimulation*Velocity: $F_{(2,66)} = .120$, $p = .887$, $\eta p^2 = .004$, $\varepsilon = .865$; Table 3.1).

Table 3.1. Descriptive statistics of embodiment questionnaire's average values in the different conditions.

Conditions	**Sham** Mean *(SD)*	**LGVS** Mean *(SD)*	**RGVS** Mean *(SD)*
Visual Capture (first)	*-0.37 (1.57)*	-0.56 *(1.73)*	-0.05 *(1.56)*
Visual Capture (second)	-0.54 *(1.61)*	-0.30 *(1.71)*	-0.13 *(1.72)*

Visual Capture (average)	-0.45 *(1.54)*	-0.43 *(1.68)*	-0.10 *(1.54)*
Slow (affective) touch	-0.36 *(1.63)*	-0.53 *(1.75)*	-0.22 (1.65*)*
Fast (neutral) touch	-0.30 *(1.60)*	-0.41 *(1.67)*	-0.19 *(1.51)*
Differential values (ST-VC)	0.05 *(0.75)*	-0.08 *(0.82)*	-0.18 *(0.89)*
Differential values (FT-VC)	0.20 *(0.79)*	0.01 *(0.81)*	0.02 *(0.85)*

Manipulation checks

Pleasantness task

A 2 (velocity: slow touch vs. fast touch) x 2 (site: forearm vs. palm of the hand) repeated measures ANOVA on the pleasantness ratings was run revealing that slow touch was perceived as more pleasant than fast touch (velocity: $F_{(1, 33)}$ = 38.205, p < 0.001, ηp^2 = .537; slow touch: M = 78.28, SD = 14.69; fast touch: M = 62.75; SD = 18.85) with no difference between the two sites (site: $F_{(1, 33)}$ = .252, p = .619, ηp^2 = .008) and no interaction between velocity and site ($F_{(1, 33)}$ = 1.268, p = .268, ηp^2 = .037). Given that slow touch ratings on the palm were not normally distributed (S-W: .924, p=.021), main effects and differential scores (using the methods described above in the data analysis section) were calculated and subsequently used to conduct non-parametric analysis with Wilcoxon-signed rank tests. The results confirmed the findings of the parametric analysis (velocity: Z =- 4.779, p = .000; slow touch: Mdn = 81.67, IQR = 20; fast touch: Mdn = 64.58; IQR = 22.46; Site: Z = .206, p = .837; Velocity*Site: Z = .535, p = .593)

Vestibular sensations

At the end of the main experiment, participants were asked to report any physical sensation associated with the stimulation in order to identify any noticeable vestibular-induced sensations between conditions. The majority of the sample (32/35) reported a tingling or itching sensation under the patches that none of the participants described as painful. About 2/3 of the sample (23/36 participants) reported vestibular-related sensations (dizziness, vertigo or loss of balance). This suggests that a 1mA stimulation has been able to trigger distinctive vestibular sensations in two thirds of the sample, in line with previous findings (see 2.3. Results, Chapter 2).

In order to control for the role of Sham stimulation as a placebo-like intervention, participants were asked to guess in which of the 3 GVS configurations they thought to have received a vestibular system's stimulation, specifying that the answer might have been all of them, 2 or 1. The majority of them guessed correctly about LGVS and RGVS (31/36 and 30/36, respectively), whereas two thirds of the sample reported Sham as a vestibular stimulation (24/36) when directly invited to compare it with the other 2 GVS configurations. A significant difference between these frequencies was found using a Likelihood Ratio Chi-square analysis ($\chi^2_{(2)} = 28.778$, $p<0.001$; $\phi_c <0.001$), suggesting that the three stimulation did not appear to have the same effects to the subjests.

3.3.2. Experiment 2

Proprioceptive drifts

Visual capture

A Friedman's ANOVA performed on the proprioceptive drift values of the two visual capture conditions (Figure 3.6A) showed a main effect of stimulation ($\chi^2_{(2)}=8.647$, $p=0.013$) and a Wilcoxon signed-rank test ($Z= 2.039$, $p=0.041$) showed a main effect of order, with the first visual capture condition being higher than the second one (First: *Mdn*=0.67, IQR= 1.77; Second: *Mdn*=0.5, IQR= 1.80), but no interaction between the factors ($\chi^2_{(2)}=.844$, $p=0.656$). To follow up the significant main effect of stimulation, Wilcoxon signed-rank tests ($\alpha=0.025$) were used, which were not significant (LGVS: Median=1.25, IQR= 1.85; Sham: Median=0.75 , IQR= 1.4; LGVS vs Sham $Z=.949$ $p=0.342$; LGVS vs RGVS: RGVS: Median=0.20; IQR= 2.25; LGVS vs RGVS: $Z=1.950$, $p=0.051$) (Figure 3.6B).

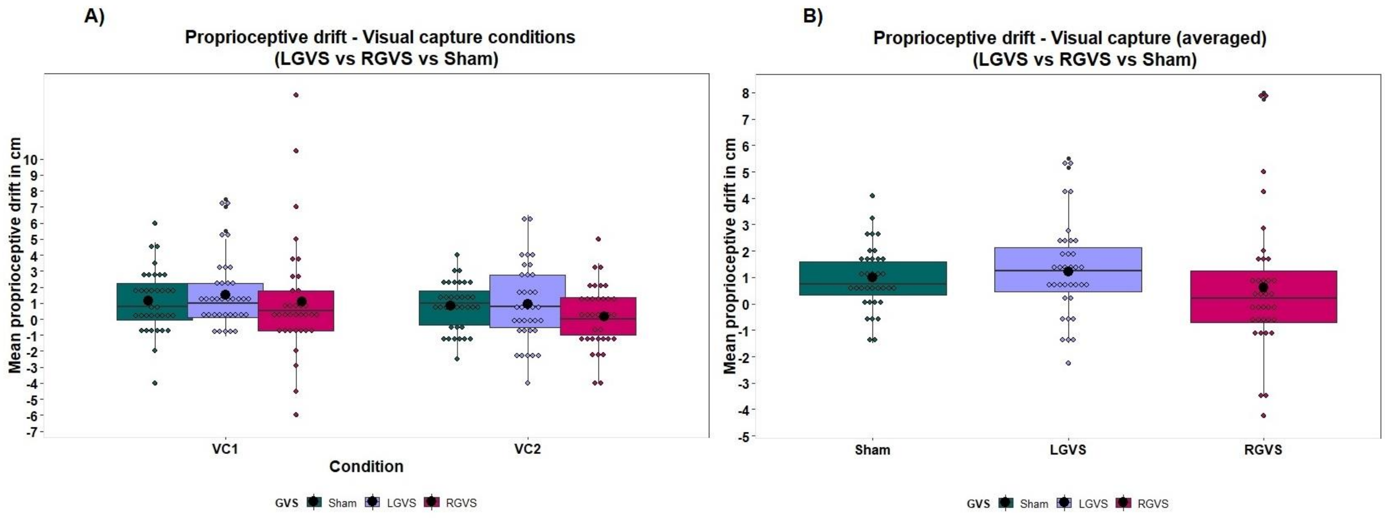


Figure 3.6. Mean values of the proprioceptive drift measured in cm in Sham, LGVS and RGVS. A) Visual capture conditions 1 and 2 as performed by the participants during the block; B) visual capture baselines averaged. *= p<0.05; Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR).

Visual capture (combined)

To check whether increasing the sample size to include data from both experiments (N=69) would lead to the same results outlined in Experiment 1 and (partly) replicated in Experiment 2, a Friedman's ANOVA was run on the average of the two visual capture conditions, revealing a main effect of stimulation ($\chi^2_{(2)}$ =19.737, p<0.0001, Figure 3.7), further investigate via post—hoc Wilcoxon signed-rank test (Bonferroni corrected, α= 0.025). Such comparisons showed that LGVS led to greater proprioceptive drifts in comparison with both Sham (Z= 3.121; p=0.002, *r*=0.27) and RGVS (Z= 2.822; p=0.005, *r*=0.24). There were no main effect of order (Z=1.193; p=0.233, *r*=0.10) or interaction ($\chi^2_{(2)}$ =.007, p=.996).

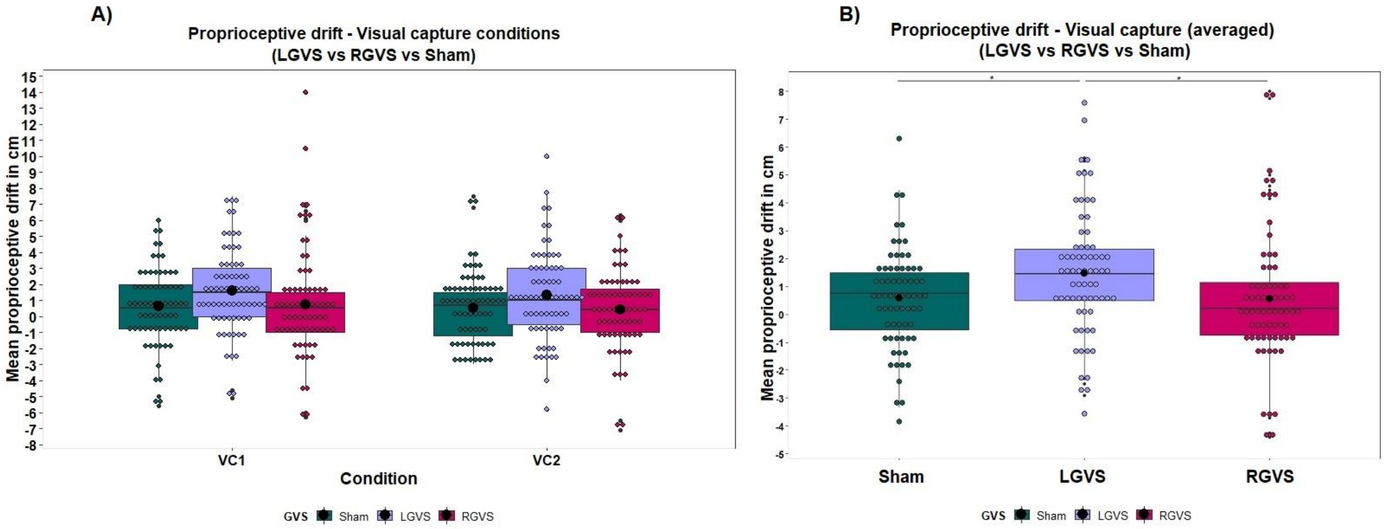


Figure 3.7. Mean values of the proprioceptive drift measured in cm in Sham, LGVS and RGVS. A) Visual capture conditions 1 and 2 as performed by the participants during the block for both experiment 1 and 2; B) visual capture baselines averaged. *= p<0.05; Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR).

Visual capture of vicarious touch

In order to examine the effects of vestibular stimulation on proprioceptive drifts following seen touch (Figure 3.8), a Friedman's ANOVA was conducted on the averaged values of the two stroking conditions, which showed a main effect of stimulation ($\chi^2_{(2)}$ = 7.667, p=0.022). To explore this main effect of stimulation, post-hoc Wilcoxon signed-rank tests were run (Bonferroni corrected, α=0.0167), confirming that LGVS increased proprioceptive drifts in comparison with Sham (LGVS: *Mdn*=0.80 , IQR=2.5; Sham: *Mdn*=0.65, IQR=2; Z=2.786, p= 0.005, *r*=0.33) but not RGVS (RGVS: *Mdn*=0.65, IQR=1.85; Z=1.223, p=0.221, *r*=0.15), with no difference between Sham and RGVS (Z=1.172 , p=0.241, *r*=0.14) and regardless of the type of touch. No effect of order (Z=0.118, p=0.732, *r*=0.01) or interaction ($\chi^2_{(2)}$ = 2.162, p=0.339) were significant.

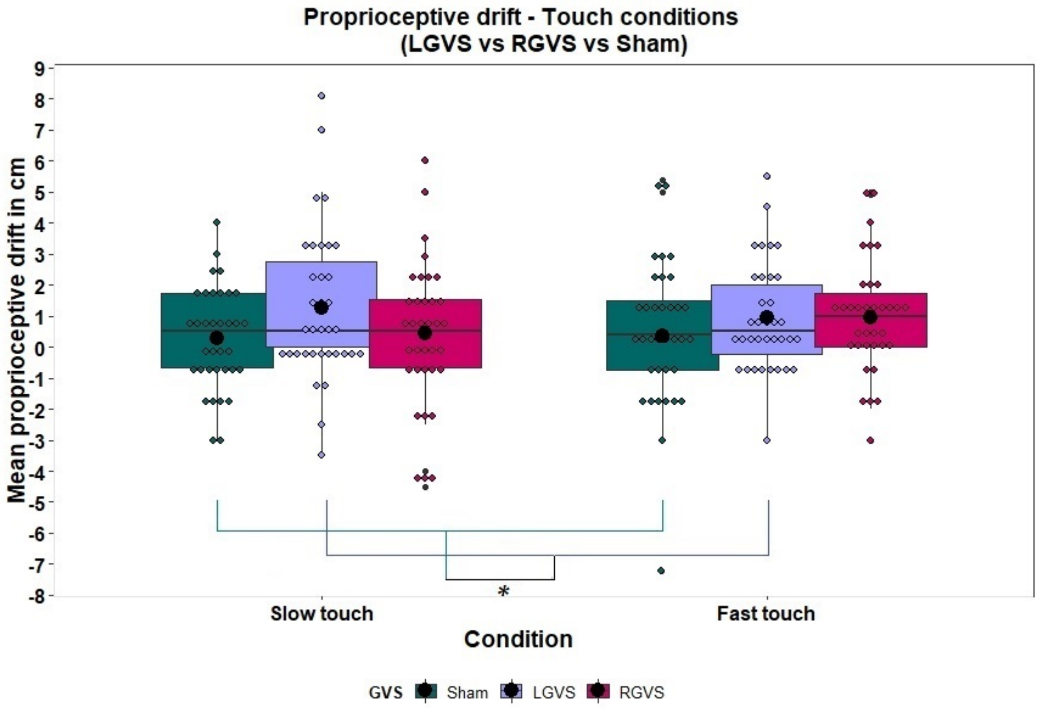


Figure 3.8. Mean values of the proprioceptive drifts in the different stroking conditions (slow, affective touch and fast, neutral touch) measured in cm and in the three different vestibular configurations (Sham, LGVS and RGVS). Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR). *p <0.05

Embodiment questionnaire values

Visual capture

To explore the effects of vestibular stimulation on embodiment, a 3 (GVS: Sham vs LGVS vs RGVS) x 2 (Order: Visual Capture First vs Visual Capture Second) repeated measures ANOVA was conducted on the questionnaire values of the two visual capture conditions. None of the main effects or interactions were significant (stimulation: $F_{(2,68)}$ = .513, p = .601, ηp^2 = .015, ε = .983; order: $F_{(1,34)}$ = .208, p = .652, ηp^2 = .006; Stimulation*Order: $F_{(2,68)}$ = .171, p = .843, ηp^2 = .005, ε = .899).

Stroking conditions

To explore the effects of vestibular stimulation on embodiment following slow, affective and fast, neutral vicarious touch on the rubber hand, a 3 (GVS: Sham vs LGVS vs RGVS) x 2 (Velocity: Slow touch vs Fast touch) repeated measures ANOVA was run on the questionnaire values of the two stroking conditions, revealing no significant main effects nor interactions (stimulation: $F_{(2,68)}$ = 1.244, p

= .295, ηp^2 = .035, ε = .985; velocity: $F_{(1,34)}$ = .399, p = .532, ηp^2 = .012; Stimulation*Velocity: $F_{(2,68)}$ = .394, p = .676, ηp^2 = .011, ε = .944; Table 3.2).

Table 3.2. Descriptive statistics of embodiment questionnaire's average values in the different conditions.

Conditions	**Sham** Mean *(SD)*	**LGVS** Mean *(SD)*	**RGVS** Mean *(SD)*
Visual Capture (first)	-.15 *(1.57)*	-*.08 (1.77)*	-.03 *(1.72)*
Visual Capture (second)	-.11 *(1.70)*	-.09 *(1.68)*	-.07 *(1.65)*
Visual Capture (average)	-.13 *(1.55)*	-.09 *(1.69)*	-.02 *(1.65)*
Slow (affective) touch	-.06 *(1.60)*	.12 *(1.62)*	-.04 (1.75*)*
Fast (neutral) touch	-.12 *(1.63)*	-.01 *(1.75)*	-.03 *(1.78)*

<u>Pleasantness task</u>

On the actual touch block, a 2 (velocity: slow touch vs. fast touch) x 2 (site: forearm vs. palm of the hand) repeated measures ANOVA on the pleasantness ratings was conducted, which confirmed that slow touch was perceived as more pleasant than fast touch (velocity: $F_{(1, 34)}$ = 24.518, p < 0.001, ηp^2 = .491; slow touch: M = 70.67, SD = 14.56; fast touch: M = 61.5, SD = 15.26) with no difference between the two sites (site: $F_{(1, 34)}$ = 2.371, p = .133, ηp^2 = .065) and no interaction between velocity and site ($F_{(1, 34)}$ = .036, p = .850, ηp^2 = .001). A paired-samples t-test was run on the vicarious rubber hand touch block, revealing that participants rated slow touch as more pleasant than fast touch (slow touch: M = 69.4, SD = 18.84; fast touch: M = 58.78, SD = 15.99; $t_{(34)}$ = 5.154, p < 0.001 d=1.25) even when touch was only seen but not felt.

Finally, a 2 (Felt touch: slow vs fast) x 2 (Vicarious touch: slow vs fast) repeated-measures ANOVA was run to check differences between slow and fast touch in the separate felt and vicarious block. In this analysis, values were averaged across sites for the felt block as there were no differences between forearm and palm. Results revealed a main effect of velocity ($F_{(1, 34)}$ = 28.407, p <

0.001, ηp^2 = .455; slow touch: *M* = 70.03, *SD* = 16.73; fast touch: *M* = 60.15; *SD* = 15.58) but no differences between the blocks (type of block: $F_{(1, 34)}$ = .445, *p* = .509, ηp^2 = .013) and no interaction between velocity and type of block ($F_{(1, 34)}$ = 1.370, *p* = .250, ηp^2 = .039). The addition of the vicarious Rubber Hand block confirmed that, as suggested by previous research, participants perceived touch administered on the rubber hand significantly more pleasant when it was slow compared with fast. Additionally, the comparison between the pleasantness reported for the felt and the seen touch did not differ and only highlighted that participants rated affective rather than neutral touch as more pleasant regardless of whether it was felt or seen (Figure 3.9).

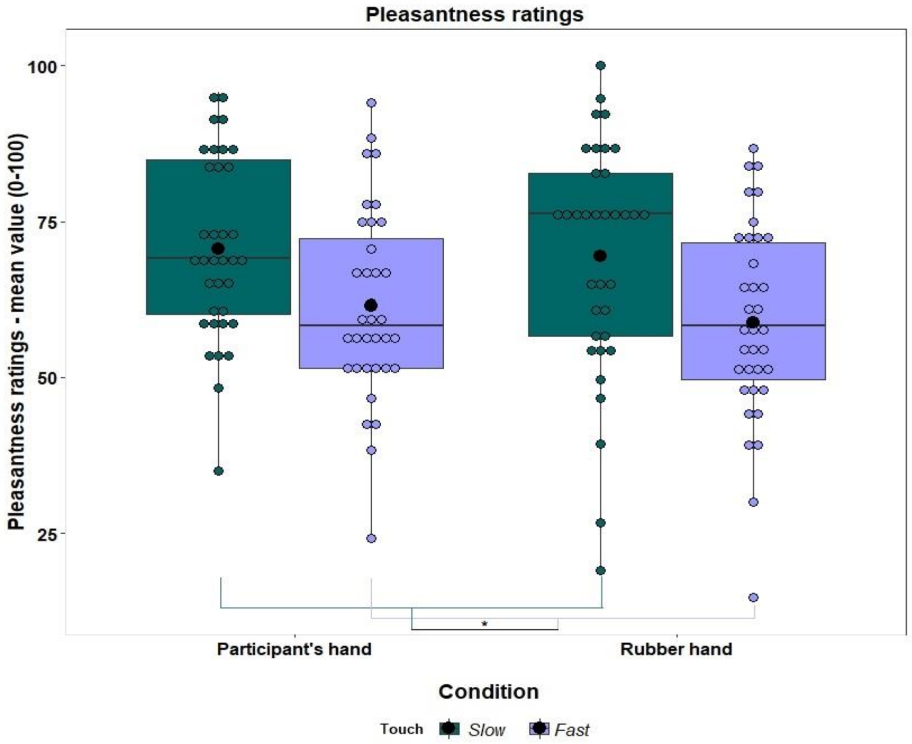


Figure 3.9. Mean values of the pleasantness ratings in the felt vs seen touch conditions according to the touch velocity (slow, affective vs fast, neutral). Ratings were on a scale from 0 "Not at all pleasant" to 100 "Extremely pleasant". Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR). *p <0.001.

Vestibular sensations

At the end of the main experiment, participants were asked to report any physical sensation associated with the stimulation in order to identify any noticeable vestibular-induced sensations between conditions. The majority of the sample (25/35) reported a tingling or itching sensation under the patches that none of the participants described as painful. About 1/3 of the sample (14/36 participants) reported vestibular-related sensations (dizziness, vertigo or loss of balance), suggesting that a 1mA stimulation has been able to trigger distinctive vestibular sensations in 1/3 of the sample, partially in line with previous findings.

To control for the role of Sham as a placebo-like intervention, participants were asked to guess in which of the 3 GVS configurations they thought to have received a vestibular stimulation, specifying that the answer might have been all of them, 2 or 1. The majority guessed correctly about LGVS and RGVS (28/35 and 19/35, respectively), whereas approximately 1/3 of the sample reported Sham as a vestibular stimulation (13/35) when directly invited to compare it with the other 2 GVS configurations. A non-significant trend for a difference between these frequencies was found using a Likelihood Ratio Chi-square analysis ($\chi^2_{(2)} = 5.541$, $p=0.063$; $\phi_c = 0.70$).

3.4. Discussion

In the current study, GVS was implemented during an adapted RHI to explore vestibular contributions to multisensory integration aiming to i) replicate the findings presented in the previous chapter, on visual capture of proprioception (i.e. LGVS leads to greater proprioceptive drifts towards the rubber hand even without touch) and ii) investigate the role of right-hemisphere vestibular stimulation in sensory conflict (i.e. touch felt but not seen and vice-versa). Specifically, it was hypothesised that i) LGVS would lead to smaller proprioceptive drifts during tactile stimulation of participants' skin (i.e. touch felt but not seen) in comparison with RGVS and Sham ("disruption of visual capture"), but in favour of vision when touch is seen but not felt ("visual capture of vicarious touch") and ii) that both effects would be enhanced by applying affective, slow touch in comparison with neutral, fast touch.

In Experiment 1, previous findings were successfully replicated: LGVS led to greater visual capture in comparison with Sham and RGVS during mere observation of a rubber hand, i.e. participants showed significantly greater proprioceptive drift towards the rubber hand following right-hemisphere vestibular stimulation. In Experiment 2, a similar, yet milder, pattern was found: LGVS led to greater proprioceptive drifts but not significantly more than RGVS and Sham. This reduction of the effect in Experiment 2 might be due to the different experimental manipulations (felt vs seen touch in the conditions following the visual capture ones) and/or higher individual variability in the sample. However, these findings suggest that stimulation of the right vestibular network may modulate multisensory integration by increasing the weight of vision over proprioception in a visuo-proprioceptive conflict. As argued in Chapter 2, such visual capture effect may be due to a temporary disruption of participants' body representation (Fink et al., 2003; Harris & Hoover, 2015). The vestibular system may reduce the relative weight of somatosensory stimuli whilst increasing the relevance of exteroceptive ones in order to allow the resolution of perceptual ambiguity (Zeller, Litvak, Friston, & Classen, 2015). This would be consistent with the visual capture effects observed in stroke patients with right peri-sylvian lesions (Martinaud et al., 2017) and with reports of symptoms remission following right-hemisphere vestibular stimulation in patients with dis-ownership feelings (Edoardo Bisiach, Rusconi, & Vallar, 1991; Rode et al., 1992).

The second main finding of the present study is that vestibular stimulation modulates visuo-tactile conflicts according to whether the touch is felt or seen. In Experiment 1, when touch was applied to participant's own hand (without concomitant tactile stimulation of the rubber hand), proprioceptive drifts were significantly smaller during LGVS in comparison with Sham stimulation (but not RGVS). In Experiment 2, seen vicarious touch delivered to the rubber hand during LGVS led to increased proprioceptive drifts in comparison with Sham (but nor RGVS). Hence, vestibular signals (not necessarily in a lateralised fashion) may be dynamically contributing to multisensory integration according to the contextual relevance of the different modalities involved. This may explain some of the previous conflicting findings in vestibular stimulation studies, with some authors reporting proprioceptive enhancement over vision during LGVS and others suggesting the opposite pattern, with vestibular stimulation increasing vision over proprioception (e.g. Lopez et al., 2010; Ponzo et al., 2018 vs Ferrè et al., 2015; Pavlidou, Ferrè, & Lopez, 2018; Pfeiffer, Serino, & Blanke, 2014). When a rubber hand is in a plausible position in space, allowing its integration in participants' body representation (as in our previous and current studies), vestibular signals may contribute to solve perceptual ambiguity by weighting visual signals more than proprioceptive ones. Conversely, when a third sensory modality (i.e. touch) is introduced in an asymmetric fashion, such that incorporation of the rubber hand into participant's body representation would generate additional conflict (i.e. feeling touch that is not seen leads to increased perceptual ambiguity), vestibular signals do not favour visual cues over proprioceptive ones. However, when touch is seen but not felt (i.e. it is vicariously perceived via vision), vestibular signals seem to favour vision, rather than proprioception, to reduce sensory conflict. In line with neuroimaging findings, suggesting an overlap between areas of the vestibular network and multisensory integration of exteroceptive and proprioceptive signals (Lopez et al., 2012; zu Eulenburg et al., 2012), it can be hypothesised that vestibular processing in the right temporo-parietal and insular areas may balance sensory inputs in order to solve ambiguous perceptual situations. Such weighting mechanism could be responsible for the enhancement or reduction of visual cues in visuo-proprioceptive-tactile conflicts according to whether the conflict between the different sensory sources can or cannot be solved via visual dominance over proprioception.

Finally, no differences between affective and neutral touch in disrupting nor enhancing visual capture were found. This contradicts the hypothesis that the results observed in the study presented in the previous chapter may be due to either the felt or the vicarious properties of affective touch. One possibility is that these previous findings, rather than representing vestibular enhancement of felt or seen components of affective touch, may be explained by the presence of both, delivered in synchrony (Filippetti, Kirsch, Crucianelli, & Fotopoulou, 2019b). Future studies should investigate differential contributions of visuo-tactile versus vicarious and tactile only affective touch to multisensory integration.

The current study also had some methodological limitations. One of the aim was to examine whether GVS effects were hemispheric specific. However, without comparing LGVS with RGVS within-subjects such conclusion could not be made. Hence, two different experiments using all three GVS configurations, including RGVS were devised. This configuration resulted in an experimental session lasting 2.5 hours. Thus, in order to avoid fatiguing participants, which might lead to a loss of focus and unreliable data, it was not possible to include further conditions to compare the felt and seen touch within-subjects. However, future studies could look at a within-subjects design, perhaps with experimental sessions spread over two consecutive days.

Additionally, the GVS device implemented in this and the previous study did not allow for fully blinded procedures. In order to reduce experimenter bias, the main experimenter who participated in the study design did not collect the data herself but was supervising data collection after having extensively trained the assisting experimenters (one for each study). Future research could employ the same design with a more sophisticated device, allowing for double-blinding.

Finally, GVS may have applications for the treatment of certain clinical conditions. For example, vestibular stimulation has been found to temporarily improve symptoms such as unilateral neglect (Saj, Honoré, & Rousseaux, 2006), anosognosia for hemiplegia (i.e. unawareness of paralysis) and somatoparaphrenia (i.e. limb disownership) (Edoardo Bisiach et al., 1991; Cappa, Sterzi, Vallar, & Bisiach, 1987). Vestibular stimulation has also been shown to reduce painful sensations in healthy volunteers (Ferre, Haggard, Bottini, & Iannetti, 2015) as well as in a single case of chronic pain following stroke (Spitoni et al., 2016). As such, future studies might explore the possible use of galvanic vestibular stimulation in the treatment of stroke-induced changes in awareness, or the reduction of chronic pain, both of which currently lack an established, effective treatment (Turk, 2002; Turk & Okifuji, 2002). For example, chronic pain might be reduced by shifting patients' attention away from the felt pain and towards more pleasurable visual experiences. Based on the present experimental findings, GVS might provide the mechanism by which this increase in the weight of visual information over proprioception could be achieved. Further clinical and experimental studies are needed to explore these ideas.

To conclude, further evidence that the vestibular system may dynamically contribute to multisensory integration by weighting different sensory modalities according to the context in which they are experienced has been provided. In the current study, vestibular stimulation led to an increased dominance of visual information over proprioception during a visuo-proprioceptive conflict as well as during vicarious touch conditions (i.e. when touch was seen on the rubber hand but not felt on participant's hand), but a decrease of visual capture effects when touch was only felt on participant's hand but not seen on the rubber hand. These findings suggest that the vestibular network may modulate multisensory experience in a dynamic fashion in an attempt to solve sensory conflicts.

In the next Chapter, alternative hypotheses for the results presented in the first two experimental studies will be taken into consideration, in order to confirm that the vestibular system modulates aspects of body representation at the net of other lower-level potential explanations.

Chapter 4

Vestibular Modulation of Body Representation: The Role of Proprioception and Space Perception in Visual Capture

4.1. Introduction

As outlined in Chapter 2, (see section 2.4. Discussion), the vestibular system contributes to shaping the way we perceive our own body, as well as our surroundings, by dynamically balancing different sensory modalities according to the context in which we experience them. Findings from the studies presented in the previous chapters showed how left-anodal/right-cathodal (i.e. LGVS) vestibular stimulation, modulates multisensory integration processes during sensory conflict (i.e. when visual and proprioceptive information mismatch) by increasing the reliability of either vision or proprioception according to contextual relevance (see Chapters 2-3 and Ponzo et al., 2018; 2019). These results were explained in terms of a temporary disruption of participants' body representation in the egocentric reference frame (Fink et al., 2003; Harris & Hoover, 2015): the vestibular system may shift the focus from a body-centred perspective to a world-based one. This mechanism could account for why LGVS led to a decreased weight of somatosensory stimuli, whilst enhancing visual (i.e. exteroceptive) ones and vice-versa. The vestibular system may hence modulate different sensory signals in an attempt to resolve sensory conflicts (Zeller, Litvak, Friston, & Classen, 2015): when visual information is deemed as more reliable, the vestibular system may enhance its relevance whilst decreasing the importance of proprioceptive one (and vice-versa – see Chapter 3). In the present chapter, three possible alternative explanations for these findings are considered: (1) instead of weighting different sensory signals at the multisensory level (i.e. when both proprioceptive and visual information have been processed by the respective primary cortices), vestibular signals may lead to a hypoactivation of somatosensory areas, thus making proprioceptive signals less reliable (i.e. down-regulation of proprioception); (2) alternatively, the vestibular system may be modulating visual space perception, by shifting the horizontal spatial plane towards the left (as discussed in section 2.4. Discussion, Chapter 2) and (3) finally, the enhanced visual capture observed in the previous studies, instead of depending on the seen object being a body part, and in a biomechanically possible position, may be due to the simple presence of an object (i.e. not necessarily related to updating body representation).

Firstly, rather than being the result of the balancing mechanism suggested above (see also Ferrè, Berlot, & Haggard, 2015), previous findings may be explained as a down-regulation of proprioceptive signals in somatosensory areas. The vestibular system may attenuate proprioceptive signals in the primary somatosensory cortex, which could then lead to a subsequent enhancement of visual cues. Thus, vestibular signals, rather than acting on multisensory integration processes, may act at an earlier stage of somatosensory perception. In line with the latter hypothesis, there is evidence that vestibular signals may decrease proprioception per se. For example, maintaining a fixed position of one's own unseen arm decreases proprioceptive awareness (Newport et al., 2001). Accordingly, Schmidt and colleagues (Schmidt, Artinger, et al., 2013) suggested that LGVS may impair proprioceptive processing in right-handers. In their study, healthy participants were required to make proprioceptive judgements after their unseen arm was moved by an experimenter-controlled robotic device, whilst simultaneously undergoing GVS. Results showed that right-handed participants were displaced towards their own trunk following LGVS (displacement was measured as the difference between estimation of arm location and actual arm's position). Furthermore, as discussed in Chapter 2, fMRI studies (e.g. Bense et al., 2001; Della-Justina et al.,2015) showed that GVS pulses of 21 seconds resulted in a decreased activation of somatosensory areas, thus supporting the hypothesis of a possible inhibition of proprioceptive processing during vestibular stimulation. Hence, if the underlying mechanism at play during LGVS is a proprioceptive down-regulation, resulting from inhibition of primary somatosensory areas, then a decreased proprioceptive ability (measured via judgement of participants' arm position) would be expected following LGVS (as in Schmidt et al., 2013). Nevertheless, given that the current study does not employ neuroimaging techniques, it can only be speculated (based on the literature) that this is the mechanism at play and future research would be needed to confirm these findings at the neurofunctional level.

A second, possible explanation for these previous findings is that the vestibular system, rather than acting on multisensory integration processes involving the body, may be influencing visual space perception. Evidence suggests that the way that a conflict between visual and proprioceptive information is resolved depends on the spatial plane (horizontal or vertical) in which the conflict occurs. Visual information is weighted more in pointing tasks performed in the horizontal space whereas proprioceptive cues are weighted more when the task requires subjects to process sensory inputs in the vertical plane (i.e. in depth) (van Beers et al., 2002). Thus, visual cues are more reliable when processing stimuli on the horizontal plane. In all the experiments reported in the previous chapters, proprioception (i.e. proprioceptive drift) was always measured on the horizontal plane (see section 2.2. Materials and methods, Chapter 2): participants watched the experimenter move the tip of a pen on the top of a box, asking her to stop when the perceived location was reached. Furthermore, previous studies showed how vestibular stimulation of the right hemisphere may induce a compensatory shift towards the left in the horizontal space (as outlined in detail in section 2.4. Discussion, Chapter 2 and reported in Ferrè, Longo, Fiori, & Haggard, 2013; Utz, Keller, Kardinal, & Kerkhoff, 2011; Wilkinson et al., 2014). The results reported in the previous chapters could hence be explained as a consequence of such shifting: when participants undergo LGVS, they may tend to report visual stimuli as shifted towards their left side (i.e. their perceived centre of space is shifted to the left). However, no study to date investigated whether the position of a visual point of reference in the horizontal space is modulated by vestibular stimulation, thus justifying the claim that previous findings may be explained away by GVS inducing a compensatory shift towards the left.

Third, it remains unclear whether the enhanced weight of vision over proprioception observed in the previous studies is due to the seen object being a body part placed in a biomechanically possible position or whether such enhancement acts at lower-levels of multisensory integration (i.e. LGVS induces visual capture of any object placed near the body). Previous studies showed how manipulating a fake hand's position in space during the rubber hand illusion can prevent subjective embodiment (i.e. rotating it 90 degrees in respect to participant's hand; Tsakiris & Haggard, 2005, or 180 degrees; Jenkinson & Preston, 2015). Similarly, proprioceptive drifts have been shown to be reduced when the rubber hand is rotated 180 degrees (i.e. with fingers facing the subject; Ide, 2013). Thus, in order for embodiment of a fake limb to occur, the fake limb needs to be in a biomechanically plausible position. In the previous chapters, LGVS caused an increase in visual capture, which was interpreted as a modulation of multisensory integration during conflictual situations (i.e. visuo-proprioceptive as well as visuo-proprioceptive-tactile). However, these previous experiments did not test whether visual capture could be enhanced even in contexts in which the rubber hand is in a bio-mechanically implausible position. If LGVS is promoting multisensory integration by updating participants' body representation to include the rubber hand, positioning the hand in a non-biomechanically plausible fashion should prevent visual capture. However, this possibility remains to be explored.

Hence, the current study set out to investigate to what extent previous results (Chapters 2 and 3) were, as hypothesised, due to the right-hemisphere vestibular network rebalancing multisensory signals in situations where visual and proprioceptive information is conflicting. Alternative hypotheses were thus tested, to exclude that vestibular stimulation influences multisensory integration via (1) a hypoactivation of somatosensory areas, leading to a decrease in reliability of proprioceptive signals; (2) a shift towards the left on the horizontal spatial plane and (3) the mere presence of a body-like object, regardless of its bio-mechanical properties. The predictions were that 1) no difference would be found between the different GVS configurations in proprioceptive drifts when there was no rubber hand in view, in contrast to when the rubber hand was positioned in line with participant's own hand; 2) no difference between the GVS configurations would be found in judgements of visual points of reference on the horizontal plane; 3) increased proprioceptive drifts would be found when a fake hand in a plausible position was in view (in continuity with findings from Chapters 2 and 3), whilst decreased proprioceptive drifts and embodiment in LGVS would occur when the rubber hand was in a bio-mechanically impossible position, in comparison with when it was in line with participant's real hand position.

To test the above hypotheses, an experimental paradigm was devised to test the effect of GVS on 1) proprioceptive ability (i.e. the ability to judge the location of one's arm with no object in view); 2) perception of space (i.e. the ability to report the position in space of a visual point of reference (in this case, the mid-point of a box) and 3) the ability to embody a rubber hand positioned either in a bio-mechanically possible (i.e. aligned with participants' own left hand) or an impossible position (i.e. rotated 180°, with palm up and fingers pointing towards the participants' trunk).

4.2. Methods

4.2.1. Participants

Thirty-six right-handed healthy participants (30 females, age range: 18 – 50 years, M=21.36, SD=5.93) were recruited through an institutional subject pool and were screened for the following exclusion criteria prior to their participation in the study: no reported neurological or psychiatric disorders, drug or alcohol abuse, history of vestibular illness, history of epilepsy, pregnancy, hearing impairment, presence of metallic head plates, electrical implants and scalp skin sensitivity. The study was approved by an NHS ethical committee and ratified by the University ethical committee. All participants provided written, informed consent.

4.2.2. Experimental design

We applied GVS (LGVS, RGVS, Sham) during a RHI task using a within-subjects, block design, with the order of the GVS blocks and order of conditions within blocks (see below for details) counterbalanced across participants. Each of the 3 GVS blocks comprised three conditions (Figure 4.1A): a pure proprioception condition (during which no rubber hand was presented) and two rubber hand conditions (one with the rubber hand in the canonical position and one with the rubber hand positioned in an anatomically impossible fashion). The pure proprioception condition (Figure 4.1B) aimed to explore whether previous visual capture effects could be due to a vestibular-dependent hypoactivation of somatosensory areas, leading to a reduced reliability of proprioceptive signals. The two rubber hand conditions were administered (in a counterbalanced order across participants) (Figure 4.1C) to investigate whether visual capture effects extend to a bio-mechanically impossible position, with the prediction that the canonical rubber hand condition would lead to greater embodiment (and specifically so following LGVS). Furthermore, in order to provide further support to the argument that the visual capture effect found in the previous studies is not the result of a compensatory leftward shift in the perception of space, a control condition was created to check whether participants' judgement of visual elements in the peri-personal space is influenced by GVS per se. If GVS, and specifically, LGVS is shifting space perception on the horizontal plane, judgement of the position of visual references (other than one's own hand or the rubber hand) should be horizontally shifted according to the type of stimulation. In order to do so, three mid-box judgements were taken across each GVS block (Figure 4.1A).

Proprioceptive drifts were collected utilising the same procedure described in Chapter 3 and participants completed the Embodiment Questionnaire (Longo, Schuur, Kammers, Tsakiris, & Haggard, 2008) following the two rubber hand conditions only (see Chapter 3 and Appendix 1). Additionally, mid-box judgements were taken i) at the beginning of the block (i.e. before any GVS occurred), ii) following the pure proprioception condition and iii) at the end of the GVS block. The procedure to obtain the mid-box judgements was the same as the proprioceptive drift one, with the exception that participants were instructed to stop the experimenter once she reached the middle of the box rather than the position of their own index finger.

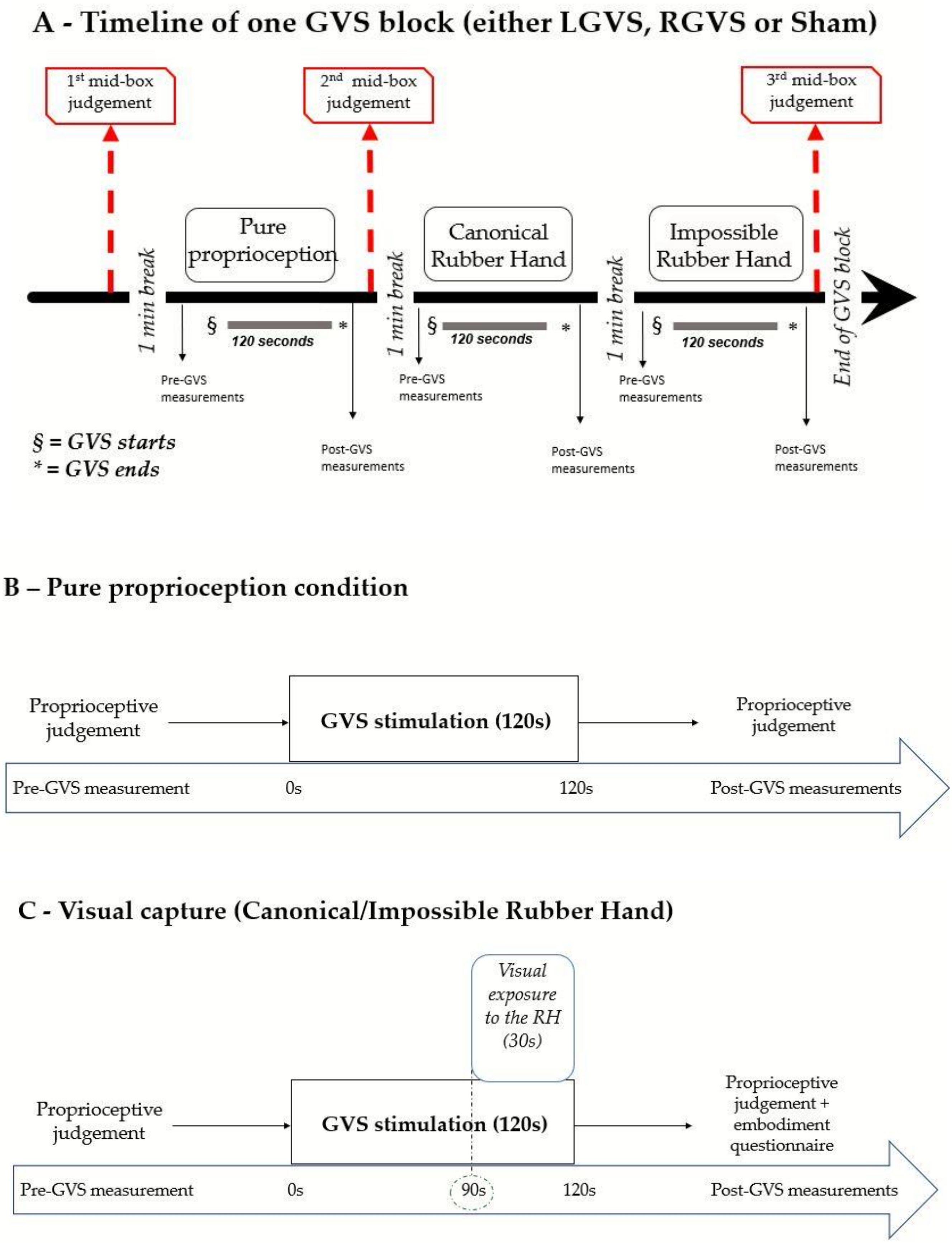

A - Timeline of one GVS block (either LGVS, RGVS or Sham)
1st mid-box judgement
2nd mid-box judgement
3rd mid-box judgement
Pure proprioception
Canonical Rubber Hand
Impossible Rubber Hand
1 min break
1 min break
1 min break
End of GVS block
§
*
120 seconds
120 seconds
120 seconds
Pre-GVS measurements
Pre-GVS measurements
Pre-GVS measurements
Post-GVS measurements
Post-GVS measurements
Post-GVS measurements
§ = GVS starts
* = GVS ends
B – Pure proprioception condition
Proprioceptive judgement
GVS stimulation (120s)
Proprioceptive judgement
Pre-GVS measurement
0s
120s
Post-GVS measurements
C - Visual capture (Canonical/Impossible Rubber Hand)
Visual exposure to the RH (30s)
Proprioceptive judgement
GVS stimulation (120s)
Proprioceptive judgement + embodiment questionnaire
Pre-GVS measurement
0s
90s
120s
Post-GVS measurements

Figure 4.1. A) *Timeline of one prototypical GVS block.* At the beginning of each of the three GVS blocks (either LGVS, RGVS or Sham), participants undertook the first mid-box judgement, before any stimulation occurred. Subsequently the pure proprioception condition began (see B for details), followed by either the canonical or the impossible rubber hand conditions (see C for details). B) *Timeline of the pure proprioception condition*. Before the pure proprioception condition started, participants performed a proprioceptive judgement (pre-GVS measurement). Immediately afterwards, the vestibular or sham stimulation commenced, lasting for 2 minutes, during which participants sat with their eyes open. After 120 seconds (total) stimulation participants immediately performed a second proprioceptive judgement, followed by a 2nd mid-box judgement.
C) *Timeline of the canonical and impossible visual capture conditions*. Before one of the two visual capture condition started (in a counterbalanced order), participants performed a proprioceptive judgement (pre-GVS measurement). Immediately afterwards, the vestibular or sham stimulation commenced, lasting for 2 minutes, during which participants sat with their eyes open. During the last 30 seconds of vestibular or sham stimulation, the experimenter opened the box lid and instructed the participant to look at the rubber hand until told otherwise. After 120 seconds (total) stimulation the lid was closed and participants immediately performed a second proprioceptive judgement and completed the embodiment questionnaire (post-GVS measurements). At the end of both rubber hand conditions, participants performed a final mid-box judgement, which signalled the end of the experimental block.

4.2.3. Experimental setup and materials

Galvanic Vestibular Stimulation

The same GVS configurations (i.e. LGVS, RGVS and Sham), electrode positions, current intensity and device described in Chapters 2 and 3 were implemented in the current study (see section 2.2. Materials and methods). The total amount of stimulation per GVS block was 6 minutes, with each experiment involving 18 minutes (including Sham) of non-continuous stimulation. Each GVS block was followed by a 20-minute break (see Chapter 2 and Utz, Dimova, Oppenländer, & Kerkhoff, 2010).

Rubber Hand Illusion

The apparatus was the same as detailed in Chapter 2 and Chapter 3, with the exception of the rubber hand's position. In the canonical rubber hand condition (Figure 4.2A), the rubber hand was positioned in line with participant's own, hidden hand, and in a bio-mechanically possible fashion. In the "impossible" rubber hand condition, the rubber hand was rotated 180°, with palm up and fingers facing the participant (Figure 4.2B).

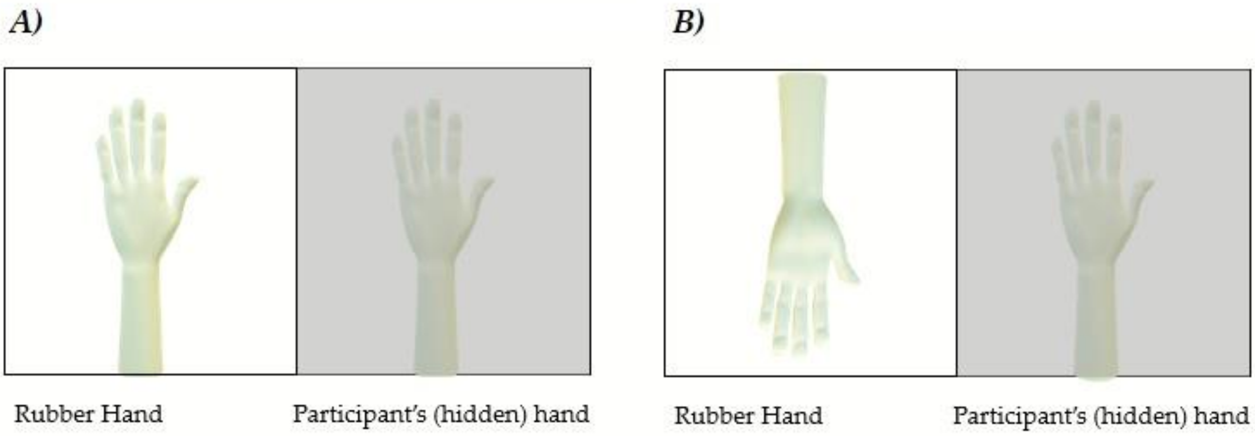


Figure 4.2. The set-up was the same described in section 3.2 of Chapter 3. According to the experimental condition, the rubber hand was positioned either A) in the canonical way (i.e. congruent with participant's body representation) or B) in an impossible to embody fashion (i.e. rotated 180° and with the palm up).

4.2.4. Experimental Procedure

Participants positioned their left forearm in the box and the experimenter aligned their index finger with the rubber hand's hidden finger when positioned in the canonical fashion (hidden from participant's view). Their body midline was aligned with the rubber hand. Each block started with a mid-box judgement, followed by a pre-stimulation proprioceptive judgement (pre-GVS measurement; see 2.2. Materials and methods, Chapter 2). Immediately afterwards, GVS stimulation started. During the first condition (pure proprioception, Figure 4.1B), participants were asked to sit still and relax. At the end of the pure proprioception condition, participants were asked to perform a post-GVS proprioceptive judgement (i.e. indicate the perceived location of their own left hand), followed by the 2nd mid-box judgement (i.e. indicate the perceived location of the middle of the box). After a one-minute break, the first rubber hand condition (either canonical or impossible, Figure 4.1C) commenced, with the experimenter obtaining the pre-GVS proprioceptive judgement (after which the stimulation started). After 1 minute and 30 seconds of stimulation, the rubber hand was revealed, and participants were asked to continuously look at it for the last 30s. Participants then performed a second proprioceptive judgement with the box closed and completed the embodiment questionnaire (post-GVS measurements). The second rubber hand condition of the block began after a one-minute break. The block ended with the 3rd mid-box judgement. At the end of the three GVS blocks, participants were asked to report any vestibular feeling associated with the stimulation as well as guess when they received vestibular stimulation (see section 2.2. Materials and methods, for further details).

4.2.5. Data analysis

In the current study, both frequentist and Bayesian analysis were used. Specifically, Bayesian analyses were used to supplement the frequentist analysis when the null hypothesis was of primary interest. Whilst frequentist approaches can inform about whether to accept or reject a null hypothesis, Bayesian statistics can be used in order to support the null hypothesis (Dienes, 2014). In particular, Bayes Factors are a measure increasingly used to assess the likelihood of one hypothesis over another in two competing models (i.e. null and alternative hypotheses). A Bayes Factor of 1 is interpreted as lack of evidence for either of the hypotheses, whereas values between 1-3 show anecdotal evidence for one of the two hypotheses, values between 3-10 indicate moderate evidence and values above 10 suggest strong evidence for one of the two hypotheses (e.g. a Bayes Factor, $BF_{(0\ 1)}= 5$ is moderately in favour of the null hypothesis over the alternative one; Lee and Wagenmakers, 2014).

In order to investigate whether GVS modulates proprioception per se, a one-way Bayesian repeated measures ANOVA was run with GVS as the independent variable (GVS: LGVS vs. RGVS vs. Sham) on the proprioceptive drifts obtained in the pure proprioceptive condition. Given that specific predictions were made about the null hypothesis (i.e. that would not be any difference between the proprioceptive drifts obtained in the three GVS configurations) Bayesian statistics were used to find support for this prediction alongside a normal repeated measures ANOVA.

To explore whether LGVS enhances vision over proprioceptive only when the rubber hand is in a biomechanically possible position, i) a 3 (GVS: LGVS vs. RGVS vs. Sham) x 2 (Rubber hand position: canonical vs. impossible) repeated-measures ANOVA was conducted on the proprioceptive drifts. Owing to violation of normality in the embodiment scores, a Friedman’s ANOVA was run on the averages of the two rubber hand conditions (to test main effects of stimulation), a Wilcoxon Signed rank test was conducted on the averages of the three GVS distributions in the canonical and impossible rubber hand (to explore main effects of condition) and finally the subtraction of the different GVS configuration in each condition (to investigate interactions) was tested via a Wilcoxon signed rank test (for further details on how main effects and interactions distributions were obtained, please refer to Appendix 2).

Finally, to test whether LGVS shifts the visuo-spatial plane towards the left, a 3 (GVS: LGVS vs. RGVS vs. Sham) x 3 (Time: 1st judgement, 2nd judgement and 3rd judgement) repeated-measures ANOVA with polynomial contrasts was conducted to check for the presence of vestibular effects on visual perception of a visual reference point over time. A Bayesian ANOVA, was run to investigate whether the null hypothesis (i.e. that nor GVS or its interaction with time would have an effect on visuo-spatial judgements) could be confirmed.

Data were analysed using the IBM Statistical Package for Social Sciences (SPSS) for Windows, version 25 (Armonk, NY) for frequentist statistics, the JASP software (Version 0.10.0) for Bayesian statistics and plotted using the "*ggplot2*" package for R (Wickam, 2009).

4.3. Results

One participant was excluded from the data analysis because his scores were more than 2.5 SD away from the mean in more than 2 proprioceptive drifts distributions. Hence the final sample consisted of a total of 35 participants (30 females, age range 18 – 50 years, M = 21.43, SD =6.01).

4.3.1. Pure proprioception condition

A frequentist one-way repeated measures ANOVA did not detect any significant main effect of GVS on proprioceptive drifts in the pure proprioception condition ($F_{(2,68)} = 0.922$, p=0.402, ηp^2=0.026; Sham: M=-0.78 cm, SD=1.84; LGVS: M=-0.62 cm, SD=2.35; LGVS: M=-0.29 cm, SD=1.69). To further confirm this finding, a one-way Bayesian repeated measures ANOVA (GVS: LGVS vs RGVS vs Sham) was conducted to further support the null hypothesis (i.e. that there would be no difference between the proprioceptive drifts in the three GVS configurations). This analysis revealed that the null model (i.e. that GVS does not have an impact on proprioception per se) was better than the alternative hypothesis by a Bayes Factor of 5.232, suggesting that the null hypothesis is moderately more likely than the alternative one.

4.3.2. Proprioceptive drifts in canonical and impossible rubber hand positions

A 3 (GVS: LGVS vs RGVS vs Sham) x 2 (RH position: canonical vs impossible rubber hand) repeated measures ANOVA revealed non-significant trend for a main effect of GVS ($F_{(2,68)} = 2.870$; $p=0.064$, $\eta p^2 =0.078$), no main effect of rubber hand position ($F_{(1,34)} =1.335$; $p=0.256$, $\eta p^2=0.038$) or interaction (GVS*RH position: $F_{(2,68)} = 0.684$, $p= 0.508$, $\eta p^2=0.020$), suggesting that there was no effect of GVS on visual capture of a rubber hand (in a canonical position) and that there was no difference in proprioceptive drifts between a possible to embody rubber hand and an implausibly positioned one (see Table 2 below).

Table 4.1: Mean and Standard deviation of proprioceptive drifts during the visual capture conditions.

Conditions	Mean (cm)	Standard Deviation
Sham canonical	0.09	2.25
LGVS canonical	0.77	1.72
RGVS canonical	0.50	1.78
Sham impossible position	-0.33	2.05
LGVS impossible position	0.15	1.94
RGVS impossible position	0.63	2.14

4.3.3. Embodiment questionnaire

As the majority of the distributions were not normal, non-parametric analysis were run on embodiment scores. A Friedman's ANOVA revealed no main effect of vestibular stimulation ($\chi^2_{(2)}$=4.299, p=0.117), while a Wilcoxon signed-rank test ran on the averages of the rubber hand canonical and impossible conditions (regardless of the stimulation type), confirmed a main effect of rubber hand's position (Z=-4.173, p<0.001, *r*=0.5), with the impossible rubber hand condition leading to less embodiment (Figure 4.3). A significant interaction was also found (Z=2.020, p=0.043, *r*=0.24), which was further analysed via Bonferroni-corrected Wilcoxon signed-rank tests (α=0.008), revealing a significant difference between RGVS and Sham impossible conditions (Z=-3.182, p=0.001; *r*=0.38; Sham IRH: *Mdn*=-2.14, IQR=1.71; RGVS IRH: *Mdn*=-1.71, IQR=1.86), with Sham leading to overall lower embodiment, and no difference between the other comparisons (Sham RH vs LGVS RH: Z=-.566, p=0.571, *r*=0.07; Sham RH: *Mdn*=0.29, IQR=3; LGVS RH: *Mdn*=-0.14, IQR=2.86; Sham RH vs RGVS RH: Z=.127, p=0.899, *r*=0.02; RGVS RH: *Mdn*=-0.29, IQR=2.86; LGVS RH vs RGVS RH: Z=0.716, p=0.474, *r*=0.09; Sham IRH vs LGVS IRH: Z=.986, p=0.324, *r*=0.12; LGVS IRH: *Mdn*=-2, IQR=1.86; LGVS IRH vs RGVS IRH: Z=2.189, p=0.029, *r*=0.26).

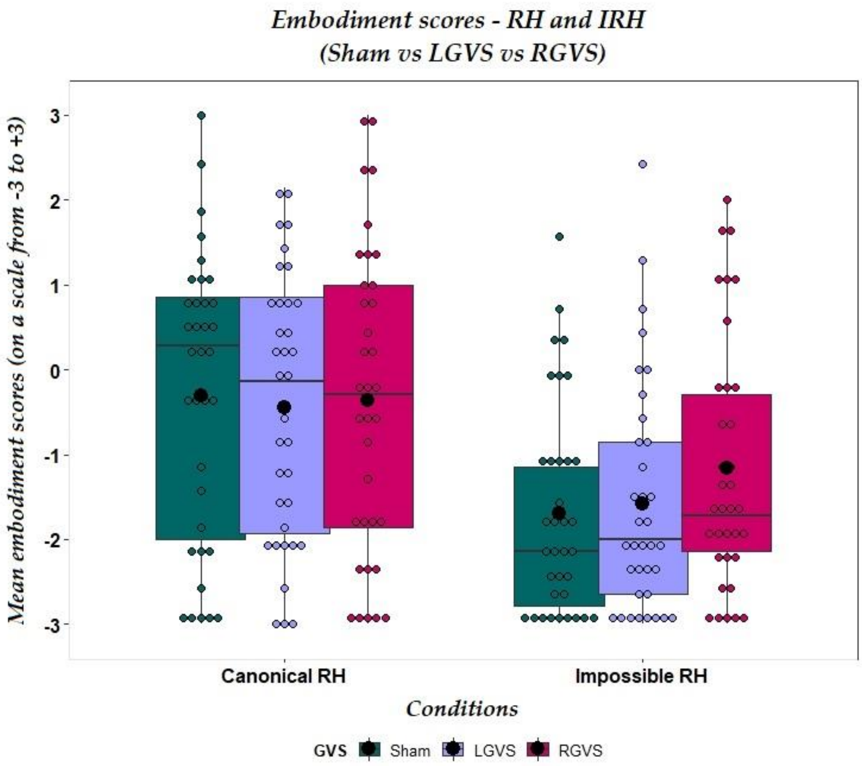


Figure 4.3. Mean values of the embodiment scores in Sham, LGVS and RGVS in Canonical and Impossible Rubber Hand positions. *= p<0.05; Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR).

4.3.4. Midpoint of the box

In order to explore whether LGVS shifts the visuo-spatial plane towards the left, a 3 (GVS: LGVS, RGVS and Sham) x 3 (Time: 1st judgement, 2nd judgement and 3rd judgement) repeated measures ANOVA was run on the mid-box judgments, using polynomial contrasts to further check for increased judgements' displacement over time. Results showed a main effect of time (Time: $F_{(4,68)}$ = 4.844, p=0.011, ηp^2=0.12) but no main effect of stimulation (GVS: $F_{(2,68)}$=0.654, p=0.523, ηp^2=.019) nor interaction (GVS*Time: F (4,136) =0.185, p=0.946, ηp^2=0.005). Polynomial contrasts were used to follow up on the main effect of time with, revealing a linear trend over time ($F_{(1,34)}$ =11.07, p=0.002, ηp^2=0.256), suggesting that participants improved in their judgements of the mid-box position over time regardless of the type of GVS involved (see Figure 4.4.). A 3 (GVS: LGVS, RGVS and Sham) x 3 (Time: 1st judgement, 2nd judgement and 3rd judgement) Bayesian repeated-measures ANOVA was conducted to find further support for the null hypothesis (i.e. that GVS nor its interaction with time would have an impact on proprioception per se). This analysis showed that the null hypothesis was moderately more likely than the alternative hypothesis by a Bayes Factor of 3.686.

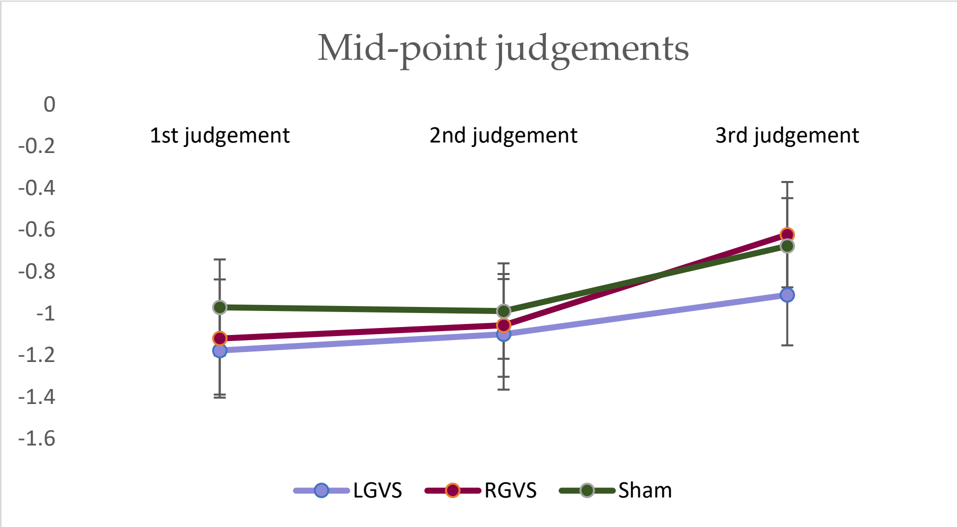


Figure 4.4. Mid-box judgements (i.e. difference between the reported and the actual mid-point of the box) in Sham, LGVS and RGVS across each GVS block (i.e. values taken from the three GVS configuration in the order they were performed). Error bars: SEM.

4.3.5. <u>Vestibular feelings</u>

At the end of the main experiment, participants were asked to report any physical sensation associated with the stimulation. The majority of the sample (29/35) reported a tingling or itching sensation under the patches that none of the participants described as painful. 26/35 participants reported mild vestibular-related sensations (dizziness, vertigo or loss of balance), suggesting that a 1mA stimulation leads to distinctive vestibular sensations in the majority of the sample, in line with previous findings.

To control for the role of Sham as a placebo-like intervention, participants were asked to guess in which of the 3 GVS configurations they thought to have received a vestibular stimulation, specifying that the answer might have been all of them, 2 or 1. The majority guessed correctly about LGVS and RGVS (30/35 and 28/35, respectively), whereas approximately 1/3 of the sample wrongly reported Sham as a vestibular stimulation (15/35). A significant difference between these frequencies was found using a Likelihood Ratio Chi-square analysis ($\chi^2_{(2)}$ = 8.17, p=0.017; ϕ_c=0.015), suggesting that the three different GVS configurations were not perceived equally by the subjects.

4.4. Discussion

In the current study, the aim was to explore whether the right-hemisphere vestibular-induced visual capture effects found in the studies presented in Chapters 2 and 3 could be explained by three alternative mechanisms: (1) a hypoactivation of somatosensory areas, with a subsequent lowering of proprioceptive signals reliability; (2) a leftward shift on the horizontal spatial plane and (3) the presence of a body-like object, regardless of whether it is positioned in a bio-mechanical fashion. The first alternative explanation was explored via a condition in which participants judged the position of their (left) index finger before and after receiving GVS. During this condition, participants were instructed to sit still with their eyes open (but without focusing on anything). No difference between the three GVS configurations was found following both frequentist and Bayesian analysis, suggesting that there was no evidence in support of a GVS effect on proprioception in this study. Previous studies (e.g. Schmidt, Artinger, et al., 2013) have found evidence for a LGVS effect on similar proprioceptive judgments, even when using a sample size lower than the one used in the current study. One possible explanation for the lack of such differences in the current study is that this experiment was not conducted in the dark as previous studies. Participants were required to keep their eyes open in order to recreate the same experimental set-up of the studies presented in the previous chapters. The aim of this condition was to explore the possibility that LGVS may downregulate proprioception during visuo-proprioceptive conflict and may hence explain away the visual capture results previously found. Furthermore, neuroimaging studies highlight a vestibular-visual reciprocal inhibition during vestibular modulation, suggesting a basic mechanism underlying visuo-vestibular interactions that might be enhanced by absence of light (Bense, Stephan, Yousry, Brandt, & Dieterich, 2001; Della-Justina et al., 2015). However, as mentioned above, future studies should explore whether the behavioural findings of the current study correspond to a downregulation of proprioceptive signals at the cortical level.

The second aim of the current study was to check whether LGVS induces a shift to the left side of participants' perceived space on the horizontal plane. No difference between the three GVS configurations in the mid-box judgements was found and further support for the null hypothesis was provided by a repeated measures Bayesian ANOVA; however, a general trend towards improvement over time (regardless of the type of vestibular stimulation) was observed. This result suggests that there was no evidence for an effect of GVS on visuo-spatial judgements. This is in contrast with the line of evidence suggesting a general leftward shift induced by right-hemisphere vestibular stimulation in both healthy subjects (Ferrè et al., 2013) and right-hemisphere stroke patients (Fink et al., 2003; Schmidt, Keller, et al., 2013). Future studies should investigate whether such discrepancy is due to methodological difference in GVS duration or insufficient statistical power (see section 2.4. Discussion).

The third aim of this study was to investigate whether the results presented in the previous chapters were directly linked to the presence of a body-like object positioned in a biomechanical position. In the current study, no difference was detected between the proprioceptive drifts in the three GVS configurations when the rubber hand was in a canonical position. As sham proprioceptive drifts values were around zero in both possible and impossible conditions, it may be possible that, in the current sample, subjects were not susceptible to the illusion. It has been previously shown (Tsakiris & Haggard, 2005) that positioning a rubber hand in a non bio-mechanically plausible fashion reduces proprioceptive drifts during synchronous (but not asynchronous) stroking conditions. Given that the current study did not include any stroking conditions, this conflicting result may be due to the lack of additional tactile information on the top of visuo-proprioceptive one. Alternatively, as discussed in Chapter 2 (section 2.4. Discussion), proprioceptive drifts may represent a lower-level integration of multisensory signals, which may not be necessarily influenced by the type of stimulus in view and thus may not be directly linked to updates in body representation. Nevertheless, there is evidence that this may not be the mechanism at play (Tsakiris and Haggard, 2005) and further research is needed to clarify the different findings of the current and previous studies. As it was predicted that a bio-mechanically possible rubber hand would have elicited visual capture, in comparison with a non-biomechanically possible position, embodiment feelings were explored to look at subjective, on the top of the objective, feelings of embodiment. As discussed in the previous chapters, feelings of embodiment may involve higher-order processes, not affected by the stimulation (Tsakiris, 2010; Martinaud et al., 2017). In line with this, a lower level of embodiment was observed when the rubber hand was displaced 180° in space in comparison with a canonical position. Embodiment scores were around zero in all GVS configurations when the hand was positioned in a canonical fashion (i.e. in line with participants' own hand). When the rubber hand was rotated, embodiment scores were negative in all GVS configurations. Hence, neither of the two experimental conditions led to positive embodiment scores. This finding is in line with the results reported in Chapter 2 and 3, indicating that visual capture conditions (i.e. with no touch administered) do not seem to elicit feelings of embodiment (in contrast with Samad, Chung, & Shams, 2015).

To summarise, in the current study i) LGVS did not lead to an impairment in proprioceptive judgements when no visual stimulus was present; ii) LGVS did not lead to a general leftward displacement of perceived space and iii) no visual capture effect was found following LGVS, regardless of whether the rubber hand was in a canonical or impossible to embody position. These findings suggest that the LGVS-induced visual capture effects observed in previous studies may indeed be related to multisensory integration processes.

The first three experimental chapters of this thesis focused on the modulation of multisensory integration in healthy subjects by the vestibular system, with findings suggesting a dynamic role of vestibular signals in multisensory integration. In the next chapter, visual capture of a motionless rubber hand will be explored in brain-damaged individuals, in order to shed light on the processes underlying multisensory integration and body ownership following lesions in right fronto-parietal areas. Studying facets of the bodily self in patients with right-hemisphere stroke can offer a unique window of insight into such processes, alongside neuromodulation studies on healthy subjects. Specifically, investigating body ownership in neuropsychological patients does not entail the use of temporary multisensory illusions and thus leads to further insight into the phenomenon of disturbances in body ownership.

Chapter 5

Body Ownership, Motor Awareness and Agency Following Right-hemisphere Stroke

5.1. Introduction

In the previous chapters, multisensory integration during vestibular stimulation in healthy subjects was explored, with a specific focus on the role of both interoceptive and exteroceptive signals in shaping the bodily self. As has been outlined above, our sense of self-awareness and body ownership relies on the continuous integration of several sensory signals (Tsakiris, 2010). Such continuous multisensory integration allows individuals to adapt to environmental and internal changes (Suzuki et al., 2013). However, following brain damage, this dynamic updating can be severely compromised. A stroke in the fronto-parietal areas of the right hemisphere (Feinberg et al., 2010; Moro et al., 2016) can result in a variety of bodily-awareness disorders, among which are Anosognosia for Hemiplegia (i.e. AHP; Babinski, 1914) and Disturbed Sensations of limb Ownership (i.e. DSO; Baier and Karnath, 2008). AHP is characterised by unawareness or denial of severe contralateral motor weakness or paralysis (Vossel et al., 2013; Fotopoulou, 2014). Often accompanying AHP, yet also found to be dissociated (Gandola et al., 2012), DSO are feelings of non-belonging or denial of ownership of the affected limb (i.e. asomatognosia; see Jenkinson et al, 2018 for a recent definition of the disorder), with or without delusional personification or attribution of the limb to somebody else (i.e. somatoparaphrenia; Feinberg and Venneri, 2014; Vallar and Ronchi, 2009).

These neuropsychological conditions can offer a unique window of insight into our understanding of how multisensory (i.e. the integration of information conveyed by different sensory modalities) and sensorimotor integration (i.e. the integration of sensory information leading to motor outputs; Sangani, Lamontagne, & Fung, 2015), give rise to various facets of body representation. In DSO patients, failure to integrate signals from different sensory modalities can underlie feelings of dis-ownership of their contralateral limb (Martinaud et al., 2017). Similarly, the inability to integrate somatosensory signals with motor planning and monitoring has been posited to be at the heart of AHP patients' unawareness (Berti et al., 2005; Fotopoulou, 2014). In addition to classic clinical-anatomical studies, which primarily sought to identify the neuroanatomy of AHP (Berti et al., 2005; Vocat et al., 2010), more recent studies have started to use experimental, psychophysical methods by the bedside to investigate multisensory and sensorimotor integration in these patients (Besharati et al., 2016; Cocchini, Beschin, Fotopoulou, & Della Sala, 2010; Fotopoulou et al., 2008; Garbarini et al., 2012; Martinaud et al., 2017; van Stralen et al., 2013; Zeller et al., 2011). Specifically, some of these studies focused on the contribution of such sensory processes to aspects of the bodily self, such as body ownership (i.e. the sense that our own body belongs to us; Gallagher, 2000), motor awareness (i.e. awareness of one's own actions) and the sense of agency (i.e. the sense of being in control of our own actions; Haggard, 2005).

One of the classic experimental paradigms used to investigate body ownership in healthy as well as clinical populations is the Rubber Hand Illusion (see also section 1.2. Exteroceptive and interoceptive sensory integration: the basis of the bodily-self, Chapter 1). In hemiplegic stroke patients, feelings of ownership of the rubber hand during the RHI are stronger in comparison with non-hemiplegic patients (Burin et al., 2015). Importantly, in right-hemisphere stroke patients, even the sight of a rubber hand can elicit both subjective feelings of ownership (Fotopoulou et al., 2008; Martinaud et al., 2017; van Stralen et al., 2013) as well as related neurophysiological responses (Llorens et al., 2017). A previous study (Martinaud et al., 2017) found that when a rubber hand is positioned congruently with patients' own left, paralysed hand (while the latter is hidden), the majority of right-hemisphere stroke patients automatically embody it, even if no visuo-tactile stimulation is performed and even when they deny ownership of their own, paralysed, limb. Such phenomenon may be due to a dominance of visual cues over proprioceptive ones, leading to feelings of ownership of a rubber hand (i.e. Visual Capture of Ownership, VoC; Martinaud et al., 2017): patients may experience aberrant sensory inputs from their own paralysed arm, thus not being able to fully integrate it in their body representation as this newly felt limb would be perceived differently than it was before the stroke. However, the rubber hand, which does not elicit such erratic signals, can be easily incorporated into patients' body representation by means of visual capture (i.e. visual signals are deemed reliable when no concomitant error signal is perceived). Strikingly, VoC appears to be present even in patients with dis-ownership of their own hand (Martinaud et al., 2017; van Stralen et al., 2013; Zeller et al., 2011), thus suggesting that the underlying mechanisms of VoC and DSO may be dissociated. Furthermore, lesion mapping analysis in Martinaud and colleagues (2017) revealed that patients who showed VoC of the rubber hand had additional lesions in the frontal operculum and the premotor cortex, in line with the reported activation in healthy subjects experiencing embodiment during the RHI (Ehrsson et al., 2004; 2005; Limanowski and Blankenburg, 2016). Accordingly, VoC effects have been reported in healthy subjects across different experimental paradigms (Crucianelli, Metcalf, Fotopoulou, & Jenkinson, 2013; Marotta, Tinazzi, Cavedini, Zampini, & Fiorio, 2016; Pavani, Spence, & Driver, 2000; Samad, Chung, & Shams, 2015).

Interestingly, it has been shown that the RHI elicits stronger feelings of ownership in younger and older individuals in comparison with middle-aged subjects (Marotta, Zampini, Tinazzi, & Fiorio, 2018). Marotta and colleagues argue that, overall, older individuals have a higher level of malleability of their body representation. Thus, the findings by Martinaud and colleagues could be explained as a result of physiological changes related to aging, possibly exacerbated by the fronto-parietal lesion. Hence, the first aim of the current study was to i) replicate and expand previous findings (behavioural as well as lesion ones) from Martinaud et al., 2017 in an increased sample size, in order to confirm the presence of VoC in the majority of right hemisphere stroke patients and to link VoC effects to previously identified lesion data; ii) explore the possibility that age-matched controls could present with VoC by comparing a sample of age-matched healthy controls and right hemisphere stroke patients, with the prediction that a percentage of healthy subjects would experience VoC but in a significantly lower proportion than in right hemisphere stroke patients, regardless of the symptoms (AHP, DSO, no symptoms).

As mentioned above, alongside the sense of body ownership, right-hemisphere stroke patients can offer insight into other aspects of body representation, such as motor awareness and agency. Specifically, it has been posited that AHP patients may rely on their motor predictions, at the expense of sensory feedback, when determining whether an action occurred or not, to the point that patients are not able to distinguish such prediction from the actually occurred movement (Berti and Pia, 2005; Fotopoulou, 2014). Previous research (Fotopoulou et al., 2008) tried to investigate the extent to which the conscious intention to move influences AHP patients' motor awareness with a bedside rubber hand paradigm similar to the one described in Martinaud and colleagues (2017). To do so, the authors showed a fake, realistic rubber hand to four AHP and four hemiplegic control patients and asked them either to try and move their paralysed limb or to stay still. At the same time, patients were provided with visual feedback in a controlled manner. Such feedback was either i) congruent with patients' motor intention (i.e. the experimenter would move the rubber hand when patients wanted to move their own hand), ii) incongruent (i.e. no movement occurred when patients wanted to move) or iii) following no intention to move (i.e. the experimenter moved or did not move the hand while asking patients not to move). After the rubber hand movement, patients were asked i) whether or not the hand moved and ii) whether they felt agency over the movement. Findings showed that all four AHP patients were more likely than controls to report the occurrence of movement, even when there was none, but only when they had the intention to move. This suggests that when motor intentions are present, they may dominate over contrasting sensory signals, thus leading to the perception of having moved. However, these findings have not yet been replicated in a larger sample size, thus providing further evidence for this hypothesis. Hence, the second aim of the current study was to replicate and expand findings from Fotopoulou and colleagues (2008) in a greater sample size by providing visual feedback of a rubber hand in either an intention-congruent (i.e. patients are asked to move and the rubber hand moves) or intention-incongruent (i.e. patients are asked to move but no rubber hand movement follows) fashion. The prediction was that AHP patients, but not fully-aware hemiplegic control patients, would incorrectly detect a movement in intention-incongruent conditions, whilst both AHP and hemiplegic controls would be able to correctly detect intention-congruent visual feedback of a moving rubber hand and that AHP patients would feel agency over detected movements.

Importantly, when AHP patients are asked to perform a movement with a moving rubber hand that they experience as their own, they also tend to feel agency over it (i.e. the sense of being the agent of an action, rather than the feeling that someone else moved their arm) (Fotopoulou et al., 2008). As described above, ownership of a fake limb can be induced in right-hemisphere stroke patients just by exposing patients to the rubber hand in a position aligned with their own hand. This, combined with the notion that AHP patients tend to feel agency over rubber hand movements (when they have the intention to move), offers the unique opportunity to investigate the relationship between ownership and agency. This relationship has been widely investigated in healthy subjects via “active” variants of the RHI (i.e. with subjects moving instead of receiving touch) in both real (Kalckert & Ehrsson, 2014; Tsakiris, Schütz-Bosbach, & Gallagher, 2007; Tsakiris et al., 2006) and virtual reality environments (Burin et al., 2019). Findings suggest that that while ownership relies on incoming sensory information and top-down representations (i.e. feeling that the hand in front of me is actually mine), agency may arise from additional information related to motor intention (i.e. “I want to move my hand and the hand moved, so I moved it”) in a more “bottom-up” driven process (Tsakiris et al., 2007). As such, these two dimensions of the bodily self have been found to dissociate (Kalckert & Ehrsson, 2012). However, it remains unclear whether there is a relationship linking the two, and what is its direction (i.e. ownership modulating agency or vice-versa). While studies suggest that ownership may drive feelings of agency in the context of willed movements (Burin et al., 2018, 2017), other posits the opposite, with agency leading to ownership feelings (Asai, 2016; Tsakiris, Prabhu, & Haggard, 2006). Put simply, the question of whether we feel that our limbs are our own because we can feel agency over them (i.e. they move congruently to our conscious motor intentions) or we attribute agency to ourselves when we feel a limb moving because we know it is our own, remains unanswered.

Hence, the current study sought to investigate whether feelings of ownership of a rubber hand would modulate the sense of agency over its movements in AHP patients. Given the conflicting findings in the existing literature, the hypothesis was two-fold: either feelings of ownership modulate the sense of agency (i.e. owning a rubber hand leads to the sense that I am the one moving it) or agency modulates ownership (i.e. feeling that I am consciously moving a hand contributes to make me feel it is mine). The experiment described in this chapter sought to investigate this question in AHP patients by investigating feelings of agency according to presence/absence of ownership as well as the opposite (i.e. feelings of ownership according to changes in feelings of agency).

To summarise, the current study had three main aims: firstly, to replicate and expand on existing findings of visual capture of ownership in right-hemisphere stroke as well as in the healthy population, suggesting that right-hemisphere stroke patients tend to embody a rubber hand just by looking at it and that this is linked to fronto-parietal lesions rather than being a product of ageing processes alone. In order to do so, an adapted, bed-side version of the RHI (Fotopoulou et al., 2008; Martinaud et al., 2017) was used. Following visual exposure to a motionless rubber hand, right hemisphere patients and age-matched healthy controls were asked whether they felt ownership over it. The prediction was that right-hemisphere patients would embody the rubber hand significantly more than the healthy group, irrespective of their clinical DSO. The second aim was to investigate the extent to which the conscious intention to move influences AHP patients' motor awareness and sense of agency over and above contrary visual feedback of a motionless arm. Accordingly, patients were asked to try to perform a movement with their paralysed limb and were provided either intention-congruent visual feedback of a moving arm or intention-incongruent feedback of a motionless arm. The prediction was that AHP patients in comparison to right hemisphere patients without AHP would be significantly more likely to detect a movement and feel agency over it, even though they received feedback of a motionless arm. By contrast, these groups should not differ in their ability to detect intention-congruent visual feedback of a moving rubber hand presented in the same spatial position, suggesting that the tendency of AHP to ignore visual feedback is not a mere matter of visuospatial neglect. Finally, the third aim was to explore the relationship between agency over the rubber hand movements and feelings of ownership of it in anosognosia. Given that it was predicted that AHP patients, but not patients without anosognosia, would feel agency over a detected movement (regardless of visual feedback), such relationship was investigated in AHP only, grouping patients according to whether or not they consistently expressed agency and ownership of the rubber hand throughout the experiment. These exploratory analyses aimed to investigate whether feeling ownership of the rubber hand in all experimental conditions could influence the extent to which patients feel agency over its movements or vice-versa (this non-directional hypothesis was due to the conflicting findings in the literature).

5.2. Materials and Methods

5.2.1. Participants

Forty-seven, adult neurological patients meeting eligibility criteria for the study (detailed below) were consecutively recruited from acute stroke units. A sub-set of this sample (n=31) had also taken part in a previous study from our group examining only visual capture of ownership (Martinaud et al., 2017). These patients, as well as sixteen additional patients were recruited in the current study in order to i) increase the sample size and confirm the visual capture phenomenon described above and ii) examine novel hypotheses about body ownership, motor awareness and their relationship, using additional experimental conditions as detailed below. Inclusion criteria comprised: (i) left upper limb hemiplegia (scores <1 in the modified version of the Medical Research Council (MRC) Scale; Florence et al., 1992); (ii) unilateral right hemisphere lesions (as detected by CT or MRI); and (iii) less than 4 months from the occurrence of the stroke. Exclusion criteria included: (i) previous neurological or psychiatric history; (ii) less than 7 years of education; (iii) medication resulting in severe cognitive impairments; and (iv) severe language impairment (i.e. not allowing successful communication between patient and experimenter). Presence of AHP was detected via a set of questions aimed at investigating awareness of motor deficits, based on the interview developed by Berti and colleagues (1996), as in previous studies, including the ones replicated here (Besharati et al., 2014; Besharati et al., 2016; Fotopoulou et al., 2008; Martinaud et al., 2017). Specifically, (i) general questions such as 'Why are you in the hospital?' were asked, then (ii) motor abilities (e.g. 'How is your left arm? Can you move it?') were assessed and finally (iii) patients were invited to perform a movement (i.e. confrontation questions): e.g. '"Please move your left arm. Have you done it?". The possible scores ranged from 0 to 2, with a score of 0 corresponding to full acknowledgement of the motor deficit (i.e. the disorder is spontaneously reported or mentioned by the patient following a general question), a score of 1 indicating partial acknowledgement (i.e. denial of motor deficit but acknowledgement of failed movement) and a score of 2 indicating complete unawareness (i.e. no acknowledgement of the disorder can be obtained). Patients were categorised as anosognosic when they scored 1 or above. As in previous studies, an additional measure of motor awareness was used, an Awareness Questionnaire developed by Feinberg et al. (2000), comprising 10 questions (including general questions, such as "'Do you have weakness anywhere?" or "Is your arm causing you any problems?", as well as specific procedures and questions aimed at confronting the patient with their own disability: i.e. the left arm is lifted and dropped in right hemispace by the experimenter, followed by the question "It seems there is some weakness. Do you agree?"). Each question was scored either 0 (full awareness of deficits), 0.5 (partial awareness) or 1 (complete unawareness) and the final score ranged from 0 to 10.

DSO was identified using a short, adapted version of Cutting's anosognosia assessment (1978) and qualitative (clinical) interviews (see Besharati et al., 2014; Besharati et al., 2016; Fotopoulou et al., 2008; Martinaud et al., 2017). Direct questions investigating ownership of the paralysed limb (e.g. "The experimenter points to the patient's left hand, asking 'Is this your hand?') were followed by specific, follow-up, questions related to the sense of non-belonging (i.e. asomatognosia; e.g. "Does it feel like it belongs to you?") as well as delusional attributions of belonging to somebody else (i.e. somatoparaphrenia; e.g. Does it ever feel like it belongs to someone else?" If yes, ask: "Anyone in particular?"). Questions were scored on a 3-point scale, including 0 (full acknowledgement of body ownership), 1 (partial acknowledgement), 2 (asomatognosia/somatoparaphrenia). Patients were classified as DSO when they scored 1 or above.

Based on the above assessments, 12 patients were identified as having AHP only (AHP group: 9 females, M=70.83 years, SD=14.60 years, age range: 36-88 years), 9 patients were categorised as having DSO only (DSO group: 4 females, M= 65.66 years, SD=13.68 years, age range: 40-83 years), 8 patients presented with both AHP and DSO (AHP+DSO group: 5 females, M=65.5 years, SD=12.02

years, age range: 41-78 years) and 18 patients were classified as hemiplegic control subjects (HP group: 6 females, M= 64.83 years, SD=13.41 years, age range: 42-88 years).

Additionally, in order to investigate the presence of VoC phenomena in the healthy population, healthy, right-handed age-matched controls (N=19, 9 females; Age: M: 57.95; SD: 10.72) were recruited from an institutional subjects pool. The study was approved by an NHS research ethical committee and all participants gave informed, written consent.

5.2.2. Neurological and neuropsychological assessment

All patients underwent neurological and neuropsychological assessment, including tests of motor strength (using the Medical Research Council scale, MRC; Guarantors of Brain, 1986), visual and tactile extinction (Bisiach et al., 1986), proprioception (Vocat et al., 2010), orientation in space and time (via the Mini-Mental State Examination, MMSE; Folstein, 1975), working memory (forward and backward digit span task, from the Wechsler Adult Intelligence Scale III; Wechsler, 1997), mood (via the Hospital Depression and Anxiety Scale, HADS; Zigmind and Snaith, 1983), visuo-spatial neglect (using the Behavioural Inattention Test, BIT; Wilson et al., 1987) as well as personal neglect (via the "one item test", Bisiach et al., 1986 and the comb/razor test, Mcintosh et al., 2000), overall cognitive functioning (assessed using the Montreal Cognitive Assessment, MoCA; Nasreddine, 2005), pre-morbid intelligence (via the Wechsler Test of Adult Reading, WTAR; Wechsler, 2001) and executive functions (investigated using the Cognitive Estimates Test, Shallice and Evans, 1978, and the Frontal Assessment Battery, FAB; Dubois et al., 2000).

5.2.3. Experimental study design

The first aim of the study was to investigate to what extent individuals (right hemisphere patients with and without DSO and healthy controls) reported subjective feelings of embodiment for a realistic rubber hand following visual exposure to it. This was done by i) presenting a motionless, life-like left rubber-hand in a realistic position in front of participants and asking right hemisphere patients and age-matched healthy controls to rate their feelings of body ownership over the rubber-hand after 15 seconds of visual exposure. In patients only, a modulation of these feelings of embodiment by the experience of the rubber hand moving, either when i) patients intended to move the arm and the rubber hand moved (congruently with their motor expectations) or when ii) the rubber hand did not move despite their effort to move it (incongruently with their motor expectations) was explored. The frequency of patients who did vs. did not state that the rubber hand was theirs was then calculated (herein referred to as Visual Capture of Ownership; VoC) and ratings were compared. VoC was tested at three time points (at the beginning of the experiment and following congruent and incongruent movements of the rubber hand).

The second main aim of the current study was to investigate whether patients with anosognosia for hemiplegia ignore sensory feedback about their paralysis when they have the intention to move their paralysed limbs. The aim was to replicate in a larger sample and for the first time, previous findings regarding the role of motor intentions in AHP (Fotopoulou et al., 2008). In order to achieve this aim, patients with right hemisphere stroke (with and without AHP) were asked to try and perform a movement that was followed by ether a congruent (i.e. the experimenter moved the rubber hand) or incongruent (i.e. the experimenter did not move the rubber hand) visual feedback. The outcomes, i.e. movement detection and agency were assessed using binary measures ("Has the hand moved?" and "Did you move it or was it someone else that moved it?" respectively).

Finally, the third aim of the current study was to investigate whether there is a relationship between feelings of ownership and agency in AHP patients and, if so, what is its direction. To do so, ownership and agency questions were used to divide AHP patients in subgroups according to i) their ownership feelings and ii) whether they felt agency over the movement. The first subgrouping aimed to explore whether agency influences feelings ownership of a rubber hand, while the latter investigated the opposite.

Due to a procedural error in the early administration of the task, the order was initially fixed and not counterbalanced. To remedy this issue and achieve an overall counterbalanced sample, the order of the condition in which the experimenter moved the rubber hand (congruent) and the condition in which the rubber hand stayed still (incongruent) was inverted in part of the sample (13/47) to avoid order effects.

Figure 5.1. Design and measures of the task. Patients' VoC was tested at three time points: at baseline, following congruent and incongruent movement. Movement detection and agency were investigated only following attempted movement with concomitant congruent (i.e. the experimenter moved the rubber hand) or incongruent (i.e. the experimenter did not move the rubber hand) visual feedback.

5.2.4. Materials and procedure

Right-hemisphere patients were tested in the hospital, either in bed or while sitting in a chair (Fotopoulou et al., 2008; Martinaud et al., 2017), whereas age-matched controls were tested in a laboratory setting. In all cases, a realistic left rubber hand was used to induce feelings of ownership following vision only in all the aforementioned groups as well as provide controlled visual feedback of movement (in right-hemisphere patients and age-matched controls).

In right-hemisphere patients, in order to position the rubber hand in an anatomically plausible fashion without the patient noticing, the experimenter directed patient's attention towards the right, while an assistant hid the patient's real hand under a pillow (directly beneath the rubber hand) and covered the rubber hand extremity (as illustrated in Figure 1). Once the set-up was finalised, the experimenter pointed to the rubber hand and asked the patient to maintain their gaze on it for 15 seconds and then proceeded to state whether or not the hand in front of them was theirs ("Is this your left hand?" – see Figure 1), followed up by a question asking to what extent they felt ownership of it ("To what extent do you feel this is your hand?") with ratings recorded on an 11-points Likert scale (ranging from 0="Not at all" to 10="Completely"). The way the questions have been phrased opens up to an important differentiation: whilst the first question ("Is this your hand?") directly tackled patients' beliefs about their own body, the second question ("To what extent do you feel this is your hand?") explored feelings of ownership, which do not necessarily translate into patients believing that the rubber hand was their real hand (Tame, Linkenauger and Longo, 2019). Following the baseline assessment of ownership of the rubber hand, the second phase of the experiment began. Patients were instructed to try and perform a movement with their paralysed limb as soon as the experimenter tapped on the table in front of them. In the congruent condition (i.e. with movement), the assistant experimenter lifted the rubber hand as if the patients successfully moved it and then proceeded to ask the motor detection, agency and ownership questions (as detailed above – Figure 5.2). In the incongruent condition (i.e. no movement), no visual feedback of movement was provided following the attempted movement, but the same questions were asked following a brief pause, equivalent to the time taken to move the hand in the congruent conditions.

Age-matched healthy controls were tested in a lab setting and they were comfortably seated in a chair in front of a table. In order to resemble as closely as feasible hemiplegic patients' motor weakness, participants' left hand was temporarily restrained with two straps, one to keep participants' forearm adhered to the table and one to prevent movement of the fingers (with exception of the thumb). Participants' real hand was then covered with a pillow and positioned the rubber hand (as in Figure 2). The same questions outlined above regarding ownership were asked following 15 seconds of exposure to the rubber hand.

5.2.5. Statistical analysis

All the data reported below are measured either at the nominal or ordinal level. Hence, Chi-squares (Likelihood ratio statistic) were employed to test for significant associations with subsequent examination of odds ratio (Field, 2017) as a measure of effect size in the case of a significant relationship between the investigated variables (corrected with Haldane-Anscombe in case of a 0 cell count; Anscombe 1956; Haldane, 1956). In all the analyses reported below, the exact, rather than the asymptotic, significance (2-sided) is used. Data were analysed using the IBM Statistical Package for Social Sciences (SPSS) for Windows, version 25 (Armonk, NY) and plotted using the "*ggplot2*" package for R (Wickham, 2016).

5.2.6. Lesion analysis

CT or MRI scans were obtained during the first days of patients' admission to the hospital wards. Five patients were excluded from the lesion analysis because of missing or unreadable scans. Lesions were manually delineated using the methods detailed in Martinaud and colleagues (2017). In order to ensure consistency between drawings of the previously reported (Martinaud et al., 2017) and additional patients, all lesions were re-drawn by a researcher (VM) and subsequently checked (to ensure accuracy) by a second researcher (SB), both blind to the patients grouping.

In order to examine the neural correlates of VoC, a Voxel-based Lesion Symptom Mapping (VLSM; Bates et al., 2003) analysis was conducted on the 11-points (0-10) VoC scores (0-10) taken at three time points: i) baseline – prior to any movement (N=39; 10 AHP, 7 AHP+DSO, 9 DSO, 13 HP), and following visual feedback that was either ii) congruent iii) incongruent with the requested movement (N=37; 10 AHP, 7 AHP+DSO, 8 DSO, 12 HP). Brünnel-Menzel tests were used for ordinal and continuous data included in the NPM (non-parametric mapping) package of MRICron (Rorden and Brett, 2000). The advantages of a VLSM approach, which consists in analysing voxels associated with cognitive deficits and comparing patients with and without a lesion in the identified voxels regardless of patients' a priori grouping, have been detailed elsewhere (Martinaud et al., 2017). Analysis were initially corrected for multiple comparisons using the permutation method (2000 permutations) and, to ensure adequate statistical power, included only voxels in which at least the 10% of the patients presented with lesions (Sperber and Karnath, 2018), however, using these strict criteria, none of the analysis survived statistical thresholding, therefore, the lesion data reported in the results section are uncorrected and for illustrative purposes only.

For further illustrative purposes of the lesion size and type, group-level overlays were produced by superimposing lesions of patients from each subgroup on the MRICron (ch2bet.nii.gz) template. As reported in Figure 5.2 below, lesions were mainly in the frontal, temporal and parietal lobes, the insular cortex as well as subcortical areas (e.g. basal ganglia) as documented via CT or MRI scans. All groups showed equivalent high lesion variability (in line with the literature; e.g. Moro et al., 2016; Vocat et al., 2010).

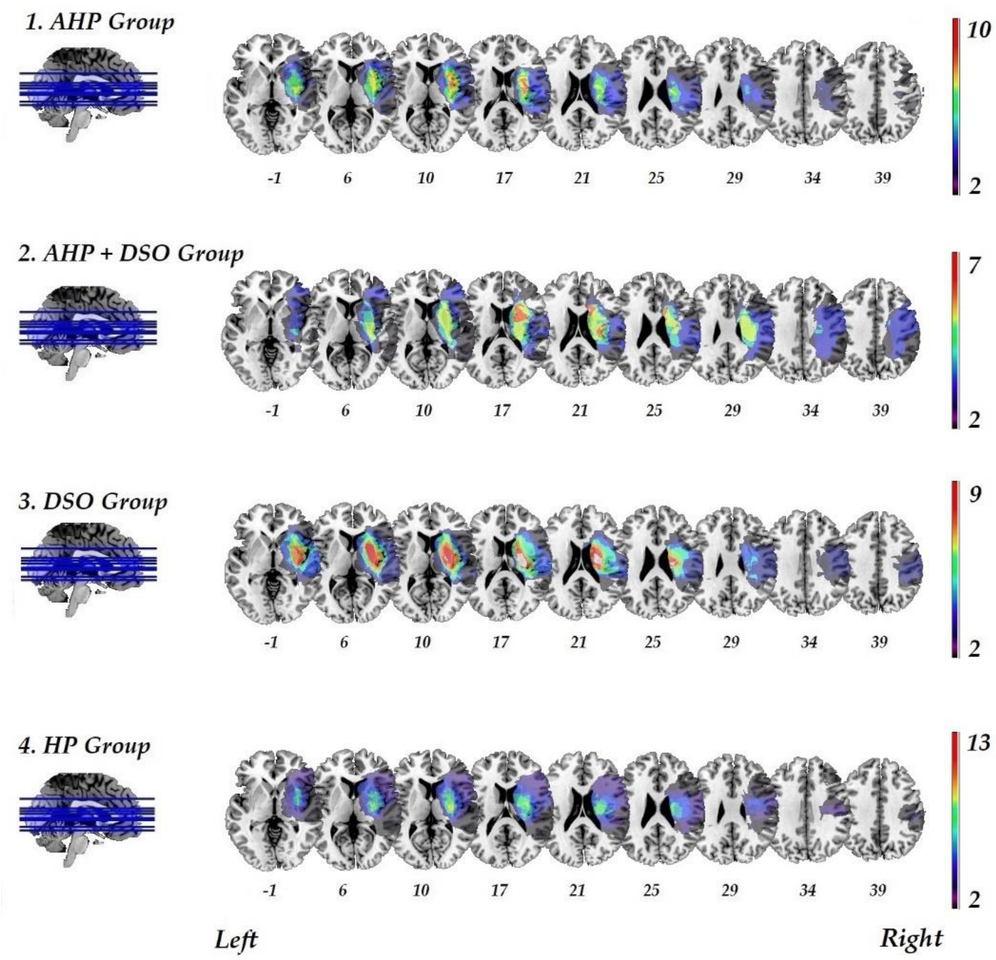


Figure 5.2. Group-level overlay of lesions in MNI coordinates for 1. AHP (N=10), 2.AHP+DSO (N=7), 3.DSO only (N=9) and HP (N=13) patients. The number of patients with overlapping lesions is signalled by the changes in coloration (see bar on the right).

5.3. Results

5.3.1. Demographics and neuropsychological results

An independent-samples Kruskal-Wallis test was conducted on demographic and neuropsychological data to investigate differences between the groups. As expected, a significant difference between the groups on awareness and ownership assessments was found (Berti Interview: $\chi^2_{(3)}$ = 39.011, *p*<0.001; Feinberg Awareness Questionnaire: $\chi^2_{(3)}$ = 31.596, *p*<0.001; Cutting Questionnaire: $\chi^2_{(3)}$ = 33.734, p<0.001). A significant difference on personal (One-item test: $\chi^2_{(3)}$ = 13.714, p=0.003) and extra-personal neglect (Star cancellation: $\chi^2_{(3)}$ = 11.060, p=0.011; Line cancellation: $\chi^2_{(3)}$ = 10.556, p=0.014) tests was also found.

To explore the direction of the abovementioned differences, post-hoc Mann-Whitney U tests (with α=0.01 to accommodate for multiple comparisons) were conducted between the groups (see Table 5.1 below), identified according to their clinical diagnosis. In line with the predictions, AHP patients (with and without concomitant DSO) showed significantly less awareness of motor impairments as tested via the Berti and Feinberg assessments in comparison with the other two groups (Berti interview: AHP vs HP: Z =-5.232 , p<0.001; AHP+DSO vs HP: Z= -4.937, p<0.001; AHP vs DSO: Z= -3.623, p<0.001; AHP+DSO vs DSO: Z=-3.367, p<0.001; DSO vs HP: Z=-2.550, p=0.176; Feinberg questionnaire: AHP vs HP: Z = -4.328 , p<0.001; AHP+DSO vs HP: Z= -3.874, p<0.001; AHP vs DSO: Z=-3.813, p<0.001; AHP+DSO vs DSO: Z=-3.431, p<0.001; DSO vs HP: Z=-1.284, p=0.229). The AHP+DSO group also showed significantly higher values in response to the Cutting questionnaire, aimed at detecting asomatognosia and somatoparaphrenia, in comparison with both controls and pure DSO (AHP+DSO vs HP: Z=-4.743, p<0.001; AHP+DSO vs DSO: Z=-3.112, p=0.002). However, pure AHP and pure DSO patients did not significantly differ from controls nor from each other (AHP vs HP:

Z = .816, p=0.819; AHP vs DSO: Z=2.494, p=0.095; DSO vs HP: Z=-2.436, p=0.106). The latter result may be possibly due to inability of this test to capture more subtle nuances of this disorder which can become clear during extensive clinical interaction and qualitative assessment (see Jenkinson et al., 2018).

Patients with AHP and concomitant DSO presented with higher scores of personal neglect in comparison with pure DSO patients (One item test: AHP+DSO vs DSO: Z=-3.112, p=0.002), whereas all the other comparisons were non-significant (AHP vs HP: Z=-.949, p=423; AHP+DSO vs HP: Z=-2.251, p=0.038; AHP vs DSO: Z=-2.763, p=0.017; DSO vs HP: Z=2.036, p=0.103). Furthermore, AHP and AHP+DSO groups also showed significantly more extra-personal neglect in comparison with controls but not pure DSO (and with no difference between controls and DSO) as investigated via two sub-component of the BIT test (Star cancellation: AHP vs HP: Z=-2.573, p=0.009; AHP+DSO vs HP: Z=-2.973, p=0.002; AHP vs DSO: Z=-.662, p=0.545; AHP+DSO vs DSO: Z=-1.108, p=0.279; DSO vs HP: Z=-1.421, p=0.169; Line cancellation: AHP vs HP: Z=2.417, p=0.017; AHP+DSO vs HP: Z=2.642, p=0.008; AHP vs DSO: Z=-.212, p=0.837; AHP+DSO vs DSO: Z=0.464, p=0.694 DSO vs HP: Z=2.129, p=0.041). Personal neglect was controlled for during the experiment by making sure patients were attending to their left side.

Table 5.1. Groups' demographic and neuropsychological profile.

	AHP			AHP+DSO			DSO			HP			Mann-Whitney
	n	Median	IQR	n	Median	IQR	n	Median	IQR	n	Median	IQR	*p*
Age (years)	12	75.5	19	8	69.5	20	9	72	21	18	65.5	25.5	*NS*
Gender (Male/Female)	12	3/12		8	3/8		9	5/9		18	12/18		*NS*
Education (years)	9	12	4	8	12	3.75	5	10	5.5	16	12.5	4.75	*NS*
Days from onset	12	9.5	10.75	8	6.5	9.25	9	6	6	18	9.5	21.25	*NS*
MRC LUL (max 5)	12	0	0	8	0	0	9	0	0	17	0	1	*NS*
MRC LLL (max 5)	12	0	1	7	0	0	6	1	2	16	1	2	*NS*
Berti - Awareness interview (max 3)	12	2	1	8	2	0.75	9	0	1	18	0	0	* # ¤
Cutting questionnaire	12	0	0	8	2	0	9	0	1	18	0	0	# ¤
Feinberg - Awareness scale (max 10)	12	6.25	4.88	8	6.5	4.38	9	1	1.25	16	0.25	2.13	* # ¤
Orientation (max 3)	11	3	0.5	7	3	0	3	3	1	15	3	0	*NS*

Digit span forward (max number repeated)	12	6	1.75	8	6	1	9	6	4	15	6	2	*NS*
Digit span backwards (max number repeated)	12	3	2	8	3	2	9	3	3.5	15	4	3	*NS*
IQ-WTAR (max 50)	6	40.5	17.5	5	38	24	3	30	26	4	33.5	11.25	*NS*
MOCA (max 30)	5	23	7	3	19	6	6	9.5	10	6	22.5	6	*NS*
Visual fields (max 6)	9	3	3.5	7	4	4	2	1.5	*n/a*	11	4	4	*NS*
Somatosensory (max 6)	9	3	2	7	2	4	2	5	*n/a*	11	2	2	*NS*
Proprioception (max 9)	11	3	3.75	8	4	3.5	8	3	1.75	12	7	2	*NS*
Comb/razor test bias (% bias)	12	-0.33	0.48	8	-0.35	0.21	8	-0.24	0.37	15	-0.29	0.55	*NS*
Comb/razor test left (number of strokes)	12	5	8	8	3.5	5.75	8	6.5	7	15	6	6	*NS*
Comb/razor test right (number of strokes)	12	12	8.5	8	13	11.75	8	15	5.75	15	13	5	*NS*
Comb/razor test ambiguous strokes	12	5	4	8	7	3.25	8	8.5	4	15	6	5	*NS*
Bisiach one item test (max 3)	12	1	1	8	1	1	7	0	0	16	0	1	¤
Star cancelation (max 54)	11	41	7	8	43	7.75	8	36.5	34.75	15	15	27	* #
Line bisection (max 9)	11	1	3	8	0	2.75	7	1	5	15	3	1	*NS*
Line cancelation (max 36)	12	15.5	25	8	12.5	14.25	7	14	14	18	32	18	* #
Copy (max 3)	11	0	1	8	0	1.38	5	0	1.5	17	1	3	*NS*
Representational drawing (max 1)	10	0	0.25	7	0	1	5	1	1	16	1	1	*NS*
Cognitive estimates (max 30)	8	16.5	6	4	20.5	9	2	13.5	*n/a*	8	12	8	*NS*
FAB total score (max 18)	8	10.5	4	5	13	3	4	12.5	7.75	11	13	5	*NS*
HADS depression (max 21)	12	5	6.75	6	6.5	6.5	5	9	11.5	11	8	6	*NS*
HADS anxiety (max 21)	12	6	4.5	6	9	8.25	5	11	10	11	7	6	*NS*

AHP = Anosognosia for hemiplegia; DSO = Disturbed sensation of limb ownership; HP = Hemiplegic patients; n = number of patients; IQR = Inter-quartile range; MRC = Medical Research Council scale; WTAR = Wechsler Test of Adult Reading; MOCA = MOntreal Cognitive Assessment; FAB = Frontal Assessment Battery; HADS = Hospital Anxiety and Depression scale. NS = not significant for all comparisons (Bonferroni corrected Mann-Whitney U tests, α=017). *significant differences between AHP and HP groups $p < 0.001$; # significant differences between AHP+DSO and HP groups $p < 0.001$; ¤ significant differences between AHP+DSO and DSO groups $p < 0.001$; § significant differences between DSO and HP groups $p < 0.001$.

5.3.2. Behavioural experimental data

Visual capture of Ownership

To replicate and expand on the findings that right-hemisphere stroke patients have a high incidence of visual capture of a rubber hand (aim 1), VoC values taken at the beginning of the experiment (i.e. before any movement occurred) of binary ("Is this your left hand?") and scale ("To what extent do you feel this is your left hand on a scale from 0 to 10?") responses were analysed. As can be seen in Table 5.2 below, among all the 47 right hemisphere patients tested, 70% spontaneously embodied a rubber hand positioned in front of them without any touch involved (i.e. 34/47 right-hemisphere patients responded "Yes" when asked whether the rubber hand belonged to them). To assess potential differences in the frequency of VoC in the patients' groups, the scale measurement of ownership was used to classify patients according to whether ownership was present (i.e. ownership score $\neq 0$) or absent (score = 0) following mere visual exposure to the rubber hand and ran a Chi-square comparing the three groups (pure AHP vs DSO vs HP). No significant difference in the proportion of VoC was found across the groups ($\chi^2_{(2)} = 0.472$, p=0.845; $\phi_c = .101$ – figure 5.3).

Table 5.2. Frequencies of *VoC* by group

Groups	***"Is this your left hand?"***	
	Yes	*No*
AHP	9	3
AHP+DSO	6	2
DSO	7	2
HP	12	6

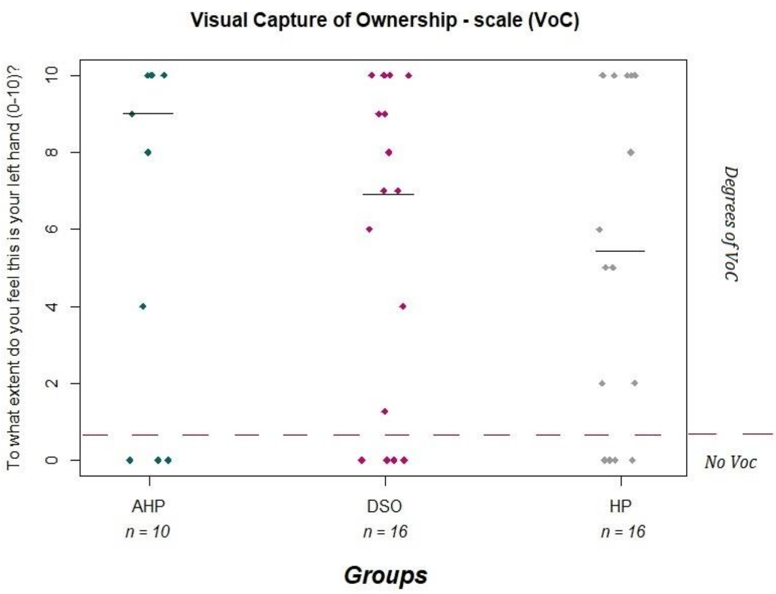


Figure 5.3. Degrees of VoC on a scale from 0 to 10. AHP+DSO patients are grouped with DSO patients. Values below 1 are considered as no ownership of the rubber hand (AHP: median= 8.5, IQR=10; DSO: median= 7, IQR=9; HP: median=5.5; IQR= 9.5).

To explore whether right-hemisphere patients were significantly more likely to report visual capture effects than age-matched controls, their binary ownership scores were compared. Results showed that 2/19 (11%) age-matched controls embodied a rubber hand without any touch being applied either to their own or the rubber arm. A Chi-square (Likelihood ratio) analysis was run which confirmed an association between this visual capture of ownership effect and groups ($\chi^2_{(1)}$ =24.335, p<0.0001, ϕ_C = .583). Specifically, right hemisphere patients were 16.22 times more likely than age-matched controls to have visual capture ownership of a rubber hand according to odds ratio.

Motor awareness and agency in right hemisphere patients

In order to test the second aim, that AHP (in comparison with HP) patients tend to detect the presence of a movement even when there is none (i.e. lack of motor awareness) and tend to experience agency over such movements when they intend to move, four Chi-squares (using the Likelihood ratio statistics when cells count were less than 5) were run. As hypothesised, when no movement occurred, a significant relationship was found between group and condition ($\chi^2_{(1)}$ = 6.959 p=0.021; ϕ_C =.405), with the odds of AHP reporting the presence of a movement which did not occur being 11.27 times more likely than HP. However, there was no relationship between agency and group following the absence of movement ($\chi^2_{(1)}$ =3.175, p=0.180, ϕ_C =.282, p=0.180). Contrary to our hypothesis, the majority of AHP patients did not feel agency over intention-incongurent movements, despite having detected them. When investigating sense of agency over an occurred movement in AHP vs HP, a significant relationship was found ($\chi^2_{(1)}$ =6.974, p=0.022; ϕ_C =.422, p=0.022) with AHP patients being 5.65 times more likely to have agency over a detected movement in comparison with HP patients (see Table 5.3 below). No relationship between the ability to correctly detect the presence of an occurring movement and group was found (AHP vs HP) ($\chi^2_{(1)}$ =1.293, p=0.340; ϕ_C =.184, p=0.340), suggesting that both groups were able to report the occurence of the movement on their left side. This goes against the idea that AHP may be explained as a severe form of neglect.

Table 5.3. Frequencies of agency values per group per group

Groups	*"Was it you or was it somebody else that moved the hand?"*			
	Congruent movement		*Incongruent (i.e.no) movement*	
	Me	*Somebody else*	*Me*	*Somebody else*
AHP	14	6	6	14
HP	5	13	1	17

Agency and Ownership

This exploratory analysis aimed to investigate whether there is a relationship between sense of agency over rubber hand movements and feelings of ownership of it in anosognosia (N=16, accounting for missing data). If such relationship exists, the aim was to investigate its direction by devising two sub-groupings, one looking at effects of agency on ownership and a second one investigating the opposite. In order to do so, firstly ownership feelings according to presence/absence of agency were explored. Three subgroups of AHP patients were created based on their answers to the agency questions: patients who *always* had agency (i.e. those who responded "Me" to the question "Was it you or was it somebody else who moved the rubber hand?", regardless of the presence or absence of rubber hand movement); patients who *never* had agency (i.e. patients who responded "Somebody else" to the question "Was it you or was it somebody else who moved the rubber hand?", regardless of the condition); and patients who *changed* their agency score as a result of the presence or absence of rubber hand movement (i.e. those who responded "Me" to the question "Was it you or was it somebody else who moved the rubber hand?" when the hand moved but responded "Somebody else" when there was no movement). Then, their responses to ownership questions, both binary yes/no responses ("Is this your left hand?": Yes [incorrect response] vs. No [correct response]) and scale ratings ("To what extent do you feel this is your left hand from 0 to 10?"), were analysed in order to see whether feeling ownership of the rubber hand would be influenced by agency feelings in the different experimental conditions.

A significant relationship between agency and ownership (indexed by the binary Yes/No responses) following movement of the rubber hand was found ($\chi^2_{(2)}$ =8.712, p=0.020; ϕ_c =.713, p=0.020), with AHP patients being more likely to feel ownership of the rubber hand rather than not, regardless of their subgrouping. Patients who changed their agency scores following congruent feedback were 2.66 and 10.66 times more likely to have ownership of the rubber hand than the “always” and “never” agency groups respectively. As for the no movement (i.e. incongruent) condition, the association between agency and ownership values was significant ($\chi^2_{(2)}$ =10.473, p=0.010, Cramer’s V: ϕ_c =.772, p=0.010), with AHP patients in the “change” group being 14 times more likely to have ownership in comparison with those in the “always” group and 56 times more than the “never agency” group, suggesting that patients who never experienced agency were less likely to feel ownership of the rubber hand (see figure 5.4 below).

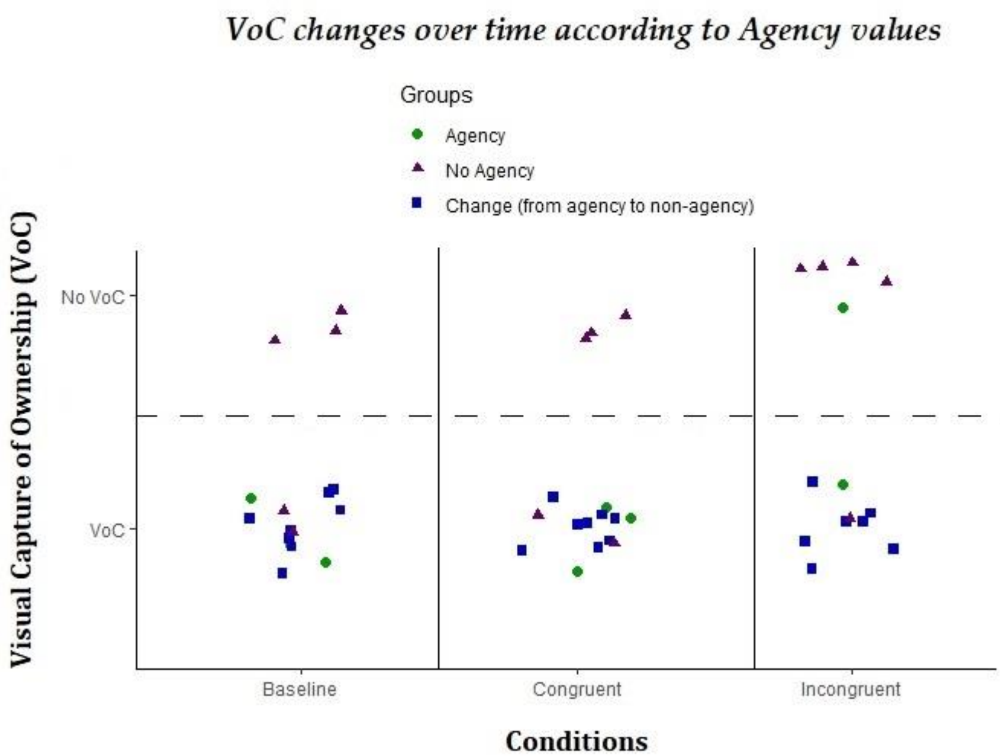


Figure 5.4. AHP patients were divided in 3 subgroups, i.e. those who had agency in both, those who didn’t and those who changed their score following the incongruent condition. These 3 groups were then further divided according to whether patients had VoC or not at the three time points (baseline, following congruent/incongruent feedback) in order to visualise the relationship between agency and VoC changes.

The 0-10 rating values obtained following the question “To what extent do you feel this is your left hand from 0 to 10?” were then analysed, categorising AHP patients (N=13 accounting for missing data) as having high values of ownership when they were equal or above 5 and low when they were below 5 using the analysis described above. No relationship was found between high and low VoC values and feelings of agency following the movement condition ($\chi^2_{(2)}$ =3.577, p=0.315; ϕ_c =.507, p=0.315), which suggests that some patients may present with lower strength of feelings of ownership than otherwise suggested by the binary Yes/No response. As for the incongruent condition (i.e. no movement of the rubber hand), a relationship between high and low values of VoC and the agency grouping was found ($\chi^2_{(2)}$ =7.199, p=0.041, ϕ_c =.698, p=0.041), with patients in the “change” group being 24 times more likely to have high rather than low ownership values even when they correctly detected absence of movement and did not report feeling agency over it, than patients in the “never agency” group (showing lower levels of VoC overall). The only patient in the “always agency” group reported low values of ownership following the no movement condition, with a clear drop between conditions (see Figure 5.5 below).

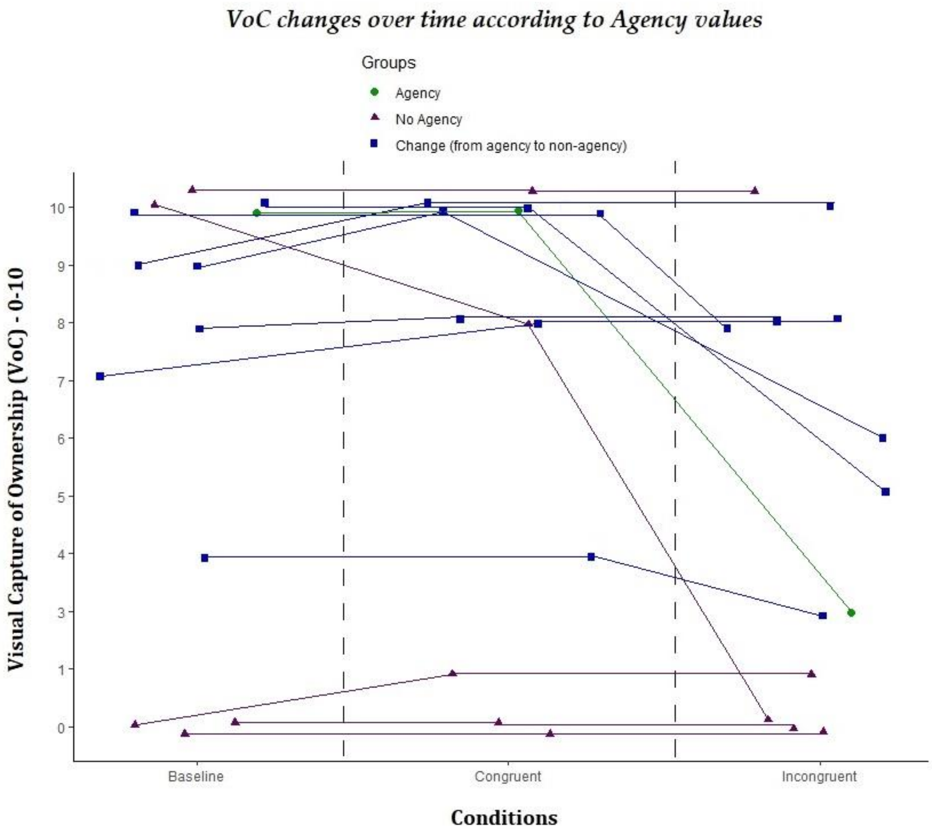


Figure 5.5. As illustrated in figure 6 above, AHP patients were divided in the same 3 subgroups and then further split according to their VoC values on a scale from 0 (No VoC) to 10 (complete VoC). Patients who never change agency (in red) are less likely to change ownership from baseline to incongruent conditions, whereas patients who changed agency scores (in blue) tend to drop their ownership values following incongruent movement even if they still maintain VoC (i.e. they have ownership but the incongruent feedback weakens VoC).

Secondly, in an attempt to further investigate the relationship between agency and ownership, patients were grouped according to whether they had ownership of the rubber hand or not following absence or presence of movements separately. These sub-groupings were used to explore changes in agency given presence or absence of ownership. 4 patients were excluded from the AHP group (3 of them were tested with incongruent first and 1 did not present with consistent VoC values at baseline and in the congruent condition), 1 patients from the DSO group (who had missing data on the second agency score), 3 from the HP groups (who could not be grouped based on lack of consistency in VoC values at baseline and in the congruent condition, i.e. they changed their score following congruent movement). The reason why patients were excluded based on congruency between baseline and the movement conditions was due to the fact that the aim was to explore differences in agency in patients with presence of ownership at baseline which was maintained during the congruent condition, yet not elicited by it. A significant relationship in the AHP group (N=16) between ownership and agency values following movement of the rubber hand was found ($\chi^2_{(1)}$ =8.712, p=0.018, ϕ_c =.713, p=0.018), with the odds of AHP patients with ownership to also have agency following movement being 22 times higher than those without ownership. When no movement occurred, the relationship between ownership and agency did not yielded significant results ($\chi^2_{(1)}$ =1.397, p=0.582, ϕ_c =.231, p=0.582), in line with the idea that the majority of the AHP patients did not report seeing a movement when it did not occur (and for which, in turn, they showed no agency – see figure 5.6 below).

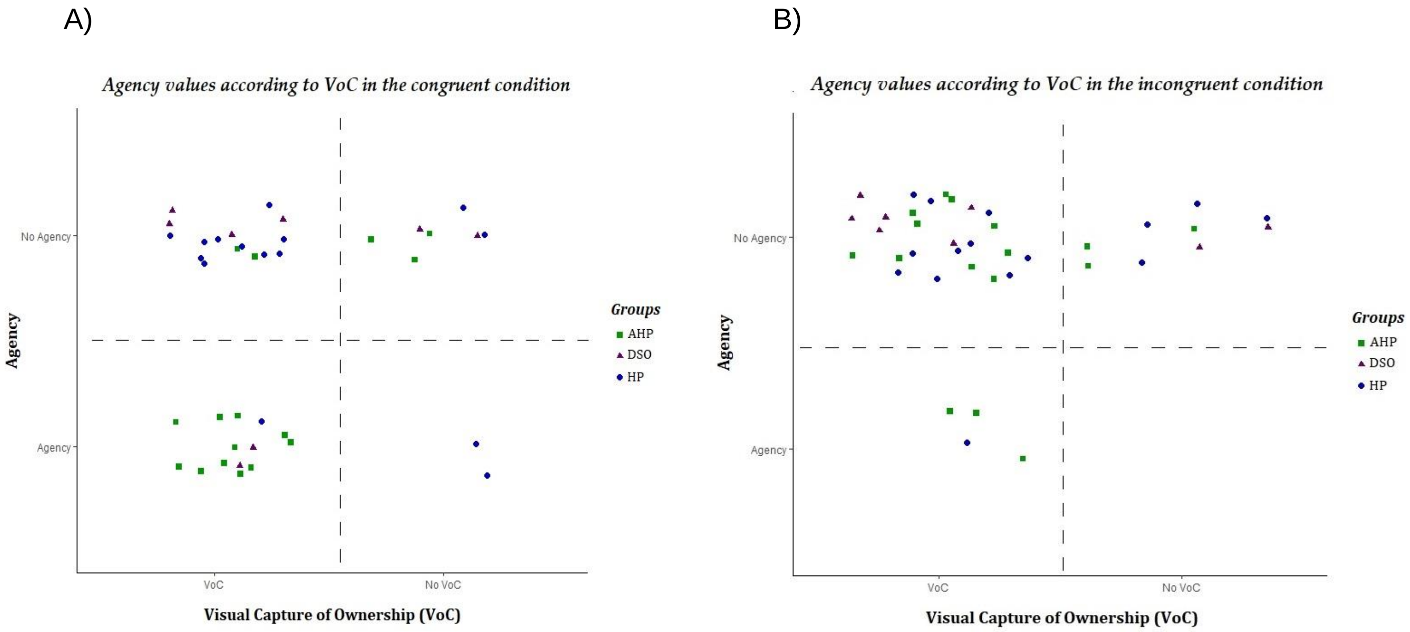


Figure 5.6. Agency scores (binary responses to the question "Was it you that moved the hand or was it somebody else?", where the answer "Me" would be categorised as agency and the answer "Somebody else" as no agency) and VoC scores according to A) congruent and B) incongruent conditions. Data from the three different groups are reported for illustratory purposes (AHP, including AHP + DSO, DSO and HP).

5.3.3. Lesion mapping analysis

As mentioned in section 5.2.6 above, when correcting for multiple comparisons using permutation methods, none of the analyses performed were significant. The uncorrected results are reported below for illustrative purposes and, as such, any conclusion based on these results should be considered cautiously. In Figure 5.7 below, the results of the VLSM investigating lesions associated with greater levels of ownership of the rubber hand at three different time points are reported. Specifically, ownership ratings were taken at baseline, following movement of the rubber hand (i.e. congruent feedback) and following lack of movement of the rubber hand (i.e. incongruent feedback) and measured via a 11-points scale, ranging from 0-10. These analyses suggest that greater visual capture of ownership is associated with damage in the basal ganglia, specifically the globus pallidus and the right putamen (in both baseline, Figure 5.7A, and following congruent movement, Figure 5.7B), the amygdala and the hippocampus (in baseline conditions prior to any movement attempts, Figure 5.7A), with an additional involvement of the insular cortex in producing visual capture following congruent visual feedback (Figure 5.7B). In addition to the above mentioned areas, patients showing VoC following incongruent movement also presented with lesions in the frontal inferior operculum (Figure 5.7C).

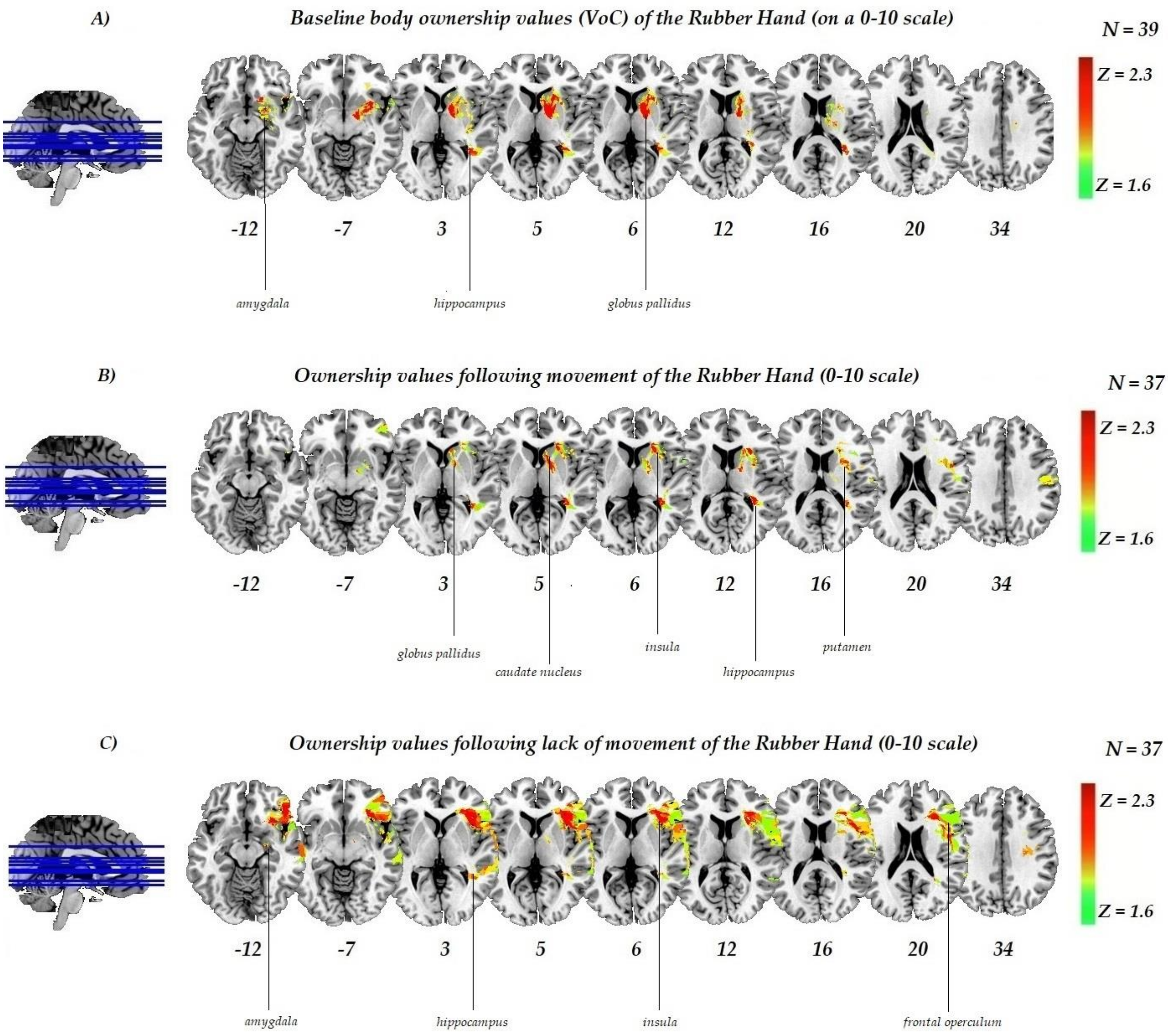


Figure 5.7. VLSM on VoC values in right-hemisphere patients at A) baseline; B) following congruent and C) incongruent feedback. The Z scores range reported in the figure is uncorrected p < .05 for z > 1.6.

Finally, the overlay of lesions of the 5 AHP patients who showed agency following lack of movement (i.e. abnormal agency) were compared with the 13 AHP patients who did not experience agency. As can be seen in Figure 5.8 below, all the 5 patients showing agency over the incongruent movement (but not necessarily VoC – 3/5 have VoC) had lesions in the rolandic operculum, right insula and right putamen (Figure 5.8A). As for the AHP patients who did not show agency, lesions were concentrated in the same areas (plus the caudate nucleus) in 10/13 patients (Figure 5.8B).

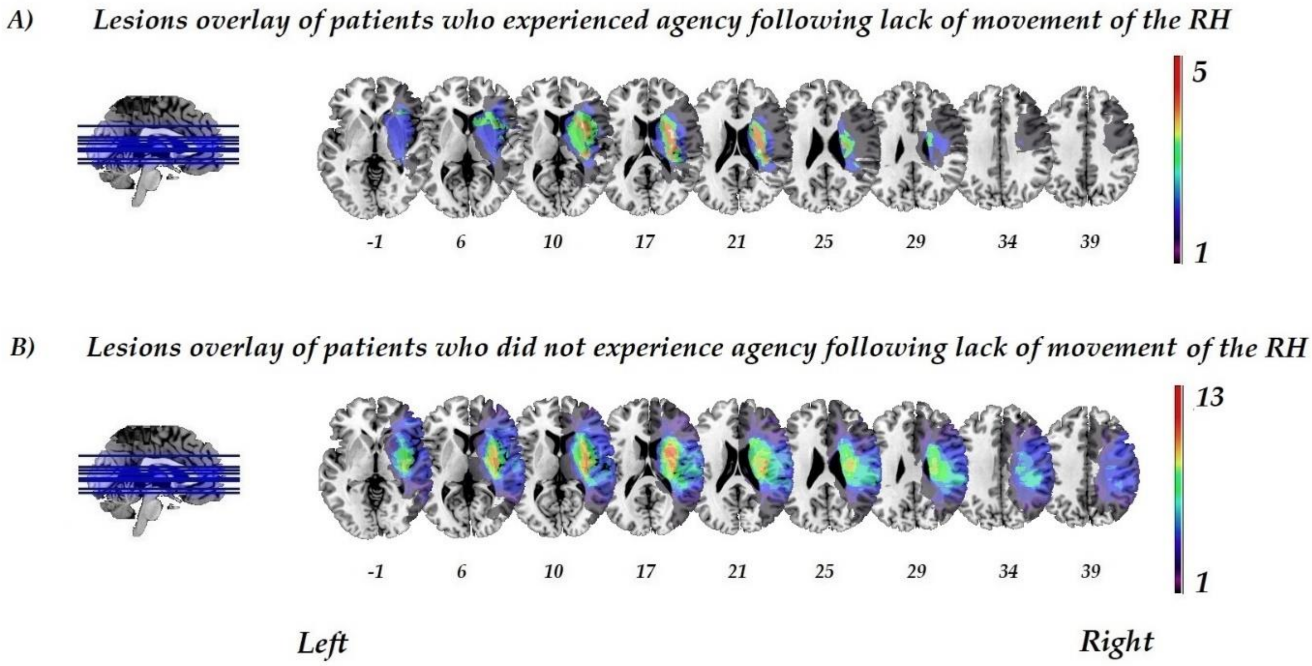


Figure 5.8. Groups overlay of AHP patients A) who showed agency and B) those who did not show agency over a movement which did not occur.

5.4. Discussion

The first aim of the current study was to replicate in a larger sample and expand in scope previous results regarding the neuropsychological mechanisms of fundamental aspects of the bodily self, such as the sense of motor awareness, agency and body ownership. Specifically, three hypotheses were investigated. The first was based on the finding that right-hemisphere patients tend to embody a realistic rubber hand seconds after it is placed in front of them. Thus, it was hypothesised that right-hemisphere patients would embody a motionless rubber hand i) regardless of their presence/absence of disorders of the self and ii) significantly more than age-matched controls. Firstly, as predicted, the majority of right-hemisphere patients experienced VoC, regardless of their clinical symptoms related to disorders of the self (i.e. AHP/DSO/HP). That is, AHP and, more importantly, control patients, presented with visual capture of the rubber hand, despite not showing dis-ownership over their own hand. Furthermore, the majority of the DSO patients showed VoC over a rubber hand, whilst still 'dis-owning' (i.e. not feeling ownership of) their own hand (3/9 DSO patients showed complete dis-ownership for their own arm according to Cutting's questionnaire and yet these same 3 patients automatically embodied the rubber hand). These results suggest that ownership of the rubber hand translated into beliefs that the rubber hand was part of patients' own body: in contrast with Tame and colleagues (2019), in the current study both questions about beliefs and feelings of ownership led to comparable answers. Even though in the current study the lesion analysis did not show significant results following statistical correction, a partial overlap with previous findings was identified in an exploratory analysis, with the frontal operculum, basal ganglia and insular cortex seemingly involved in feelings of ownership over a fake limb in right-hemisphere patients. Nevertheless, further research is needed in order to investigate the underlying neuroanatomical profile of VoC.

Secondly, ownership values from age-matched healthy controls were compared with right-hemisphere patients scores to explore whether visual dominance over proprioception could be due to normal ageing processes rather than a lesion-specific mechanism. As expected, VoC was significantly higher in patients with right hemisphere damage compared with healthy controls. The increased VoC found in right-hemisphere patients was not related to the presence (or absence) of DSO. The idea of increased malleability in body representation following right hemisphere stroke has been already put forward (Burin et al., 2015; Martinaud et al., 2017) and there are studies suggesting that, at least in a percentage of healthy individuals, vision can capture ownership, leading to embodiment of a rubber hand (Samad et al., 2015). In right-hemisphere stroke patients, this visual capture of ownership could be due to lesions impacting proprioceptive processing and thus compromising normal multisensory integration. In support of this, in all the four groups of patients (controls included), the majority presented proprioceptive impairment as well as lesions in the right insular cortex, a multisensory area linked to the establishment and maintenance of the sense of self (Blanke et al., 2015; Craig, 2002; 2009).

The second aim of the current study was to investigate whether AHP patients (vs HP) would detect a movement even when there is none (thus showing lack of motor awareness) and experience agency over it (Fotopoulou et al., 2008). In line with the hypotheses, in the intention-incongruent condition (i.e. lack of movement), AHP patients were far more likely to report occurrence of movement than HP. Previous studies (Fotopoulou et al., 2008) explained these findings as a dominance of motor intentions over actual motor output (i.e. “I want to move, hence I moved”), due to compromised motor monitoring abilities in anosognosic patients. Such explanation holds true for the current study: AHP patients showed lack of awareness when they had the intention to move and no movement occurred. However, contrary to the predictions, motor unawareness was not accompanied by associated sense of agency: AHP patients did not significantly show higher agency when no movement occurred in comparison with HP. Nonetheless, a subset of AHP patients still reported agency in intention-incongruent conditions (in line with reported behaviour of anosognosic patients; Jenkinson and Fotopoulou, 2014) and qualitative investigation of the data revealed that only 1 control patient reported agency over a movement which he did not even detect, suggesting the presence of confabulatory behavior. Finally, as predicted, in intention-congruent conditions, the majority of right hemisphere patients detected the presence of a movement when occurring in the contra-lesional side, thus ruling out the hypothesis that VoC may be due to neglect. In terms of agency, as predicted, AHP patients were more likely than HP patients to feel agency over the rubber hand movement. Future studies could expand on the lack of agency found in AHP patients following intention-incongruent conditions by increasing the number of trials and thus increasing the possibility of detecting confabulatory behaviours.

To further investigate whether there is a relationship between ownership and agency (aim 3), and what its direction may be, in the AHP group possible modulations of ownership on agency (and vice-versa) were explored. Results of this exploratory analyses suggest that even when patients do not experience agency over a movement (i.e. following intention-incongruent conditions), they still maintain ownership over the fake arm. However, at the same time, patients who never experienced agency over the congruent movement also did not show ownership of the rubber hand, suggesting a link between agency and ownership but not a clear direction (i.e. none of them is necessary for the other to occur). No relationship between high and low ownership values and agency following movement of the rubber hand was found, suggesting that some patients may present with lower ownership “strength” than otherwise suggested by the binary Yes/No response. As for the no movement condition, the sub-group of patients who changed their agency from intention-congurent (i.e. movement) to intention-incongruent (i.e. no movement) conditions had higher VoC, even when they correctly detected absence of movement and did not report agency over it, in comparison with patients who never experienced agency (who consistently showed low levels of VoC overall). Patients who never changed their agency scores tended to be less likely to change ownership values from baseline to the no movement condition. Conversely, patients who changed their agency score from congruent to incongruent conditions (i.e. the had agency over the movement in the congruent but not in the incongruent condition) remained relatively stable within the high and low categories of ownership but still drop their ownership values when the feedback is incongruent with their motor expectations. Moreover, patients tended to report overall higher VoC and agency scores in the congruent condition, whereas, even when they did not report feelings of agency following the incongruent condition, the majority of the patients still maintained VoC of the rubber hand. Taken together, these findings suggest that ownership may be modulated by agency (i.e. when there is no agency, ownership is less strong), but not necessarily so. This is in line with the idea that agency can be influenced by the sensory integration of internal and external changes (e.g. presence vs absence of a movement), whereas ownership over a fake limb may be linked to a top-down visual dominance, suppressing bottom-up information (Tsakiris et al., 2006; Burin et al., 2019). Further research is needed in order to determine the direction of the relationship between top-down and bottom-up aspects of ownership and agency both in the healthy and the stroke populations.

Findings of the current study confirm that Visual Capture of Ownership may be linked to a dominance of visual signals over other sensory modalities, possibly due to a compromised multisensory integration process following lesions in the right fronto-parietal areas. Furthermore, some insights into the relationship between agency and ownership in anosognosia in the context of willed movements were identified: whilst agency seems to be more susceptible to contextual changes (i.e. presence of movement), ownership feelings are more stable, possibly due to a top-down suppression of incoming sensory information (i.e. presence or absence of movement).

In this chapter, the multisensory integration processes leading to body ownership and motor awareness in patients with dis-ownership and unawareness of their motor deficits were investigated. In the next chapter, the possibility of a modulation of ownership and motor awareness based on the perspective from which patients observe themselves (i.e. either from their 1st person perspective or from a 3rd, external, one) will be examined.

Chapter 6

Motor awareness and body ownership from different spatial perspectives

6.1. Introduction

Early work in the field of Anosognosia for Hemiplegia (AHP; Babinski, 1914) established that providing patients with direct visual or somatosensory feedback of their paralysis did not lead to an improvement in awareness (e.g. Ramachandran & Rogers-Ramachandran, 1996). This was explained as a dominance of motor intentions over sensory feedback: when patients are asked to move, they disregard mismatching sensory inputs signalling that the action did not occur (Berti & Pia, 2006; Fotopoulou, 2014). When AHP patients are confronted with their motor weakness, they may create confabulatory accounts and alternative explanations (e.g. “I don’t feel like moving right now”) to justify the absence of movement of their left arm (Bisiach & Geminiani, 1991; Ramachandran, 1996). However, some AHP patients seem to be able to recognise paralysis in other patients (Moro, Pernigo, Zapparoli, Cordioli, & Aglioti, 2011; Ramachandran & Rogers-Ramachandran, 1996) and, whilst unable to acknowledge their weaknesses when confronted with them directly (e.g. “Can you move your arm?”), their awareness improves when questions are asked from the examiner’s point of view (e.g. “If I were you, could I move my arm?”; Marcel, Tegnér, & Nimmo-Smith, 2004).

These findings led to the idea that AHP might involve an impairment of the first-person (i.e. directly experienced) representation of the body, whilst a third-person representation (i.e. the body as seen from the outside) remains intact but is unable to inform and update awareness of the body and its motor ability. Such an impairment in perspective-taking has also been described in other psychiatric (e.g. schizophrenia; Langdon, Coltheart, Ward, & Catts, 2001) as well as neurodegenerative disorders (e.g. Alzheimer's; Marková, Laczó, Andel, Hort, & Vlček, 2015), entailing dissociations between individuals’ perception and external, “objective”, accounts (e.g. during a psychotic episode in schizophrenia). In a single case report of a patient with chronic AHP, Fotopoulou and colleagues (2009) video-recorded the patient during a formal assessment of motor awareness, including questions assessing the patient's ability to recognise her motor deficits prior to any request to move (i.e. anticipatory awareness, e.g. "Can you move your left arm?") as well as questions following confrontation with the disability (i.e. emergent awareness, e.g. "Please try to move your left arm. Have you done it?"). During the assessment, the patient consistently denied her paralysis and remained convinced of her ability to perform bimanual tasks (e.g. clapping her hands) without help, despite existing evidence that, in some cases, repeated confrontation with AHP patient's impairment may improve their motor awareness (i.e. emergent awareness is better than anticipatory; Berti, Làdavas, & Della Corte, 1996). However, when the examiners showed her the video-replay of her previous assessment (immediately after it), she instantly and permanently acknowledged her weakness ("I have not been realistic about my left-side not being able to move at all". […] "The video. I did not realize I looked like this"; Fotopoulou, Rudd, Holmes, & Kopelman, 2009, p. 1258). Hence, the same assessment shown via an external, 3rd person perspective reinstated patient's motor awareness. Subsequent replications of this effect have found a significant improvement in awareness of motor deficits in two more patients (Besharati, Kopelman, Avesani, Moro, & Fotopoulou, 2015), although the generalisation of the effect across motor and awareness domains was not present in all patients. For example, some patients improved their awareness only for the body part (left arm) shown during the video self-observation but continued to believe that they could walk (Besharati et al., 2014). Furthermore, some of these patients improved immediately after the video-replay but returned to be unaware of their disabilities shortly thereafter. Thus, video-replay is a potential way of reinstating awareness in AHP patients; however, the reason why self-observation leads to such a variety of results remains to be understood and may be due to specific characteristics of self-observation in videoclips rather than to perspective-taking alone. Specifically, given that the video-replay was a recording of a real assessment the patient underwent, the possible explanations for these findings are either the change in perspective (from 1st to 3rd) and/or its 'offline' nature (i.e. the fact that when the video was played the patient did not intend to move).

In the studies reported above employing video self-observation, patients have been recorded whilst being asked to move by the experimenter and have been subsequently shown the video-replay.

However, while watching the clips, patients were not asked to perform a movement and were, therefore, not influenced by the consequences of “online” motor planning and monitoring. Given that one of the main explanations of AHP is that it may be the result of a dominance of motor intentions over sensory feedback (e.g. Fotopoulou et al., 2008), the lack of intention to move during self-observation in videoclips might explain this gain in insight. In fact, videos offer the unique opportunity to show patients how they behaved whilst their intention to move is not present (i.e. in an “offline” fashion). If AHP is the result of a compromised ability to monitor the outcome of one’s own actions while they are happening, the remission of unawareness following video-replays may be due to the lack of any action occurring rather than being only a result of implementing a 3rd person perspective. Nevertheless, no study to date used “online” perspective-taking protocols (such as via mirrors) to explore this possibility.

Similarly to AHP patients, patients with Disturbed Sensation of limb Ownership (i.e. DSO; Baier and Karnath, 2008) seem to be unable to integrate sensory feedback experienced in their 1st person perspective to update their body representation and hence feel ownership of their arm (Feinberg & Venneri, 2014). The idea that a change in perspective may improve body ownership in patients with dis-ownership has been investigated in two previous somatoparaphrenic patients (Fotopoulou et al., 2011). When viewing their own arm directly (i.e. from their 1st person perspective), these patients would attribute ownership of their own left limb to somebody else (in this instance, family members); however, when asked whether their left arm belonged to them whilst looking at it in the mirror (i.e. thereby implementing a 3rd person perspective, as experienced by an external observer), their ownership dramatically improved. Nonetheless, such improvement was only temporary and related to the presence of the mirror. Another single case study of a somatoparaphrenic patient further explored the possibility of using mirrors to reinstate ownership by testing the role of attention and space in such improvement (Jenkinson, Haggard, Ferreira, & Fotopoulou, 2013). Results suggests that when patients’ attention was drawn to the peri-personal space (i.e. the space directly surrounding individuals) using an audio cue, whilst looking at their arm in the mirror, the patient would regain ownership only in some of the trials. However, when patients’ attention was directed to the extra-personal space (i.e. the portion of space outside individual’s reach), the somatoparaphrenic patient always acknowledged ownership of her own hand. The aforementioned findings indicate that 3rd person perspective-taking may be at least partially spared in DSO patients, especially when attention is directed away from patients' body. However, no study to date confirmed this effect in a group of DSO patients (rather than a few single cases) nor whether it was lasting after the mirror was removed.

The abovementioned fluctuation in awareness following video-replay in AHP and the transient return of ownership via mirrors in DSO suggests that perspective-taking may not be the only mechanism at play. Rather than being due to employing a different perspective (from 1st to 3rd), these findings may be the result of a temporary integration of both perspectives, which in turn leads to a coherent representation of the body as well as the surroundings from the perceiver's point of view (Filimon, 2015). Accordingly, Serino and Riva (2017) hypothesised that a continuous syncing of egocentric (i.e. based on the perceiver) and allocentric (i.e. based on external landmarks) information is crucial to spatial navigation and bodily awareness. A key area allowing such syncing between frames of reference is the hippocampus, which may be responsible for creating an allocentric representation of space that still maintains a body-centred viewpoint (Behrendt, 2013). Such spatial representation may be informed by activity of other areas of the fronto-limbic circuit. For instance, a study by Zhang and colleagues (2012) suggested that the inferior frontal gyrus may be responsible, in healthy subjects, for converting world-based coordinates to viewpoint dependent ones. Hence, frontal areas may play a role in this translational process from allocentric to egocentric frames of reference, thus providing integration between allocentric and egocentric cues. As such, lesions in fronto-parietal areas may compromise the integration of these two different perspectives, even if they are individually spared, thus impairing the ability of DSO patients to distinguish between themselves and others (Saxe, Jamal, & Powell, 2006). However, research investigating differences in awareness and ownership following the integration of 1st and 3rd person perspective (i.e. both are made available to the individual) and the presence of only one perspective at a time (either 1st or 3rd) is lacking.

To summarise, the current study aimed to explore i) whether AHP patients' motor awareness would improve by looking at their own arm in a mirror vs direct view (whilst trying to perform a movement) and ii) whether feelings of ownership in DSO patients would ameliorate when looking at their own arm in a mirror vs direct view. In order to explore these possibilities, i) two main designs, investigating changes in AHP patients' motor awareness and DSO patients' feelings of ownership, and ii) two control designs, investigating the role of integration of 1st and 3rd person perspective on motor awareness and ownership vs 1st and 3rd person perspective only, were devised. In terms of the main aims, in AHP patients, higher emergent awareness (i.e. following failure to execute the movement) in comparison with anticipatory awareness (i.e. motor awareness before trying to perform a movement) in both views as well as increased anticipatory and emergent awareness in the mirror view were expected. In terms of DSO patients, higher ownership feelings were expected in the mirror view in comparison with the direct view. As for the two control designs, it was expected that the integration of 1st and 3rd person perspectives (in the mirror view, with direct view available) rather than 3rd person perspective only (with direct view blocked) would improve AHP patients' awareness and DSO patients' ownership. To do so, an extra condition was included, in which a subset of patients also completed a mirror condition whilst direct view of their own arm was blocked. Finally, neural correlates of improvements in awareness and ownership in the mirror versus direct view were explored. No study to date explored whether changes in awareness and ownership (or lack thereof) could be linked to specific brain lesions. Hence, change scores from the different blocks were analysed using lesion mapping techniques (see Chapter 5 for further details on VLSM).

6.2. Materials and Methods

6.2.1. Participants

Forty-seven adult neurological patients were recruited from acute stroke units in London. The same inclusion criteria detailed in section 5.2.1 (Chapter 5) were applied to select the sample. The sample consisted of 12 AHP patients (AHP group: 8 females, mean age = 70.25 years, SD = 16.54 years, age range: 36-88 years), 8 DSO patients (DSO group: 4 females, mean age = 64.88 years, SD

= 14.41 years, age range: 40-83 years), 7 patients with both AHP and DSO symptoms (AHP+DSO group: 4 females, mean age = 64.43 years, SD = 13.67 years, age range: 41-78 years) and 20 hemiplegic control patients (HP group: 6 females, mean age = 62.25 years, SD = 14.11 years, age range: 38-88 years).

6.2.2. Neurological and neuropsychological assessment

The study was approved by a National Health Service (NHS) Research Ethics Committee and all patients underwent neurological and neuropsychological assessment after they gave informed, written consent. The same tests described in Chapter 5 (as specified in section 5.2.2) were used to assess motor strength, proprioception, left-right disorientation, perceptual extinction; premorbid intelligence, general cognitive function, orientation and mood; working memory and executive functioning; and personal and visuo-spatial neglect.

6.2.3. Experimental study design

The main aims of the study were to investigate i) whether AHP patients' unawareness of motor deficits would improve following confrontation in the mirror vs direct view and ii) whether ownership feelings in DSO patients would improve following mirror vs direct view of their left limb. To do so, i) two main designs (to test changes in motor awareness and limb ownership) and ii) two related control designs (to check for the role of integration of 1st and 3rd person perspective on motor awareness and ownership) were devised.

The main *motor awareness* design was a 2 (Groups: AHP vs HP) x 2 (Visual feedback: direct view vs mirror view) x 2 (Time: Anticipatory vs Emergent awareness) mixed design. The main *limb ownership* design was a 2 (Groups: DSO vs HP) x 2 (Visual feedback: direct view vs mirror view) mixed design. All patients underwent the same set of questions. Ownership feelings were assessed via a question asked at the beginning of each block (direct or mirror view): Q1. "Is this your hand?". Awareness was assessed via 2 questions: one investigating motor awareness prior to a request to move (Q2. anticipatory awareness - “Can you move this arm?”) and one following attempted movement (Q3. emergent awareness - “Has the arm moved?”). All questions were scored on a 3-points scale (0= complete awareness/ownership/agency; 0.5=partial awareness/ownership/agency; 1= lack of awareness/ownership/agency).

In order to check for left-right confusion, patients were asked to identify whether the hand the experimenter was pointing at (either directly or in the mirror) was their left or right one (scored as 0 when patients correctly identified their left hand, 0.5 if they showed difficulties at first but managed to eventually distinguish them and 1 when they mistook heir left for their right hand). In all designs, statistical analyses were first conducted without patients with issues in right/left distinction in the mirror block to ensure these difficulties were not impacting the results. The same analyses were then re-run including these patients. In the main motor awareness design, patients with hand dis-ownership were included in the control group (and vice-versa for the main ownership design), in order to differentiate between mirror effects on anosognosia and on DSO.

Two additional control manipulations were devised to explore whether the integration of both 1st and 3rd person perspectives, in comparison with 3rd person perspective only, would further improve i) awareness in a 2 (Groups: AHP vs HP) x 2 (Time: Anticipatory vs Emergent awareness) x 3 (View: Direct vs Mirror vs 3rd pp only) mixed design in a subset of patients (N=12, AHP group=4, with 2 pure AHP and 2 AHP+DSO, and HP=8) (see Figure 6.1) and ii) ownership in a 2 (Groups: DSO vs HP+AHP) x 2 (Time: Pre vs Post) x 3 (View: direct vs mirror vs 3rd pp only) mixed design. In order to explore the latter, a subset of patients (N= 16, with 2 pure AHP patients, 1 AHP+DSO, 6 DSO and 7 HP) were asked whether they felt ownership of their left hand (Q6 – “Whose hand is this?”) followed by a question scored on an 11-points Likert scale, assessing degree of ownership (Q7 - “To what extent do you feel this is your left hand?” 0=”Not at all”; 10=”Completely).

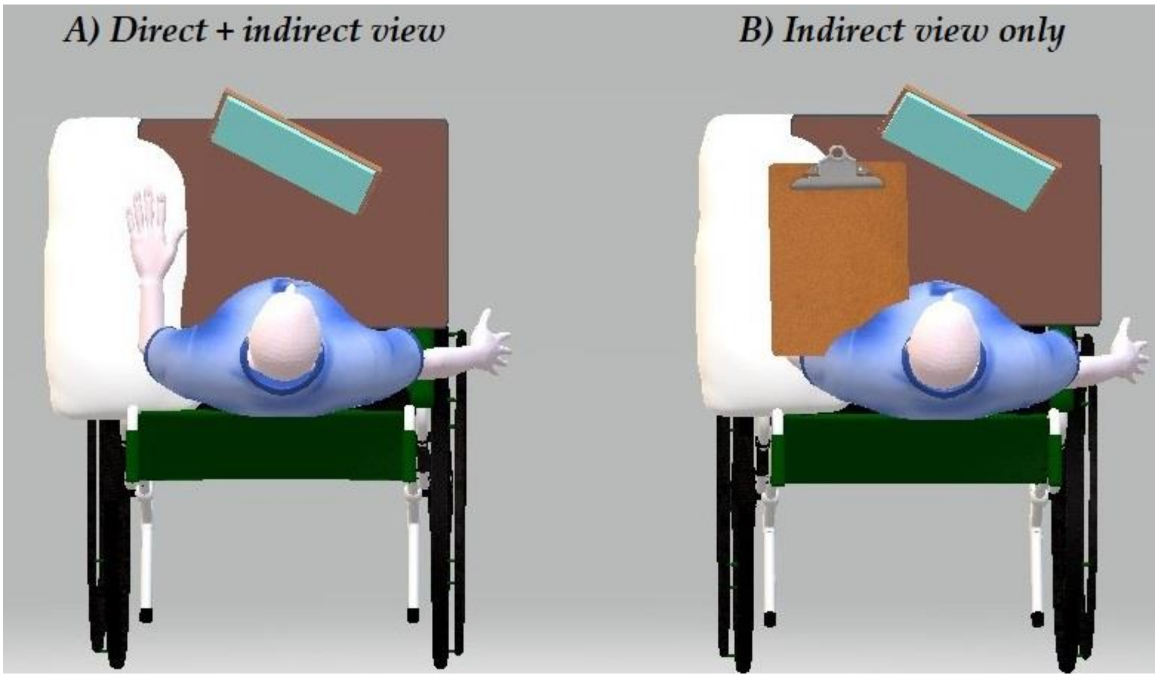


Figure 6.1. Set up of the task (panel A) and additional 3rd pp only condition (panel B). Panel A): Patients' are comfortably sat in a chair whilst their left, paralysed limb is kept in position on a pillow and the mirror is on the table, capturing the left limb. Panel B): patients' direct view of their own left arm is prevented by using a clipboard. The experimenter made sure patients were able to see their left hand in the mirror before proceeding with the questions.

6.2.4. Materials and procedure

The experiment involved a 36 cm x 25 cm single plane mirror and a 34 x 23 cm black clipboard (used during the 3rd person perspective only block). During the experiment, patients sat upright in their bed or an armchair. The left arm was positioned comfortably to the left of the patient's midline with the hand extending to the mid-sagittal plane. To avoid confusion, the right hand was located to the right of the body in a relaxed position throughout the experiment. In the direct view block, the mirror was not present, and questions were asked directly by referring to patient's left limb positioned in full view in front of them (see Figure 6.1 above). In the mirror view block, the mirror was positioned on the bed or the armchair table such that patients could clearly see their own left arm in the mirror. During this block, patients looked at their own limb in the mirror whilst direct view of their own arm remained available. However, the experimenter pointed to the reflection, rather than the real limb, whilst asking the questions. Finally, in the 3rd person perspective only block (i.e. mirror and clipboard), patients could only see the reflection of their arm in the mirror whilst the direct view of their arm was blocked by positioning the black clipboard above patients' own limb (at shoulder's height, in order to obstruct direct view whilst allowing the patients to properly see the mirror). Body ownership and motor awareness were evaluated by the questionnaire described in section 6.2.3 in all the experimental blocks in the whole sample.

In a subsample (17/48) of patients, the order of the blocks was inverted by starting with the mirror rather than the direct view to avoid order effects (for the same reasons reported in section 5.2.3).

6.2.5. Statistical analysis

All the data reported below are non-parametric and measured either at the nominal or ordinal level. In order to test whether AHP patients' unawareness of motor deficits would improve following confrontation in the mirror, main effects of i) group (i.e. AHP vs HP), ii) view (direct vs mirror) and iii) time (anticipatory vs emergent awareness) were calculated. Main effects of groups were obtained by averaging the values of Q2 (i.e. anticipatory awareness) and Q3 (i.e. emergent awareness) across the different visual conditions and comparing them between groups using a Mann-Whitney test. Main effects of view were calculated by averaging the values of Q2 and Q3 in direct vs mirror view and tested the obtained scores via a Wilcoxon Signed-Rank Test. Lastly, main effects of time were obtained by averaging the values of Q2 in direct and mirror view and Q3 in direct and mirror view, in order to compare anticipatory and emergent awareness regardless of both groups and view (tested via a Wilcoxon Signed-Rank Test).

To assess the presence of 2-ways interactions between group and view, the values of Q2 and Q3 in the mirror view were averaged and then this value was subtracted from the average of Q2 and Q3 in the direct view. To test the interaction between group and time, the values of Q2 in the direct view and Q2 in the mirror view were averaged and then this value was subtracted from the average of Q3 in the direct view and Q3 in the mirror view. Then the presence of differences between the two groups was tested using Mann-Whitney U tests. In order to investigate the 2-way interaction between time and view, the values of Q3 from Q2 in the direct view (Direct Emergent-Anticipatory Awareness) were subtracted and compared with the same subtraction in the mirror view (Mirror Emergent-Anticipatory Awareness) using a Wilcoxon Signed-Rank test. Finally, in order to check for 3 ways interactions, the Direct Emergent-Anticipatory Awareness was subtracted from the Mirror Emergent-Anticipatory Awareness and these values were compared in AHP patients only using planned comparisons (Bonferroni corrected $\alpha=0.025$) via Wilcoxon-Signed Rank Tests.

To assess the effect of mirror vs direct view on ownership the same methods and analyses outlined above were applied on ownership scores in the two different groups (DSO vs HP) following direct and mirror view to obtain main effects of i) group and ii) view as well as their interaction.

As for the control conditions, the abovementioned analyses were implemented on awareness and ownership scores to obtain main effects of i) group, ii) time, iii) view as well as the 2 and 3-ways interactions between the factors. Main effects of view were investigated using Friedman's ANOVA.

Data were analysed using the IBM Statistical Package for Social Sciences (SPSS) for Windows, version 25 (Armonk, NY) and plotted using the "ggplot2" package for R (Wickham, 2016).

6.2.6. Lesion mapping analysis

CT or MRI scans were obtained during the first week of patients' admission to the hospital wards. Three patients (1 AHP and 2 HP) were excluded from the analysis because of missing or unreadable scans. The native structural scan of each patient was reoriented and aligned to match the stereotaxic space of the T1-weighted MRI scan template from the MNI (Montréal Neurological Institute), provided within the MRIcron software (http://www.mccauslandcenter.sc.edu/mricro/mricron/; Rorden and Brett, 2000). All the lesions were drawn onto the MNI template, whilst using all available scans to guide the delineation by a researcher (VM) and double-checked by another researcher (SB), both blind to the patients grouping.

Voxel-based Lesion Symptom Mapping (VLSM) was used to explore neural correlates of awareness and ownership values in direct and mirror view in the different groups. Specifically, the change in ownership and awareness scores in the different perspectives was explored. However, none of the analysis survived statistical thresholding and even uncorrected lesions were not informative in terms of either views or groups and are hence not reported.

To illustrate the lesion size and type, group-level overlays were produced by superimposing lesions of patients from each subgroup on the MRICron (ch2bet.nii.gz) template. As reported in Figure 6.2, lesions were mainly concentrated in the frontal, temporal and parietal lobes. Specifically, the involvement of the insular cortex as well as subcortical areas (e.g. basal ganglia) as documented via CT or MRI scans was present in all four groups. Such variability is in line with the literature findings (e.g. Moro et al., 2016; Vocat et al., 2010).

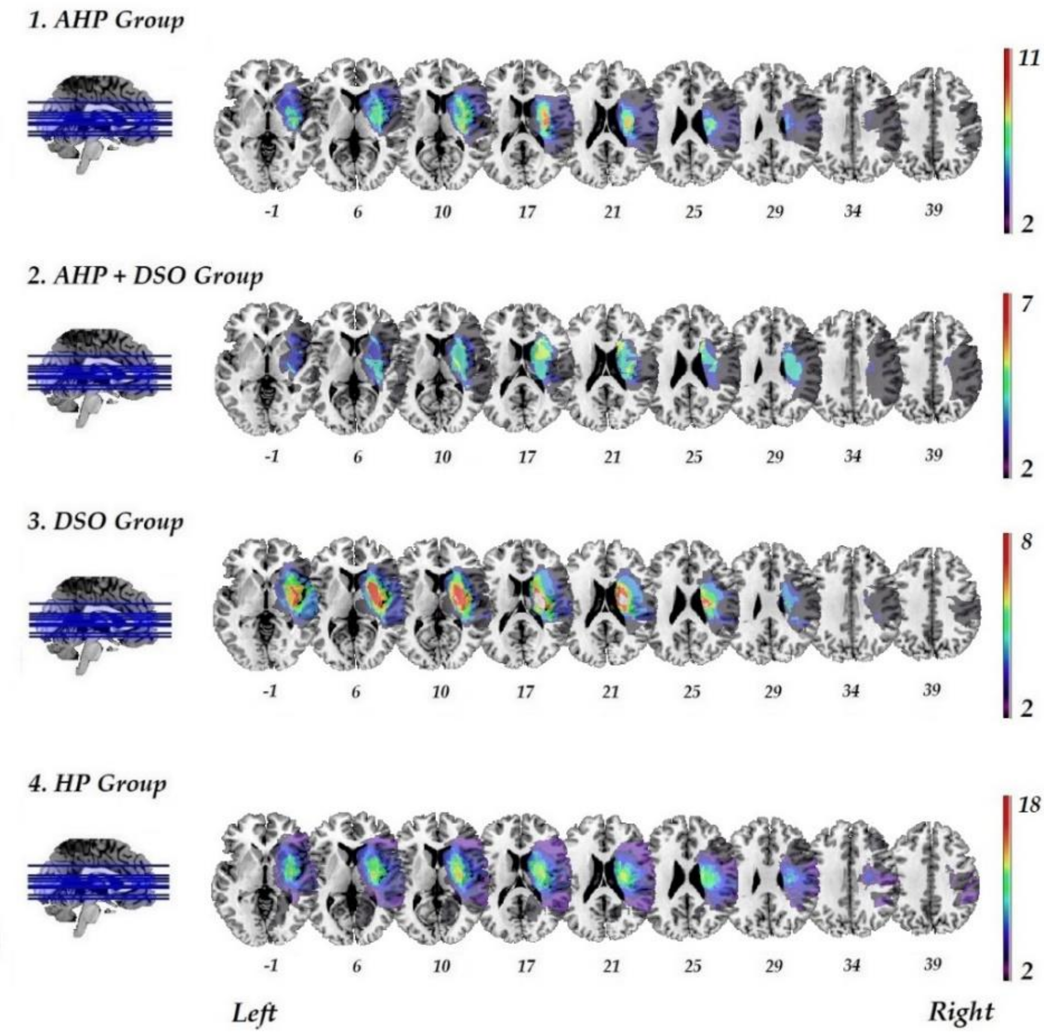


Figure 6.2. Group-level overlay of lesions in MNI coordinates for 1. AHP (N=11), 2.AHP+DSO (N=7), 3.DSO only (N=8) and HP (N=18) patients. The number of patients with overlapping lesions is signalled by the changes in coloration (see bar on the right).

6.3. Results

6.3.1. Demographics and neuropsychological results

An independent-samples Kruskal-Wallis test was conducted on demographic and neuropsychological data to investigate differences between the groups. As expected, a significant difference between the groups on awareness and ownership assessments was found (Berti Interview: $\chi^2_{(3)}$=40.145 , *p*<0.001; Feinberg Awareness Questionnaire: $\chi^2_{(3)}$=30.516, *p*<0.001; Cutting Questionnaire: $\chi^2_{(3)}$=29.934, p<0.001), alongside a significant difference on personal (One-item test: $\chi^2_{(3)}$=12.356, p=0.006) and extra-personal neglect (Star cancellation: $\chi^2_{(3)}$=10.640, p=0.014; Line cancellation: $\chi^2_{(3)}$=10.404, p=0.015) as well as in executive functioning (FAB: $\chi^2_{(3)}$=9.768, p=0.021).

To explore the direction of the abovementioned differences, post-hoc Mann-Whitney U tests (with fixed α=0.01 to accommodate for multiple comparisons) were conducted between the four groups. As predicted (see Table 6.1), AHP patients (including AHP+DSO) showed significantly less awareness of motor deficits, assessed via both the Berti and Feinberg assessments (Berti interview: AHP vs HP: Z =-5.232 , p<0.001; AHP+DSO vs HP: Z= -4.937, p<0.001; AHP vs DSO: Z= -3.623, p<0.001; AHP+DSO vs DSO: Z=-3.367, p<0.001; DSO vs HP: Z=-2.550, p=0.176; Feinberg questionnaire: AHP vs HP: Z = -4.328 , p<0.001; AHP+DSO vs HP: Z= -3.874, p<0.001; AHP vs DSO: Z=-3.813, p<0.001; AHP+DSO vs DSO: Z=-3.431, p<0.001; DSO vs HP: Z=-1.284, p=0.229). Moreover, AHP and AHP+DSO groups showed significantly more visuo-spatial neglect in comparison with the control group as tested via a sub-component of the BIT test (Star cancellation: AHP vs HP: -2.812, p=0.004; AHP+DSO vs HP: Z= -2.666, p<0.01). Finally, the AHP group showed a poorer performance on the Frontal assessment Battery in comparison with controls (AHP vs HP= Z= 2.962, p<0.01). The

AHP+DSO group also showed significantly higher scores in the Cutting questionnaire, signalling lack of ownership over the paralysed limb (AHP+DSO vs HP: Z = -4.588, p<0.001). However, pure DSO patients did not present with the same pattern. One possibility is that the Cutting questionnaire may be less sensitive to more subtle nuances of asomatognosia, which can in turn be captured during clinical interaction and qualitative assessments (see Jenkinson et al., 2018).

In order to control for symptoms-specific differences between the groups, all patients with AHP (including AHP + DSO) as well as all patients with DSO (including AHP + DSO) were grouped and separately compared with HP patients (using Bonferroni correction with α=0.025). Very similar profiles with a few exceptions were identified. In both the AHP vs HP and the DSO vs HP comparison, a significant difference between the groups on Vocat proprioceptive task was found (AHP vs HP: Z=2.411, p=0.015; DSO vs HP: Z= 2.536, p=0.011), indicating worse proprioception in both AHP and DSO. Following the AHP vs HP comparison, a significant difference in the Line Bisection subtest of the BIT was found (AHP vs HP: Z=2.435, p=0.019), with AHP patients performing worse than HP on the task, and a difference in cognitive estimates (Z=-2.292, p=0.022), with AHP patients scoring higher values than HP. The DSO (including AHP + DSO) vs HP comparison additionally revealed a significant difference in the Cutting questionnaire (DSO vs HP: Z= -3.650, p=0.002), with DSO showing higher lack of ownership in comparison with controls.

Table 6.1. Groups' demographic and neuropsychological profile.

	AHP			AHP+DSO			DSO			HP			Mann-Whitney
	n	Median	IQR	*n*	Median	IQR	*n*	Median	IQR	*n*	Median	IQR	*p*
Age (years)	*12*	76.5	23	*7*	66	24	*8*	70	21.5	*20*	62	18.5	*NS*
Gender (Male/Female)	*12*	4/12		*7*	3/7		*8*	4/8		*20*	14/20		*NS*
Education (years)	*10*	10.5	4	*7*	12	3	*4*	8.5	6	*15*	12	4	*NS*
Days from onset	*12*	8.5	13.25	*7*	6	6	*8*	5.5	7.5	*20*	9.5	16	*NS*
MRC LUL (max 5)	*12*	0	0	*7*	0	0	*8*	0	0	*20*	0	0.75	*NS*
MRC LLL (max 5)	*12*	0	1	*6*	0	0.5	*6*	1	2	*18*	0.5	2	*NS*
Berti - Awareness interview (max 3)	*11*	2	0	*7*	2	2	*8*	0	0.75	*20*	0	0	* # § ¤
Cutting questionnaire	*11*	0	0	*7*	2	0	*8*	0	1	*20*	0	0	# ¤
Feinberg - Awareness scale (max 10)	*11*	6	4.5	*7*	6.5	5	*8*	1	1.38	*18*	0.5	1.38	* # § ¤

Orientation (max 3)	*10*	3	0	*6*	3	0.25	*3*	3	1	*16*	3	0	*NS*
Digit span forward (max number repeated)	*11*	6	2	*7*	6	1	*8*	6	2.5	*19*	6	1	*NS*
Digit span backwards (max number repeated)	*11*	3	2	*7*	3	2	*8*	3.5	4.25	*19*	4	3	*NS*
IQ-WTAR (max 50)	*5*	42	19	*5*	38	24	*3*	30	26	*6*	38	12.75	*NS*
MOCA (max 30)	*4*	23.5	7.75	*2*	20	*N/A*	*6*	19.5	10	*9*	23	4.5	*NS*
Visual fields (max 6)	*9*	2	2.5	*6*	4	2.75	*2*	1.5	*N/A*	*13*	2	4	*NS*
Somatosensory (max 6)	*9*	3	2	*6*	3	4.5	*2*	5	*N/A*	*12*	2	3.75	*NS*
Proprioception (max 9)	*9*	3	4.5	*7*	4	3	*7*	3	2	*11*	7	2	§ ¤
Left/Right distinction (max 14)	*10*	12	1	*6*	11	3.25	*5*	13	2	*15*	12	3	*NS*
Comb/razor test bias (tot. bias)	*11*	-0.43	0.44	*7*	-0.33	0.22	*7*	-0.21	0.20	*18*	-0.30	0.45	*NS*
Comb/razor test left (number of strokes)	*11*	3	6	*7*	3	7	*7*	7	5	*18*	5.5	6.75	*NS*
Comb/razor test right (number of strokes)	*11*	12	4	*7*	12	13	*7*	15	3	*18*	15	8	*NS*
Comb/razor test ambiguous strokes	*11*	6	4	*7*	7	3	*7*	9	2	*18*	6	5.25	*NS*
Bisiach one item test (max 3)	*11*	1	1	*7*	1	1	*6*	0	0	*16*	0	1	*NS*
Star cancelation (max 54)	*11*	41	5	*7*	43	8	*7*	41	37	*18*	22.5	27.25	* # § ¤
Line bisection (max 9)	*11*	1	3	*7*	0	3	*6*	0.5	2.75	*17*	3	1	§
Line cancelation (max 36)	*11*	15	22	*7*	13	18	*6*	13.5	18	*20*	31.5	18	NS
Copy (max 3)	*10*	0	1	*7*	0	1.5	*5*	0	1.5	*17*	1	3	*NS*
Representational drawing (max 1)	*10*	0	0.25	*6*	0	1	*4*	0.5	1	*16*	1	1	*NS*
Cognitive estimates (max 30)	*8*	16.5	1.5	*4*	20.5	9	*2*	13.5	*N/A*	*7*	12	11	§
FAB total score (max 18)	*9*	8	6	*5*	13	3	*4*	12.5	7.75	*10*	14	2.5	* §
HADS depression (max 21)	*10*	5	7.25	*5*	6	6	*5*	9	11.5	*14*	7.5	6.25	*NS*
HADS anxiety (max 21)	*10*	6	5.5	*5*	10	9.5	*5*	11	10	*14*	7	4.75	*NS*

AHP = Anosognosia for hemiplegia; DSO = Disturbed sensation of limb ownership; HP = Hemiplegic patients; n = number of patients; IQR = Inter-quartile range; MRC = Medical Research Council scale; WTAR = Wechsler Test of Adult Reading; MOCA = MOntreal Cognitive Assessment; FAB = Frontal Assessment Battery; HADS = Hospital Anxiety and Depression scale. NS = not significant for all comparisons (Bonferroni corrected Mann-Whitney U tests, α=0.1). *significant differences between AHP and HP groups at $p < 0.01$; # significant differences between AHP+DSO and HP groups $p < 0.01$; § significant differences between AHP (including AHP+DSO) and HP groups $p < 0.025$; ¤ significant differences between DSO (including AHP+DSO) and HP groups $p < 0.025$.

6.3.2. Behavioural experimental data

Motor awareness

The first main aim of the current study was to explore whether viewing their own arm in a mirror rather than directly would increase AHP patients' awareness of their left side motor weakness by assessing pre and post components of motor awareness (anticipatory and emergent). To analyse the between-subjects factor of this 2 (Groups: AHP vs HP) x 2 (View: Direct vs Mirror) x 2 (Time: Anticipatory vs Emergent) mixed design, Mann-Whitney U tests were used, whereas within-subjects factors were analysed via Wilcoxon-signed rank tests. A main effect of group was found (Z=5.066, p<0.001, *r*=0.93), with AHP showing higher level of unawareness in comparison with HP (AHP: Mdn= 0.38, IQR=0.44; HP: Mdn=0, IQR=0) (Figure 6.3A). Furthermore, a significant 2-way interaction between Groups and Time was highlighted (Z=4.494 p<0.001, *r*=0.82), which was followed up by comparing the two groups (AHP vs HP) in Anticipatory vs Emergent awareness (Bonferroni corrected, α=0.025). A significant difference between groups was found in Anticipatory awareness only (Z= 5.271, p<0.001, *r*=0.96), with AHP patients presenting with higher unawareness in anticipatory (AHP: Mdn=0.5, IQR=0.5; HP: Mdn=0, IQR=0), but not in emergent awareness (Z=2.268, p=0.114, *r*=0.41; AHP: Mdn=0, IQR=0.63 ; HP: Mdn=0, IQR=0) in comparison with controls. The interaction between Time and View was also significant (Z=2.434, p=0.015, *r*=0.44) but it was not further explored as the majority of the HP patients (apart from 2 cases), as expected, reported complete awareness in all the conditions. However, the 3-way interaction between Group, Time and View was significant (Z=4.033, p=0.001, *r*=0.74) and was followed up by comparing anticipatory and emergent awareness scores with a Bonferroni corrected (α=0.025) Wilcoxon-Signed Rank Tests in AHP patients only in direct (Z= 2.070, p=0.038, *r*=0.49; Anticipatory: Mdn=1, IQR=0.5; Emergent: Mdn=0, IQR=1) and mirror views (Z= 2.121, p=0.034, *r*=0.5; Anticipatory: Mdn=0.5, IQR=0.75; Emergent: Mdn=0, IQR=0.5) separately. These comparisons did not withstand the correction for multiple comparisons but suggest a difference between anticipatory and emergent awareness which is higher in the mirror view. No other main effect or interaction was significant (Main effect of view: Z=0.602, p=0.547, *r*=0.11; Main effect of time: Z=-1.781, p=0.075, *r*=0.33; Group*View: Z=0.611, p=0.541, *r*=0.11).

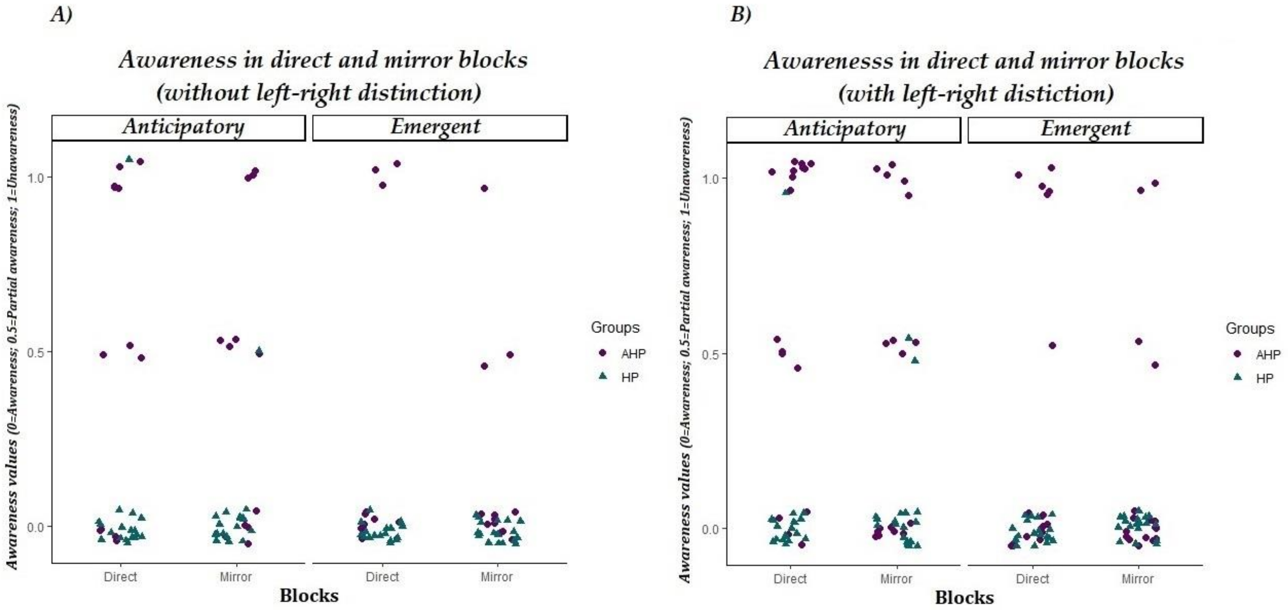


Figure 6.3. Awareness scores were calculated on a 3-points scale (0=awareness; 0.5=partial awareness and 1=unawareness) and compared between the different experimental blocks (i.e. direct vs mirror view) as well as between the different time points (i.e. anticipatory vs emergent) in A) patients without left-right distinction In the (N=30; AHP=9, HP=21), issues and B) in patients with left-right distinction issues (N=36; AHP=14, HP=22).

When adding patients with left-right distinction issues, the same pattern of significance and direction highlighted above was found (see Figure 6.3B) with significant main effects of Group (Z=5.389 , p<0.001, *r*=0.9) as well as significant 2-way and 3-way interactions (Group*Time: Z=3.962, p<0.001, *r*=0.66; Group*View*Time: Z=4.055, p=0.001, *r*=0.66). Time was also significant (Z=3.372, p=0.001, *r*=0.56), with anticipatory awareness being higher than emergent (Anticipatory: Mdn= 0.38, IQR=0.44; Emergent: Mdn=0, IQR=0). 2 and 3-way interactions were followed up with Mann-Whitney U test and Wilcoxon-signed Rank Test respectively. The comparison between AHP and HP in Anticipatory vs emergent awareness (irrespective of view) revealed that AHP patients have higher unawareness scores in anticipatory (Z=5.191, p<0.001, *r*=0.87; AHP: Mdn=0.5, IQR=0.5; HP: Mdn=0, IQR=0) as well emergent (Z=3.618, p=0.012, *r*=0.6; AHP: Mdn=0.13, IQR=0.56; HP: Mdn=0, IQR=0) awareness in comparison to controls. The follow up analysis on the significant 3-way interaction survived the Bonferroni correction, with AHP patients showing improved awareness in emergent rather than anticipatory awareness in both direct (Z=2.598, p=0.009, *r*=0.49; Anticipatory: Mdn=1, IQR=0.5; Emergent: Mdn=0, IQR=1) and mirror (Z=2.271, p=0.023, *r*=0.43; Anticipatory: Mdn=0.5, IQR=1;

Emergent: Mdn=0, IQR=0.5) views. No other main effect or interaction was significant (Main effect of view: Z=1.820, p=0.069, *r*=0.3; Group*View Z=1.722, p=0.141, *r*=0.29; Time*view: Z=0.690, p=0.490, *r*=0.12).

Ownership

The second main aim of the current study was to explore whether viewing their own arm in a mirror rather than directly would increase DSO patients' ownership. A 2 (Groups: DSO vs HP) x 2 (View: Direct vs Mirror) mixed design revealed no main effects of Group (Z=3.553, p=0.051, *r*=0.6) or View (Z=1.414, p=0.157, *r*=0.24) nor the interaction between them (Z=2.440, p=0.342, *r*=0.41) when excluding patients with left-right distinction issues (Figure 6.4). However, when including patients with left-right distinction issues the main effect of group (Z=3.774, p<0.001, *r*=0.56) was significant, with DSO patients reporting higher levels of dis-ownership (Mdn=0; IQR=0.75) in comparison with hemiplegic controls (Mdn=0; IQR=0). Likewise, the interaction between group and view was also significant (Z=3.012, p=0.003, *r*=0.45) and was followed up by Wilcoxon-Signed Rank Test (Bonferroni corrected, α=0.025) comparing direct and mirror views in DSO (Z=1.890, p=0.059, *r*=0.36; Direct: *Mdn= 0.25* IQR=1; Mirror: *Mdn*=0, IQR=0) and HP (Z=1.000, p=0.317, *r*=0.13; Direct: *Mdn*=0 IQR=0; Mirror: *Mdn*=0, IQR=0) separately. These comparisons did not survive Bonferroni correction, thus suggesting that the mirror effect might be milder than expected. As can be observed in Figure 6.4, 4 DSO patients changed their ownership score from 1 (i.e. dis-ownership) and 0.5 (i.e. partial dis-ownership) to 0 (i.e. ownership) in the mirror condition in comparison with the direct view. Finally, the main effect of view was not significant (Z=1.131, p=0.258, *r*=0.17).

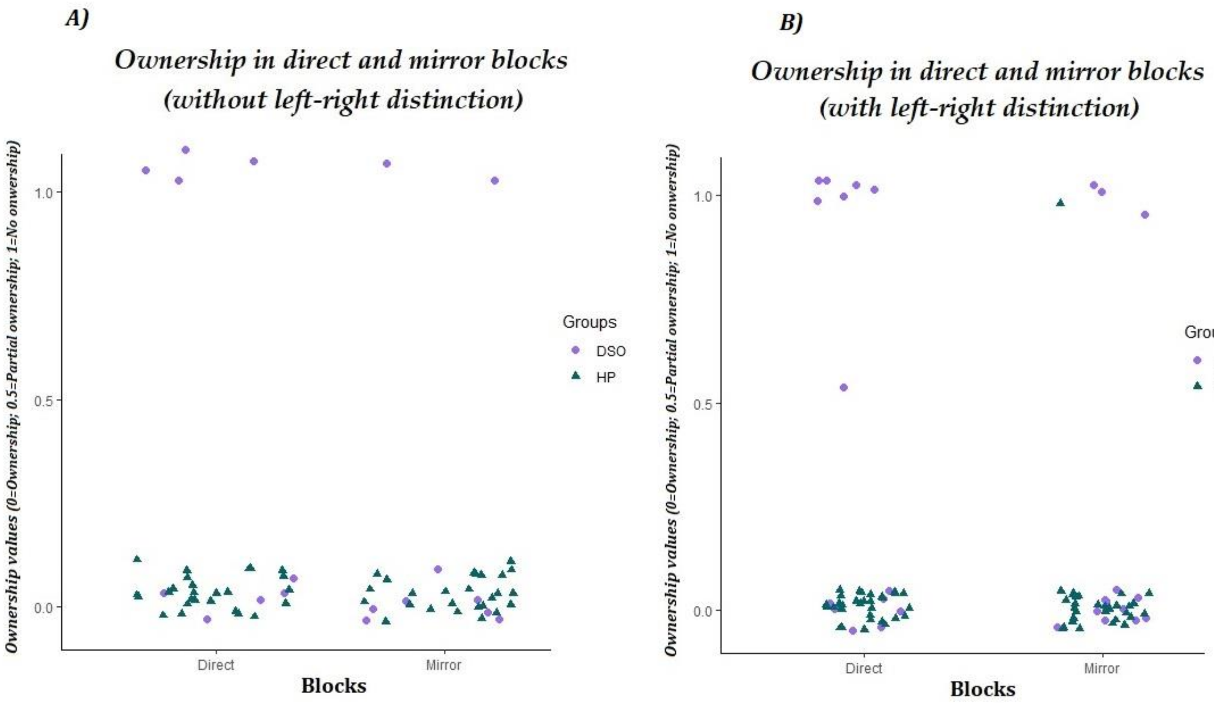


Figure 6.4. Ownership scores were calculated on a 3-points scale (0=ownership; 0.5=partial ownership and 1=dis-ownership) and compared between the different experimental blocks (i.e. direct vs mirror view) in A) patients without left-right distinction issues (N=35; DSO=9, HP=26) and B) in patients with left-right distinction issues (N=45; DSO=14, HP=31).

Control designs: motor awareness and ownership in integration of 1st and 3rd person perspective

In order to explore the hypothesis that motor awareness would improve with the integration of 1st and 3rd person perspective more than in 1st and 3rd person perspective separately, a 2 (Group: AHP vs HP) x 3 (View: Direct, Mirror, 3rd pp only) x 2 (Time: Anticipatory vs emergent) mixed design was employed in a sub-set of patients. The main effect of group, analysed using Mann-Whitney U tests, was significant (Z=2.752, p=0.008, *r*=0.8), with anosognosic patients presenting with higher levels of unawareness in comparison with controls (AHP: *Mdn*=0.46, IQR=0.83; HP: *Mdn*=0, IQR=0 – Figure 6.5). The significant 3-way interaction (Group*View*Time: Z= 2.683, p=0.048, *r*=0.78), followed up by Bonferroni corrected multiple comparisons (α=0.0125) with Friedman's ANOVA, did not reveal any significant pattern (AHP Anticipatory awareness: $\chi^2_{(2)}$= 0.667, p=0.717; Direct: *Mdn*=0.75, IQR=0.88; Mirror: *Mdn*=0.5, IQR=0.38; 3rd pp only: *Mdn*=0.5, IQR=1; AHP Emergent awareness: $\chi^2_{(2)}$= 2.000, p=0.368; Direct: *Mdn*=0.25, IQR=0.88; Mirror: *Mdn*=0.25, IQR=0.88; 3rd pp only: *Mdn*=0.5, IQR=1; HP Anticipatory awareness: $\chi^2_{(2)}$= 2.000, p=0.368; Direct *Mdn*=0, IQR=0; Mirror: *Mdn*=0, IQR=0; 3rd pp only: *Mdn*=0, IQR=0; HP Emergent awareness: $\chi^2_{(2)}$= 0.0, p=0.1; Direct: *Mdn*=0, IQR=0; Mirror: *Mdn*=0, IQR=0; 3rd pp only: *Mdn*=0, IQR=0). No other interaction or main effect was significant (View: $\chi^2_{(2)}$= 0.615, p=0.735; Group*Time: Z=1.828, p=0.154, *r*=0.53; Group*view: Z=2.122, p=0.73, *r*=0.61).

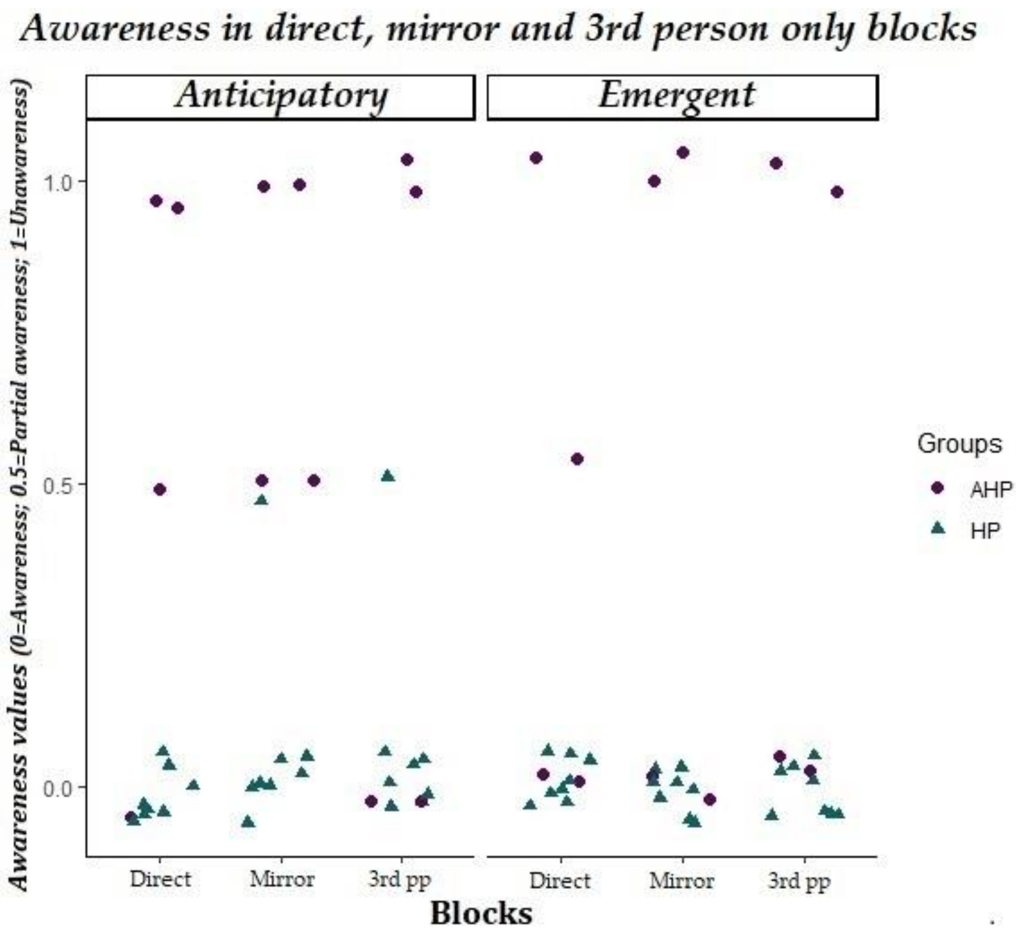


Figure 6.5. Awareness scores were calculated on a 3-points scale (0=awareness; 0.5=partial awareness and 1=unawareness) and compared between the different experimental blocks (i.e. direct vs mirror vs 3rd pp only) as well as between the different time points (i.e. anticipatory vs emergent) in a sub-group of patients (N=12, AHP=4; HP=8).

To investigate the possibility that ownership would improve with the integration of 1st and 3rd person perspective more than 1st and 3rd person perspective separately, a 2 (Group: DSO vs HP) x 3 (View: Direct, Mirror, 3rd pp only) x 2 (Time: Pre vs Post-experimental block) mixed design was used. No interaction or main effect was significant (Figure 6.6 – Friedman's ANOVA: View: $\chi^2_{(2)}$= 0.353, p=0.838; Mann-Whitney U tests: Group: Z=1.901, p=0.106, *r*=0.55; Group*Time: Z=0.746, p=0.639, *r*=0.22; Group*view: Z=1.353, p=0.268, *r*=0.39; Group*View*Time: Z=2.238, p=0.106, *r*=0.65).

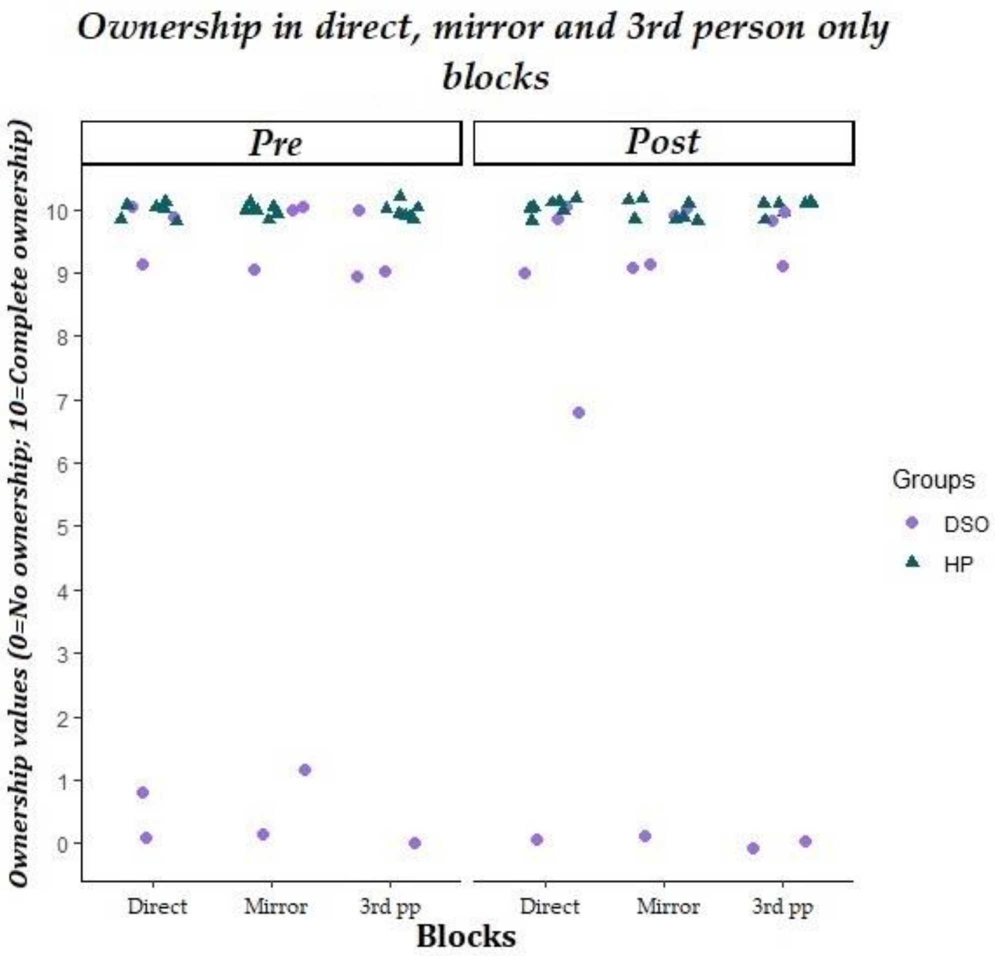


Figure 6.6. Awareness scores were calculated on a 11-points Likert scale (0=No ownership; 10=Complete ownership) and compared between the different experimental blocks (i.e. direct vs mirror vs 3rd pp only) as well as between the different time points (i.e. pre vs post) in a sub-group of patients (N=12, DSO=5; HP=7).

6.4. Discussion

The current study aimed to investigate whether the unawareness of left paralysis and dis-ownership of the left arm seen in patients with right-hemisphere stroke could be reduced when they were provided with visual feedback of their affected limb (before and after failing to perform a movement) in a mirror (i.e. 3rd perspective) rather than directly (i.e. 1st person perspective). The study also examined two secondary objectives, namely i) to what extent different types of perspective (i.e. 1^{st} person, 1^{st} and 3^{rd} person and 3^{rd} person only) would influence patients' unawareness and dis-ownership and ii) whether DSO patients would show higher degrees of ownership over time following each of the three experimental blocks.

Results showed that AHP patients improved their emergent (i.e. after having tried to perform a movement) motor awareness following a failed movement in both direct and mirror view of their own arm, with no significant difference between the two views. A potential explanation for this finding is that AHP patients may benefit more from repeated confrontation (i.e. being asked multiple times to perform a movement and assess the result of its absence) rather than viewing their own arm in different perspectives. This may be due to the repetitive nature of the task: as mentioned above, confrontation techniques have been showed to improve awareness in some AHP cases (Berti et al., 1996). Hence, in the current study, asking the same questions multiple times in a short period could have led to an improvement on the top of the experimental manipulation. Furthermore, these results could suggest that the remission found in previous studies employing videoclips may be linked to the "offline" nature of the self-observation rather than the perspective itself (Besharati et al., 2014; Fotopoulou et al., 2009). Motor intentions have been recognised as a dominating factor in the maintenance of AHP symptoms (Berti and Pia, 2005; Fotopoulou, 2014). When AHP patients intend to move, they may fail to monitor the outcome of their own actions because their motor planning overrides incoming sensory signals. Thus, when assessing patients' emergent awareness after a failed movement observed in the mirror, the presence of motor intention may eliminate the advantage of employing an intact 3^{rd} person perspective. When exploring the effect of 3^{rd} person perspective only (i.e. by blocking patients' view of their own arm), to investigate whether integration of both 1^{st} and 3^{rd} person perspective would be more effective in improving AHP patients' awareness, no difference between the blocks was found. As mentioned above, the lack of improvement in emergent awareness according to the different perspectives could be due to the presence of online motor planning. Future studies could directly compare the results of online vs offline interventions in patients with unawareness of motor deficits, whilst controlling for visual perspective (i.e. providing offline feedback from the 1^{st} person perspective).

In terms of DSO patients, in line with previous findings (Fotopoulou et al., 2011; Jenkinson et al., 2013), some of the patients (4 out of 7) changed their ownership scores when viewing their own arm in the mirror in comparison with the direct view. These results would suggest that viewing their dis-owned limb from an external perspective, whilst both direct and mirror views are available, could improve feelings of ownership in DSO patients. Even though no lesion data has confirmed this hypothesis in the current study, dis-ownership in right-hemisphere stroke patients may be linked to damage in fronto-parietal areas, necessary to integrate incoming sensory information from 1st and 3rd person perspectives into a stable body representation (Serino & Riva, 2017). Thus, dis-ownership could be explained as a dissociation between the "*subjectively felt*" (as directly experienced by the patients) and "*objectively seen*" body (as experienced from an outsider's perspective in extra-personal space) (Fotopoulou et al., 2011). Given that it was not possible to re-test these patients at different time points, the extent to which such change is long-lasting remains to be explored, together with the neural correlates of such phenomenon.

To further investigate the extent to which patients maintained their changes in ownership scores over time and differently according to the specific type of view implemented, a subgroup of patients were asked to rate their degree of ownership before and after each experimental block in 1st person perspective (i.e. direct view), 1st and 3rd person perspective (i.e. mirror view) and 3rd person perspective alone (i.e. mirror with direct view blocked). Findings suggest that time plays a more relevant role than view, with 3 out of 6 patients feeling low degrees of ownership at the beginning of each block, then increasing their ownership at the end of the same block (returning to the original low level of ownership at the beginning of the following one), with no difference between the blocks. Future research could focus on repeated treatments involving integration of different perspectives in order to induce long-lasting changes in DSO patients rather than temporary changes.

Finally, an overall limitation of the current study (at least for the two control designs) was the low sample size: in both groups only 12 patients were tested and thus these results must be interpreted with caution. Further research, with bigger sample sizes, would be required to reach a conclusive finding about the influence of different perspectives in remitting unawareness of motor deficits and dis-ownership feelings as well as identifying neural correlates of changes in ownership and awareness.

In conclusion, the current study revealed that motor awareness is not influenced by changes in views (direct vs mirror) and that it improves, regardless of the view, following a failed attempted movement (i.e. emergent awareness). The lack of specific perspective-driven effects in emergent awareness in the current study despite previous findings of an effect of perspective on motor awareness (i.e. Fotopoulou et al., 2009), may be due to the "online" nature of mirror self-observation in comparison with video-replay. This would suggest that AHP patients may be unable to integrate incoming sensory feedback informing their emergent awareness, even when presented with an intact 3rd person perspective, due to dominance of their motor intentions whilst attempting to move. In terms of ownership, DSO patients' feelings of arm ownership were improved only when they viewed their own limb in a mirror rather than directly, but not when direct view was unavailable (i.e. in the 3rd person perspective only block). These results suggest that the integration of both 1st and 3rd person perspectives, rather than the 3rd person perspective only, may temporarily reinstate a normal body representation.

Finally, in the next chapter of this thesis, the question of how healthy subjects use information from different spatial frames of reference to inform awareness was examined. This builds on the neuropsychological work reported in chapters 5 and 6 which addressed the question of how patients with right-hemisphere stroke process stimuli in order to obtain a sense of self. In particular, the final empirical chapter builds on the findings of the current chapter on perspective-taking and asks the question of whether healthy subjects are less aware of their own performance when information is processed in an egocentric (i.e. body-centred) vs an allocentric (world-centred) frame of reference.

Chapter 7

Metacognition of perceptual judgements in egocentric and allocentric frames of reference

7.1. Introduction

In Chapter 6, the possibility of influencing ownership and motor awareness by changing the spatial visual perspective from 1st to 3rd person (Fotopoulou et al., 2011) was investigated in right-hemisphere stroke patients. The rationale of the study was that patients with AHP and Disturbed Sensations of limb Ownership (DSO) may be impaired in processing information regarding their left, paralysed limb in the 1st person perspective due to a lack of integration between information coming from the body and experienced with an egocentric (i.e. centred on the body; e.g. Fogassi et al., 1992; Graziano and Gross, 1998) perspective. Results suggested that an integration between information coming from both 1st and 3rd person perspective may lead to improvements in ownership but not awareness.

These findings suggest that anosognosic patients may be less able to interpret information originating from their body, regardless of the perspective taken. When their motor intention is present, they seem unable to disengage from their first person perspective, even when confronted with an additional, 3rd person, one. This may be due to their inability to monitor their own cognitive processes (i.e. metacognition; Flavell, 1979) when asked to express a judgement about their motor weakness. It might be possible that such metacognitive impairment in AHP patients, rather than being linked to perspective-taking per se, may be due to a failure in integrating different Frames of References (i.e. a set of criteria in relation to which judgements can be made; FoRs). For instance, in neglect patients, several studies looked at egocentric and allocentric deficits as two traditionally dissociated aspects of the syndrome (e.g. Chechlacz et al., 2010; Marsh & Hillis, 2008). However, new evidence suggests that they might instead be strongly associated: the majority of patients who presented allocentric neglect, also showed egocentric neglect, whilst the opposite pattern was not found (Rorden et al., 2012;

Yeu et al., 2012). Thus, neglect may arise as a consequence of a failure in integrating egocentric and allocentric spatial information, with egocentric processing being necessary for the allocentric one to arise. Similarly, in AHP patients, an integration failure of egocentric and allocentric processing may lead to a metacognitive deficit when patients judge their own performance in an egocentric (i.e. centred on one's own body) FoR. In the current chapter, the possibility of an egocentric bias in metacognitive abilities will be explored in healthy subjects, with the idea that this mechanism may be crucial in establishing and maintaining a sense of self-awareness and that its impairment may underlie anosognosic patients' behaviour.

To successfully navigate and process stimuli from their own environment, individuals rely on the integration of information coming from a body-centred representation of space (i.e. egocentric frame of reference) with a world-based one (e.g. Maguire et al., 1998; Burgess, 2006), in which the reference point for perception and processing of stimuli (in relation to one another) is in the extra-personal space and independent from the perceiver (i.e. allocentric frame of reference; Ball, Birch, Lane, Ellison, & Schenk, 2017; Camors, Jouffrais, Cottereau, & Durand, 2015; Chen et al., 2018). Such process comprises an integration of 1st and 3rd person perspective during spatial navigation in one's own environment. Specifically, both 1st and 3rd person perspectives lead to better navigational performance when experienced egocentrically on the ground level, whereas both perspectives in the allocentric frame of reference are more efficient when navigating an environment from an aerial view. Hence, in order to successfully navigate in our immediate surrounding, both perspectives need to be integrated in an egocentric frame of reference, which is subsequently integrated with an allocentric reference frame to allow spatial navigation not centred on the body (Török et al., 2014). Thus, spatial processing may start from an integration of different perspectives grounded on the body: an egocentric representation of the body in space, as well as its surroundings, may be a necessary first step to develop an allocentric viewpoint (Filimon, 2015). As discussed in the previous chapter (section 6.1), Serino and Riva (2017) proposed that integrating egocentric and allocentric FoRs is crucial for creating and maintaining awareness of one's own body as well as one's surrounding. This idea that spatial perception may play a role in AHP has been put forward by Besharati and colleagues (2016; see section

6.1. Introduction of the previous chapter). The authors found a dissociation between 1st and 3rd person visuo-spatial and mental perspective-taking in AHP patients: their ability to take an outsider's perspective seems to be impaired, with patients being unable to disengage from their own 1st person perspective during visuo-spatial (i.e. perceiving the same stimuli from the experimenter's visual perspective) as well as mentalization (i.e. reflecting on stories presented with the patient as the agent vs stories regarding an external agent) tasks.

A complementary theoretical account suggests that anosognosia for hemiplegia may be the result of an inability to update prior beliefs (internal models of the world stemming from previous experiences and genetic predispositions; Friston, 2010) about their own body in light of disproving evidence (i.e. the fact that their arm is paralysed) (Fotopoulou, 2014). Belief updating entails the individuals' capacity to update prior beliefs according to differences between intended (e.g. the fact that I want to move my arm) and observed outcomes (e.g. the lack of movement of my paralysed arm) in a Bayes-optimal fashion. In the context of predictive coding accounts (e.g. Friston & Kiebel, 2009), the brain generates probabilistic predictions approximating Bayes rule. That is, the posterior probability of an event (e.g. the movement of my arm) is a consequence of its prior conditions (e.g. the current state of my body) as well as the likelihood of the event occurring (e.g. how likely is it that my arm will move given its current conditions). For example, a new intern in a stroke ward might not be fully aware of a specific patient's condition. If, during the round, the doctor asks a patient "Can you move your left arm?" and the patient replies "Yes", the intern would tend to predict the patient can move. Given she has no extra information about the condition of that patient, the probability of the patient moving is higher than not ("why would the doctor ask otherwise?"). Following lack of movement of the patient's arm, the intern would then be prompted to update her original prediction in light of this new evidence (i.e. the patient is likely anosognosic). This will allow her to minimise prediction errors (i.e. the difference between predicted and observed outcomes; Adams, Shipp, & Friston, 2013) in following encounters with that patient but also other patients in the ward (i.e. she now knows this is a possibility, so the probability of this event occurring is changed).

In AHP patients, this lack of belief updating could account for some of the evidence reported in clinical studies. For instance, when faced with their own disability, patients are unable to recognise the failure of their intended action (Fotopoulou et al., 2008). Similarly, AHP patients seem to be resistant to change their prior knowledge even in light of insufficient or dubious evidence and express overly confident judgements regardless of their performance (on tasks related as well as unrelated to their motor disabilities; Jenkinson et al., 2009; Vocat et al., 2013). Taken together, these findings suggest that the lack of awareness showed by AHP patients may entail an impairment in metacognitive processing and belief updating. However, all the studies reported above always investigated self-awareness adopting an egocentric frame of reference, i.e. no study to date investigate self-awareness for stimuli presented allocentrically, thus making it difficult to pinpoint the role of reference frames in this updating process.

In the metacognition literature, metacognitive abilities are often indexed by confidence judgements in individuals' perceptual choices in a behavioural task (Fleming & Lau, 2014). Whilst metacognition is a broad, widely investigated concept (see Fleming & Daw, 2017 for a review), the majority of the research so far focused on uni-sensory perception and memory. Neuroimaging and lesion studies showed that selective activation of neural populations in the right pre-frontal cortex encode domain-specific metacognition (i.e. different areas are activated during perceptual vs memory metacognitive judgements; Fleming et al., 2014; Morales, Lau, & Fleming, 2018). Nevertheless, the authors also found evidence for a domain general metacognitive ability sub-served by a widespread fronto-parietal network (Morales et al., 2018). This latter finding is partially in line with a more global, multisensory account of metacognition: evidence from neuroimaging and behavioural sensory tasks points toward a shared mechanism sub-serving metacognitive judgements across different sensory modalities (Faivre, Filevich, Solovey, Kuhn, & Blanke, 2018). These findings could hence sustain the hypothesis of a domain-specific (i.e. motor related), accompanied by a more global metacognitive impairment in self-awareness in AHP patients.

Furthermore, a dissociation between different aspects of metacognitive abilities has been found in both perceptual and memory domains. For instance, Fleming and colleagues (2016) asked individuals, in a visual discrimination task (i.e. left or right position of a target stimulus), to express their confidence both retrospectively (i.e. after having performed the task) as well as prospectively (i.e. every five trials, they were asked to express their confidence on the probability of getting the next trial right before seeing the stimuli and performing the trial). Findings from this study showed that prospective judgements were predicted by previous confidence ratings in preceding trials (previous four retrospective confidence judgements) whereas retrospective ones seemed to be influenced by the decision immediately preceding the current judgement (Fleming, Massoni, Gajdos, & Vergnaud, 2016).

Another dissociation between prospective and retrospective confidence judgements has been found in their accuracy. Findings of a memory tasks, on which individuals were asked to express prospective as well as retrospective judgements, showed that while confidence ratings are less accurate given prospectively (i.e. before individuals are given the chance to see the target response), they are more accurate were expressed retrospectively (i.e. after having assessed the difficulty of the task; Siedlecka, Paulewicz, & Wierzchon, 2016). Hence, it might be possible that, when self-awareness is impaired, patients may not be able to use information arising from their own body to inform their prospective judgements about what they can or cannot do. This is in line with the clinical observation that, while some AHP patients may recognise failures in moving their left arm following direct confrontation with their disability, they might return to a state of unawareness shortly after the assessment (Orfei et al., 2007).

As such, an impairment in metacognitive awareness (i.e. the ability of an observer to correctly use the information available during a given task in order to make confidence judgements on such task; Fleming, 2017; Fleming, Weil, Nagy, Dolan, & Rees, 2010) may underlie AHP patients' bias in correctly judging the output of their own actions as perceived egocentrically. In the current study, the hypothesis that metacognition of one's own action may be differentially influenced according to the frame of reference in which such action occurred will be explored. Specifically, investigating how healthy individuals process stimuli in the egocentric and allocentric reference frames could provide insight into processes underlying self-awareness (and lack thereof). If allocentric processing depends on a functioning egocentric one, and even healthy individuals are less metacognitively aware when judging their own performance in an egocentric FoR, it may be possible that metacognitive processes are influenced by spatial frames of references, with egocentric FoR leading to a lower awareness (in comparison with an allocentric FoR). Nevertheless, despite the idea that AHP patients may be lacking the ability to update their prior beliefs about their own selves when adopting an egocentric FoR, no study to date investigated the possibility that such impairment may be due to a general tendency to overestimate one's own ability when presented with egocentric views in basic perceptual tasks in healthy subjects (i.e. an "egocentric bias" in metacognitive judgements).

Hence, this study aims to investigate in healthy subjects i) whether any differences exist in peoples' prior beliefs about their ability to perform a perceptual judgment task using egocentric versus allocentric FoRs; ii) accuracy and metacognitive awareness in perceptual decisions after performing a perceptual judgment in a task using egocentric versus allocentric FoR; iii) differences between Bayes-optimal belief updating (i.e. expected prospective judgements given both prior estimates and actual performance during the task) and participants' actual belief updating based on their own reported responses (i.e. their prospective judgements on how well they will perform on the same task in the future). In order to do this, in a pilot study and two follow-up separate experiments, subjects completed a task in which they encoded spatial information (i.e. the location of a visual target) using either an allocentric or egocentric FoR and subsequently made a visual discrimination between 2 targets positioned at different distances (only one being the correct one) presented in either an allocentric or egocentric FoR (matched to the encoding phase, i.e. discrimination was always in the same FoR as encoding). In an initial pilot study, the aim was to test the task and check whether the two conditions were similar in their levels of difficulty (by analysing performance levels). In experiment one, the aim was to establish whether there was a significant difference in both performance and metacognition when participants were presented with stimuli in egocentric and allocentric FoR in a larger sample size and a fully randomised presentation of the stimuli. However, given that the two tasks may still present with differing levels of difficulty, the results on metacognition may be biased by differences in performance. Hence, in the second experiment, performance was equalised across participants by using a staircase procedure (as in Fleming et al., 2010 and Patel et al., 2012). Such staircase approach aims to achieve a set level (~70%) of correct responses in both egocentric and allocentric condition by increasing or decreasing the task difficulty according to participants' own responses. This allows us to test differences in metacognitive abilities in egocentric and allocentric FoR regardless of task differences. Furthermore, belief updating abilities were investigated by devising two separate blocks. The priors block assessed participant's belief of how well they thought they would carry out the task in egocentric and allocentric conditions prior to actually performing it and the posteriors block assessed the same but after participants finished the task (by asking them how well they thought they would perform the task again in the future).

The first aim of the current study was to assess whether subjects were less metacognitively aware of their own perceptual choices when experiencing stimuli egocentrically rather than allocentrically. Specifically, it was hypothesised that subjects would be more confident regarding the accuracy of their perceptual decisions when they were right and less confident when wrong in the allocentric condition compared to the egocentric one (due to the presence of an "egocentric bias"). The second aim of the present study was to test whether subjects would update their beliefs regarding their own performance in a Bayes-like fashion when rating allocentric, but not egocentric, stimuli. As such, it was hypothesised that participants would be biased by their original beliefs when judging their ability prospectively in the egocentric FoR (in comparison with the allocentric one), i.e. that they would not base their judgement on their actual performance but rather on their original belief about it.

7.2. Methods

7.2.1. Participants:

Pilot study

Twenty right-handed healthy participants (11 females, age range: 18-71 years, M=29.6, SD=13.12) were recruited through an institutional subject pool in exchange for university credit or monetary compensation (£7.50/hour according to University's regulations). One participant was excluded from the final analysis as performance was more than 2 SD away from the group mean. Hence, the final sample comprised nineteen participants (11 females, age range: 18-71 years, M=29.37, SD=13.44). The study was approved by UCL ethical committee and ratified by UH ethical committee. All participants provided written, informed consent.

Experiment 1

Thirty-six additional right-handed healthy participants (26 females, age range: 18-35 years, M=21, SD=4.54) were recruited to take part in experiment 1 as described above.

Experiment 2

Thirty-six right-handed new healthy participants (21 females, age range: 18-40 years, M=22.7, SD=5.5) were recruited to take part in experiment 2 with the same criteria described above.

7.2.2. Experimental design

7.2.2.1. General design

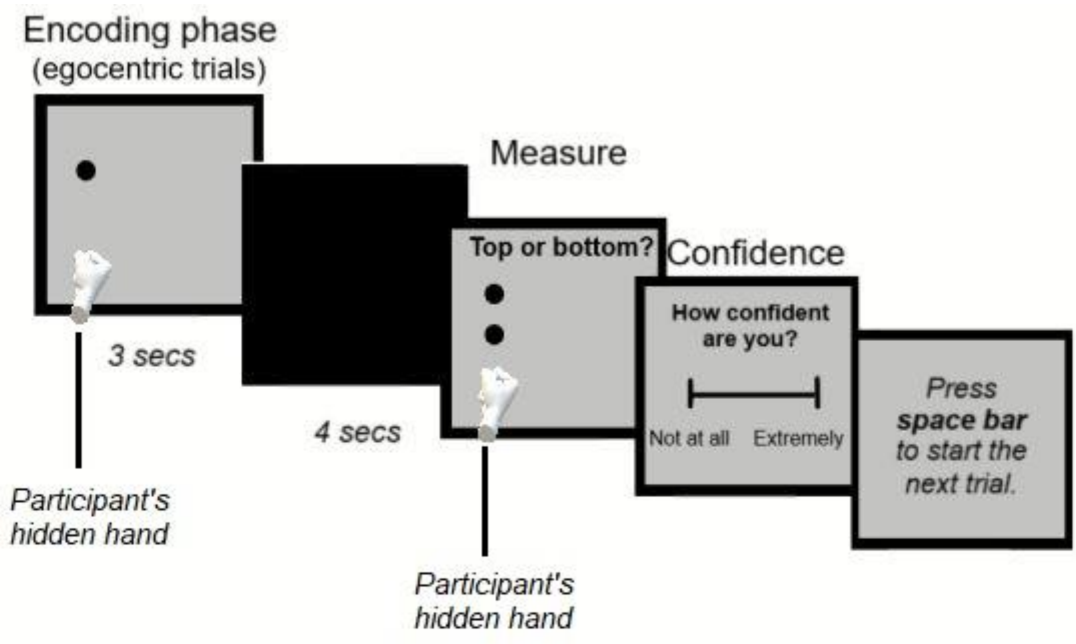
Main task:

In all the experiments, a within-subjects design, with FoRs (egocentric vs. allocentric) as the independent variable, was employed. Egocentric and allocentric FoRs were manipulated by asking participants to position their right hand as follows. In egocentric conditions, participants were asked to remember the distance between their hidden hand and a visual stimulus (i.e. a black circle) positioned vertically above it, i.e. their hand was the reference for the judgement. In allocentric conditions, the participant's hand was positioned alongside their body, so that their own hand could not act as a point of reference for remembering the distance between two vertically aligned stimuli (i.e. a cross and a circle) in a world-based fashion. This manipulation ensured that relevant proprioceptive information was available only during egocentric encoding but not during allocentric one: in the former, the position of the participant's hand was informative in relation to the visual stimulus presented on screen, thereby contributing to calculate the distance, whereas in the latter the hand was resting alongside the participant's body and could not be used as a reference while calculating the distance between the stimuli shown (i.e. there would be no apparent advantage in using proprioceptive information when it was not on the same plane as visual one; van Beers, Wolpert, & Haggard, 2002). In the egocentric condition, participants maintained their hand positioned in the same place they were in during encoding and they were asked to judge which one among two black circles was at the same distance from their own hand as the one they had been exposed to during the previous phase (i.e. "*Which of the 2 circles is at the right distance*?"). The circles were positioned one above the other and only one of them was at the correct distance (figure 7.1A). In the allocentric outcome, participants were asked to keep their hand outside of the graphic tablet (to avoid interference from proprioceptive information) and were asked to judge which one among two black circles was at the same distance from a black cross as the distance they had been exposed to during the encoding phase (figure 7.1B). The correct stimuli were presented in the same position as during encoding. Participants' responses to the 2 alternatives forced-choice (i.e. 2afc) question (i.e. “*Which of the 2 circles is at the right distance*?”) as well as related confidence ratings in their responses were the dependent variables. Performance scores (i.e. amount of correct responses on the total amount of trials) were used to calculate accuracy and confidence ratings were used to calculate metacognitive awareness (see section 7.2.5).

Priors/posteriors blocks:

In order to investigate change in belief updating, two additional short blocks were devised: one performed before and one after the main task. Following an initial phase of familiarisation and instructions (see section 7.2.4. below), before performing the main task, participants were asked to express their beliefs on how they would carry out the task using the same stimuli described above for the encoding phase but without asking them to choose between to targets (i.e. without the measure phase). Specifically, participants were asked to report how well they thought they would be able to remember a distance encoded either egocentrically or allocentrically (i.e. “*How well would you be able to remember the distance between 2 points you have just seen?*”) and how confident they were in their own answer using a visual-analogue scale (ranging from Not at all to Extremely, which was converted into a 0-100 scale). During the posteriors block, participants answered the same questions as in the priors block, but taking into consideration the fact that they performed the main task (i.e. the instructions specified participants had to think about how well they would do on the main task if asked to do it again in the future). These two extra blocks were used to gain insight into participants’ belief updating throughout the task via analysing their estimates and confidence ratings in egocentric vs allocentric trials.

A)



B)

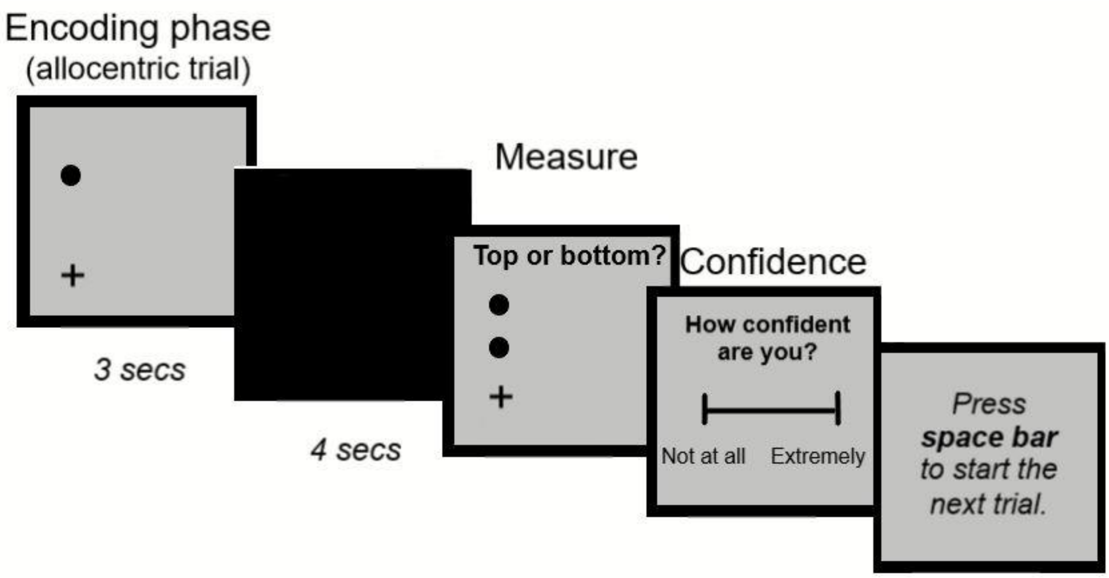


Figure 7.1. A) Example of an egocentric trial during the main task. Participants had their own hidden hand placed on the graphic tablet by the experimenter. During the encoding phase, they saw a black circle appearing vertically above their hand. They were then presented with a 2-alternative forced choice question, asking them to identify which among the two circles was at the same distance from their hand as they saw during the previous phase (i.e.: "*Which of the 2 circles is at the right distance*? *Answer using the up/down arrow keys*"). After the training phase and during the actual task, participants were prompted by a shorter version of the question *(Top/Bottom?).* Confidence ratings were collected in response to the question "*How confident are you about your answer*?" (VAS response 0-100, *"Not at all confident"; "Extremely confident*"). B) Example of an allocentric trial during the main task. Participant's hand was place alongside their body and they were presented with 2

vertically aligned stimuli (a cross and a circle). During the measure phase, they were asked which of the 2 circles was at the right distance in respect to the cross. The same questions reported above for egocentric trials were asked.

Control tasks and questionnaires:

In order to control for the influence of general visuo-spatial and working memory abilities on the experimental task, the Digit Span (Wechsler, 1997), Corsi blocks (Corsi, 1972) and the Benton Judgement of Line Orientation (Benton, Varney, & deS Hamsher, 1978) tasks were used (see 7.2.3. below for details). To assess participants general self-efficacy and perspective-taking abilities, two different questionnaires (GSE; Schwarzer & Jerusalem, 1995 and IRI-perspective-taking subscale; Davis, 1983) were used. These control tasks and questionnaires were subsequently included in the linear mixed model as controls for working memory, spatial judgements and attitudes towards general self-awareness and mentalisation.

7.2.2.2. <u>Design variations:</u>

Pilot study:

In the pilot, the correctly positioned circle among the two circles in the measure phase was positioned either at the top or the bottom using two different pseudo-randomised fixed orders. Each order had a complementary presentation of up and down circles and half of the sample carried out the task with one order and the other half with the second order.

Experiment 1:

In this variation of the experiment outlined above, the distance between the two circles in the measuring phase was fully randomised (i.e. in the pilot study, the distance between the right and wrong circle was predetermined for each trial).

Experiment 2:

This variation of the experiment outlined above, aimed to explore participants' metacognitive abilities per se without looking at performance by levelling task difficulty in the two conditions. A staircase procedure (Fleming et al., 2010; Patel et al., 2012) was employed during the outcome phase in order to equalise performance across the two conditions. Given that metacognitive measures are calculated based on their associated performance, if there is a difference in difficulty at the performance level, this could influence metacognitive measures (Rahnev & Fleming, 2019). Hence, the position of the 2 circles during the measure phase (i.e. when participants were asked to judge which, among the two circles, was at the right distance by selecting one of two option in a 2-alternative forced choice fashion) was varied using a two-up/one-down staircase procedure aimed at achieving approximately 70% of correct responses. The staircase procedure worked as follow: following 2 correct responses, the distance between the correct circle and the wrongly positioned circle decreased in the subsequent trial by 0.25 cm (going up if the wrong circle was below the correct one and down in the opposite condition), thus increasing the difficulty of the task. On the contrary, following 1 incorrect response, the distance increased by 0.25 cm (going down if the wrong circle was below the correct one and up in the opposite condition), hence decreasing the difficulty of the task by making it easier to differentiate between the two circles. The steps used by the staircase procedure were the same ones implemented in the perceptual task (see section 7.2.3 below).

7.2.3. <u>Experimental setup and materials</u>

Materials:

Prior to the experimental session, participants were asked to complete a set of questionnaires via an anonymous Qualtrics link (which included consent form and information sheet of the study) aimed at exploring i) General Self-Efficacy abilities (via the 10-items GSE questionnaire; Schwarzer & Jerusalem, 1995) and ii) perspective taking attitudes (via the perspective taking subscale of the Interpersonal Reactivity Index, IRI; Davis, 1983). Upon arrival, participants taking part in experiments 1 and 2 were also asked to complete a series of tasks to control for i) visuo-spatial abilities (via the Benton's Judgement of line orientation test; Benton, Varney, & deS Hamsher, 1978), ii) verbal working memory (via the digit span task from the Wechsler Adult Intelligence Scale III; Wechsler, 1997) and iii) spatial working memory (via the Corsi span block; Corsi, 1972).

Apparatus and stimuli:

Participants were comfortably seated on a chair in front of a table, facing a graphic tablet (size: 43w x 28.7l x 0.8h cm; active drawing area: 31.1w x 21.6l) positioned underneath a customised shelf (size: 45w x 30l x 15h) on which an ASUS flat monitor (size: 34.4 x 19.4 cm) was located. On their left there was a keyboard, used to move to the next screen by pressing the space bar as well as choosing the top or bottom circle in the main task using the up/down arrows. Attached to participant's own right index finger, there was an active pen (i.e. a stylus pen used to interact with the tablet). Their hand, alongside the active pen, was hidden from view and inserted in the box (see Figure 7.2) during egocentric trials. The graphic tablet active area was mapped to perfectly match the monitor size (e.g. when the pen was positioned on the far right of the graphic tablet, the cursor would appear on the corresponding vertical location of the monitor). This was done to ensure that the experimenter could passively position participant's hand in the right spot at the beginning of egocentric trials (see procedure below).

The stimuli used throughout the experiments were displayed on the ASUS monitor. In the egocentric encoding phase, one black circle was located vertically above the participant's hand. In the allocentric encoding phase, a vertically aligned black circle and black cross were presented. During the measuring phase, two circles were positioned one above the other and only one of them was at the correct distance. The wrongly positioned circle was above the correct circle in half of the trials and below in the other half. The distances between the 2 circles were equally distributed among four different possible distances: 0.5, 0.75, 1 and 1.25 cm. Stimuli were presented equally in all available quadrants of space (top left, top right, bottom left, bottom right, with 0 being in the middle of the screen). There were 16 unique trials for the egocentric condition and 16 for the allocentric (with a total of 32 unique trials), repeated 6 times (with a total of 160 trials) in a randomised order (for the encoding phase – see above for randomisation related to measuring phases).

A) B)

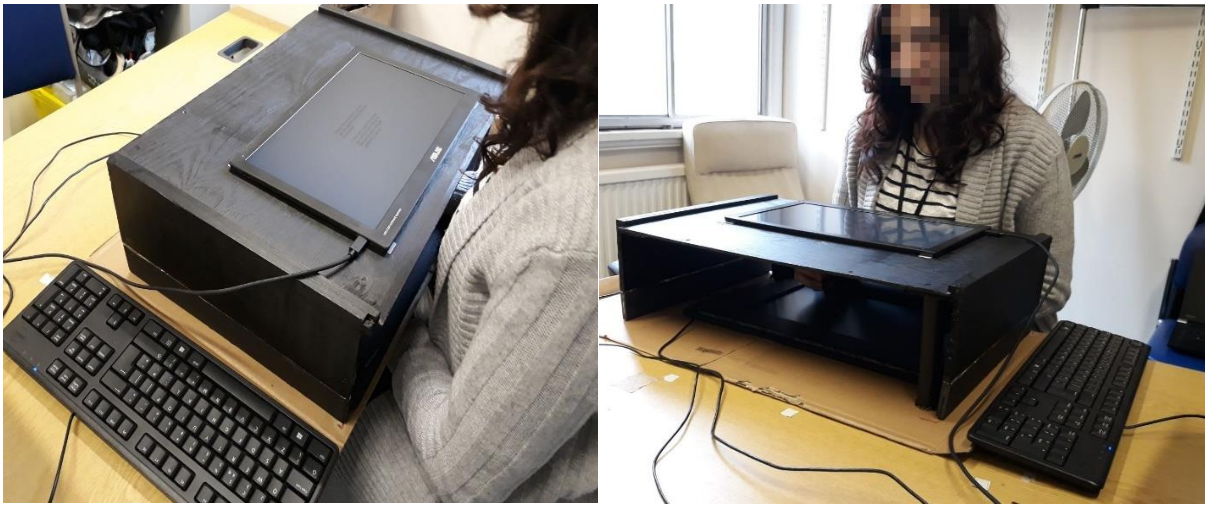


Figure 7.2. Stimuli are shown on a flat ASUS monitor (panel A), of which display area corresponds to the active drawing area of the graphic tablet hidden underneath the black monitor stand (panel B). Participants were never able to see their own hand on the graphic tablet during the experiment.

7.2.4. <u>Procedure</u>

Upon arrival participants underwent a set of control tasks described in section 7.2.3 above. Then, participants sat on a chair in front of the tablet (see figure 7.2). The first five minutes were dedicated to familiarisation with the equipment (e.g. seeing how the pen responded to the participant's right hand position in space and how this was mapped onto the monitor) as well as explanation of the instructions, including interactive training (i.e. the experimenter showed the participant how the task would work and how they would be required to use the active pen to answer questions on the tablet). Following the initial training phase, the room lights were turned off to avoid excessive visual interference, and the procedure continued as follows (figure 7.3):

1. Priors block: participants were asked to perform 6 trials (2 buffer and 4 actual trials, 3 egocentric and 3 allocentric ones). In the egocentric condition trials, the participant's right hand was positioned by the experimenter on a point (signalled by a red cross for egocentric conditions together with a written warning indicating whether the trial was egocentric or allocentric) on the unseen graphics tablet while their vision was blocked by the experimenter via a black carton panel. Following this passive positioning of the hand, the participant was presented with a black circle on the flat ASUS monitor. The position of the circle was vertically aligned with their own hidden hand on the tablet below. Stimulus presentation lasted 3 seconds, followed by a 4 seconds inter-stimulus interval (signalled by a black screen) preceding the questions screens (see section 7.2.2.1 above). In the allocentric conditions, the experimenter positioned participants' right hand (while their vision was blocked) outside of the box, aligned with their body. Stimuli (a black circle and a black cross) were presented for 3 seconds, followed by a 4 seconds inter-stimulus interval which preceded the questions. After their responses were recorded, participants were asked to press the space bar to begin the subsequent trial.

2. Main task: The encoding phase for egocentric and allocentric trials was the same described for the priors block. However, following the inter-stimulus interval, participants were presented with either i) two black circles (only one of them displayed at the correct distance in relation to the stimulus shown during the encoding phase) vertically aligned with their unseen hand or ii) 3 vertically aligned stimuli (2 black circles and a black cross), with one of them displayed at the correct distance in relation to the black cross. Participants answered by using the up/down arrow keys on the keyboard for the 2afc questions (selecting what they thought was the right circle) and the active pen to select the desired point on the VAS scale. At the middle of the experiment, participants had a 5 minutes break.

3. Posteriors block: made of 4 trials and resembling the priors block, marked the end of the experiment.

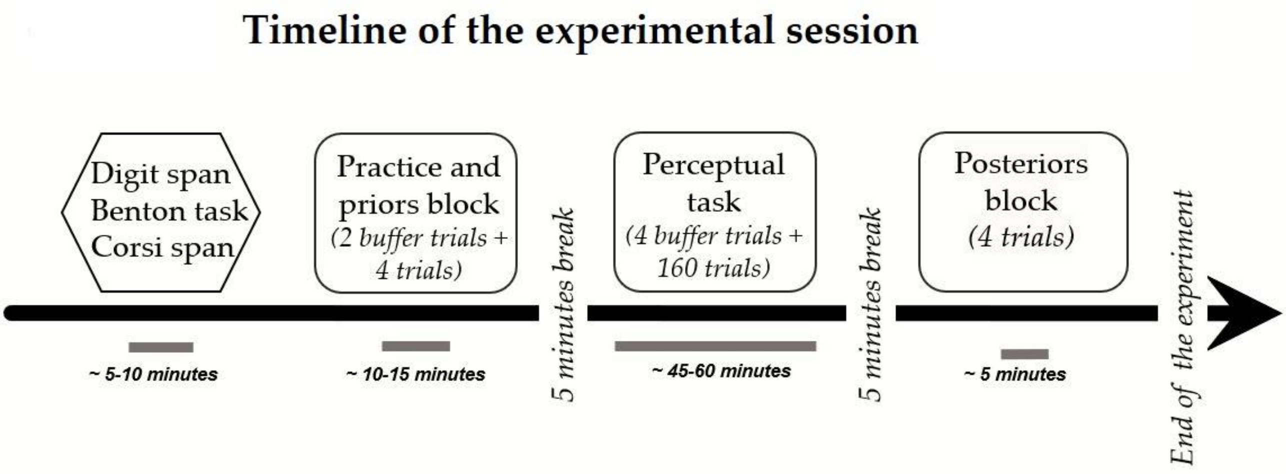


Figure 7.3. Timeline of the experimental session. Participants were first asked to complete a set of control tasks (Benton Line Orientation task in the pilot, with the Digit Span and Corsi blocks tasks added in experiment 1 and 2). They were then positioned in front of the graphic tablet and carried out the first block (priors),comprising 2 buffer trials and 4 actual trials. Following the priors block, participants started the main task, which lasted 45 to 60 minutes with a break in between. They were then asked to complete the final block (posteriors), which signalled the end of the experiment.

7.2.5. Data analysis

In order to investigate the first aim, i.e. that participants would be less metacognitively aware in egocentric rather than allocentric conditions, accuracy during task performance as well as metacognitive awareness (indexed by participants' confidence in their responses), were obtained using the raw performance and confidence scores. Specifically, accuracy was calculated per each condition by applying the following formula, returning values from 0 (total inaccuracy) to 1 (complete accuracy):

$$Accuracy = \frac{N\ correct\ responses}{N\ total\ trials}$$

In order to test metacognitive awareness, a non-parametric estimate of the probability of being correct for each level of confidence, namely receiver-operating characteristic (ROC) curves, was used (Fleming et al., 2010; Patel et al., 2012). The area under the ROC curve (A_{ROC}) is a measure of participants' ability to express confidence on their perceptual decisions. It is calculated by the sum of the area between the ROC curve and the area under the area of the half square triangle below the major diagonal. In order to calculate A_{ROC}, a vector with the correct and wrong responses as well as a vector containing the binned version of the confidence scores (11 bins, ranging from 0 to 10 following transformation from a 0-100 to a 0-10 scale) was obtained for each separate condition (egocentric and allocentric) in each of the three experiments. Data were pre-processed using the "*tidyverse"* package for R (Wickham, 2017). These vectors were subsequently used as arguments for the MatLab function implementing the A_{ROC} formula used by Patel and colleagues (2012), together with the total amount of possible ratings (in this instance, 11). hi=p(confidence=I | correct) and fi=p(confidence=I | incorrect) were obtained for each bin, with "hi" representing a correct response (i.e. hit) and "fi" a wrong response (i.e. false alarm). The obtained probabilities were transformed into cumulative probabilities and plotted to produce the ROC curve:

$$A_{ROC} = 0.25 \sum_{k=1}^{0} [(h_{K+1} - f_K)2 - (h_K - f_{k+1})2] \mid + 0.5$$

Once accuracy and A_{ROC} values were obtained, paired-samples t-tests (or Wilcoxon signed rank test) were used to explore differences between conditions. Data were then entered in R and subsequently analysed using linear mixed models (i.e. LMM), with *lmer4* and *lmerTest* packages with Satterthwaite approximation ($S_e = \sqrt{}\ (s_1^2/n_1 + s_2^2/n_2)$) for p-values calculation of estimates (Luke, 2017). Using LMMs instead of multiple regressions is advised with repeated measures design as it allows to control for both random (e.g. intra-subject variability) as well as fixed (e.g. egocentric and allocentric FoRs) effects (Hesselmann, 2018). The first LMM aimed at investigating the effects of condition (i.e. egocentric or allocentric), awareness (i.e. A_{ROC} values), priors estimates (as well as the interaction between these three factors), questionnaires scores (GSE and IRI perspective taking subscales) and control tasks for experiments 1 and 2 only (Benton, Digit Span and Corsi blocks) on accuracy as the predicted variable. Participants IDs were used as the random intercept. In terms of metacognitive awareness, the same method was used but with accuracy values instead of awareness values as a predictor.

In order to test the second aim, i.e. that participants would not optimally update their beliefs in the egocentric conditions, participants' prior estimates and confidence ratings in egocentric and allocentric trials were compared by averaging egocentric and allocentric responses across trials (separately for allocentric and egocentric conditions) and subsequently performing a paired-sample t-test (or Wilcoxon signed rank test, when distributions were not normal) to examine any difference in prior beliefs according to the experimental condition. Furthermore, in order to examine differences between the participants' posterior estimates with the computed Bayes optimal posterior distributions (i.e. the actual responses vs the expected responses are analysed to explore whether individuals update their beliefs in a Bayes-optimal fashion), the following formula was used. This formula takes into account participants prior beliefs (i.e. estimates of how well they would carry out the task) as well as their actual performance, in order to compute a posterior distribution approximating Bayes' values. Accuracy values were multiplied by 100 and rounded to nearest integer too allow uniformity with priors and posteriors measures (which were taken on a VAS ranging from 0 to 100, rounded to the nearest integer):

$$\mu_{\theta|y} = \mu_\theta + \frac{\pi_\varepsilon}{\pi_{\theta|y}}(y - \mu_\theta)$$

In the equation above, $\mu_{\theta|y}$ corresponds to the computed posterior estimate, given the prior estimate (μ_θ) plus the ratio of the execution confidence (π_ε) on the probability of the prior confidence on the execution confidence ($\pi_{\theta|y} = \pi_\varepsilon + \pi_\theta$ where π_θ = prior confidence) multiplied by the difference between execution accuracy (y) and prior estimate (μ_θ). The difference between egocentric and allocentric conditions in Bayes-optimal and observed posteriors was analysed with separate paired-samples t-tests.

Given the minimal difference between pilot and study 1 (i.e. quasi randomised vs fully randomised presentation of choice stimuli, with ratio of up/down maintained equal across the two studies), the data from these two experiments together was analysed, in order to increase statistical power. For paired sample t-tests, effect sizes were obtained using Cohen's d (see section 2.6.6.)

Data were analysed and plotted using the type2roc function for MatLab (Patel et al., 2012), the "*tydiverse*" , "*ggplot2*" (Wickham, 2016), "*lmer4*" (Bates, Mächler, Bolker, & Walker, 2015) and *"lmerTest"* (Kuznetsova, Brockhoff, & Christensen, 2017) packages for R.

7.3. Results

7.3.1. Pilot study

Priors block

Paired-samples t-tests were employed to explore the difference between egocentric and allocentric conditions in prior estimates and confidence values. A significant difference in the prior estimates was found, with allocentric trials being rated as easier than egocentric ones ($t_{(18)}$= 2.392, p = 0.028, *d*= 0.549; allocentric estimates: M= 63.84, SD= 10.42; egocentric estimates: M=54.47, SD= 19.57, figure 7.4A). As for confidence values, this comparison did not reveal significant differences between the conditions ($t_{(18)}$= 1.574, p = 0.132, *d*= 0.360; allocentric confidence: M= 63.84, SD= 10.42; egocentric confidence: M=54.47, SD= 19.57, figure 7.4B). These results suggest that participants believed they would perform better in allocentric trials they could monitor visually (i.e. in an allocentric way) compared with egocentric trials, which entailed using proprioception as a point of reference (i.e. egocentric).

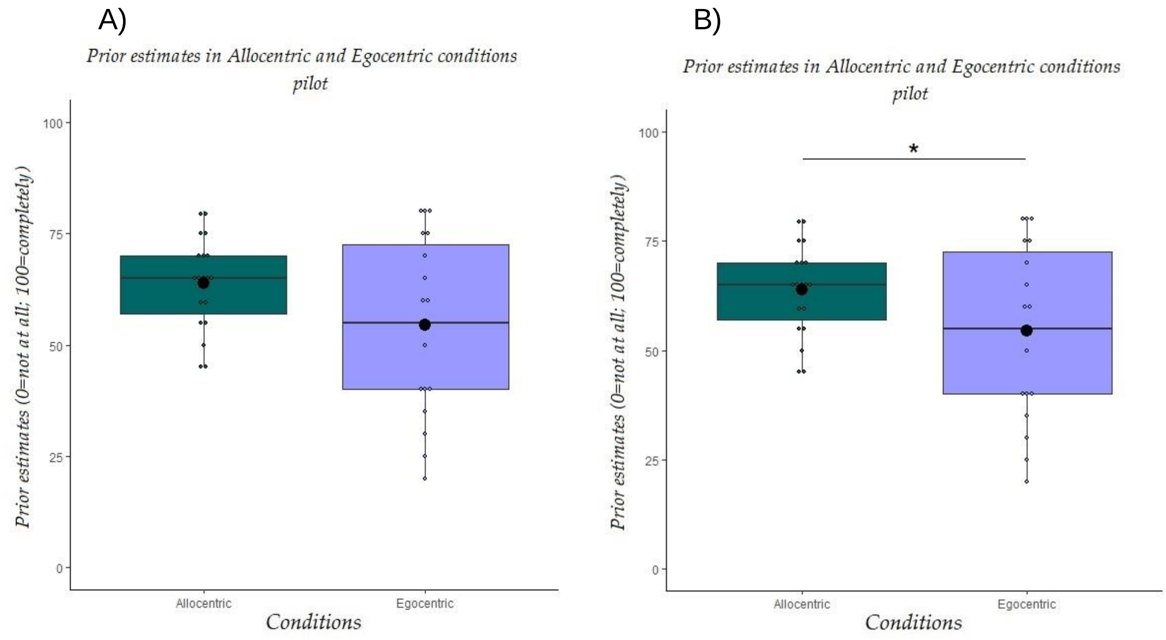


Figure 7.4. Participants' responses in the priors block to the questions A) "*How well would you be able to remember the distance between 2 points you have just seen?*" ranging from 0="Not at all well" to 100="Completely") and B) *"How confident are you in your answer?"* ranging from 0="Not at all confident" to 100="Completely". Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR). *p <0.05

Accuracy and metacognitive awareness - main task

A paired-samples t-tests between egocentric and allocentric conditions revealed a significant difference in accuracy ($t_{(18)}$ = -2.586, p= 0.019, *d*=0.692; Allocentric: M=0.79 SD=0.08; Egocentric: M=0.84, SD=0.09), with egocentric trials leading to higher accuracy (Figure 7.5), suggesting that subjects were more accurate during egocentric trials (despite their prior beliefs).

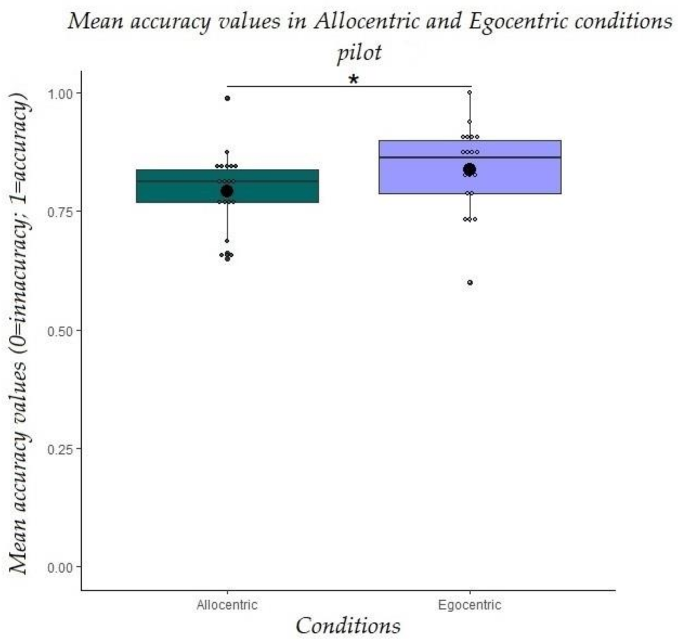


Figure 7.5. Mean accuracy values in egocentric and allocentric conditions. Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR). *p <0.05

As for metacognitive awareness, a second paired-sample t-test showed no difference between the two conditions ($t_{(18)}$ = -0.879, p=0.39, *d*=0.180; Allocentric: M=0.66, SD=0.07; Egocentric: M=0.67, SD=0.08) (Figure 7.6), indicating that there was no difference in their awareness of their own performance in both egocentric and allocentric trials.

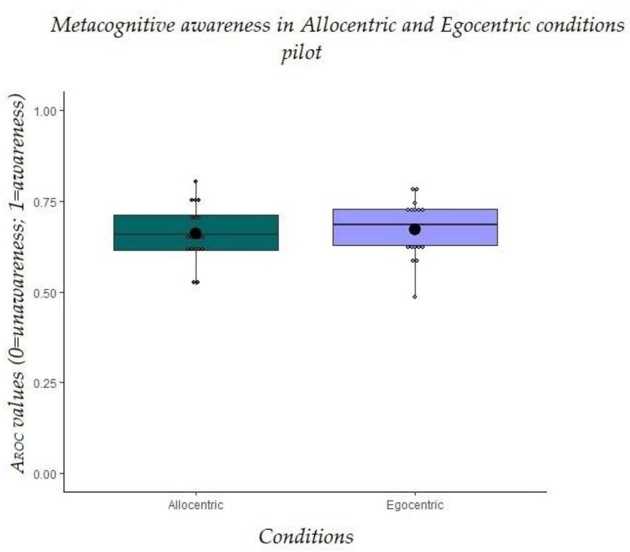


Figure 7.6. Mean A_{ROC} values in egocentric and allocentric conditions. Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR).

A linear mixed model with accuracy as the predicted variable and condition (i.e. egocentric or allocentric), awareness (i.e. A_{ROC} values), priors estimates and questionnaires scores (GSE and IRI perspective taking subscales) as predictors revealed a significant positive main effect of Metacognitive awareness and prior estimates in predicting accuracy, as well as a significant negative interaction between these two factors (see Table 7.1. below for a summary of the LMMs). This suggests that both awareness of one's own performance as well as prior estimates on it would predict accuracy levels, yet regardless of the condition (i.e. allocentric or egocentric). A linear mixed model with metacognitive awareness (i.e. A_{ROC} values – Figure 7.6.) as the predicted variable and condition (i.e. egocentric or allocentric), accuracy, priors estimates and questionnaires scores (GSE and IRI perspective taking subscales) as predictors revealed no effect of any of the factors (all p values for fixed effects were above 0.5 – see Table 7.1 below).

Table 7.1. Summary of fixed and random effects of linear mixed models for Accuracy and Metacognitive awareness in the pilot.

	Accuracy			**Metacognitive awareness**		
Predictors	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*
(Intercept)	-1.00	-1.88 – -0.11	**0.039**	0.13	-0.77 – 1.02	0.785
Metacognitive awareness	2.28	0.86 – 3.69	**0.005**			
Condition	0.30	-0.00 – 0.60	0.069	0.15	-0.15 – 0.44	0.347
Prior estimates	0.02	0.01 – 0.03	**<0.001**	0.01	-0.01 – 0.02	0.331
Metacognitive awareness* Condition	-0.22	-0.73 – 0.28	0.394			
Condition*Prior estimates	-0.00	-0.00 – 0.00	0.335	0.00	-0.00 – 0.00	0.980
Metacognitive awareness* Prior estimates	-0.03	-0.04 – -0.01	**0.001**			
Accuracy				0.70	-0.35 – 1.76	0.210
GSE				-0.00	-0.02 – 0.01	0.406
IRI – PT				0.00	-0.01 – 0.01	0.871
Condition*Accuracy				-0.16	-0.54 – 0.22	0.431
Accuracy*Prior estimates				-0.01	-0.02 – 0.01	0.410
Random Effects						
σ^2	0.00			0.00		

τ_{00}	0.00 Participants	0.00 Participants
ICC	0.75	0.66
N	18 Participants	18 Participants
Observations	36	36
Marginal R^2	0.367	0.215
Conditional R^2	0.841	0.734

Bayes-optimal and observed posteriors

In order to test whether participants updated their beliefs more in the egocentric rather than allocentric condition (due to their higher performance) and according to expected updating (i.e. Bayes-optimal posterior distributions), two separate paired-samples t-tests were carried out on i) actual reported estimates in egocentric and allocentric trials and ii) Bayes-optimal calculated estimates in egocentric and allocentric trials. There was no significant difference in either of the comparisons, suggesting successful belief updating on egocentric conditions following the main task (Bayes-optimal estimates: $t_{(18)}$= 0.951, p = 0.354, *d*= 0.218; allocentric: M= 71.84, SD= 7.76 ; egocentric: M= 69.32, SD= 13.17; observed estimates: $t_{(18)}$=-0.036, p = 0.972, *d*= 0.008; allocentric: M=67, SD=16.62 ; egocentric: M=67.1, SD=17.14, figure 7.7.A and B).

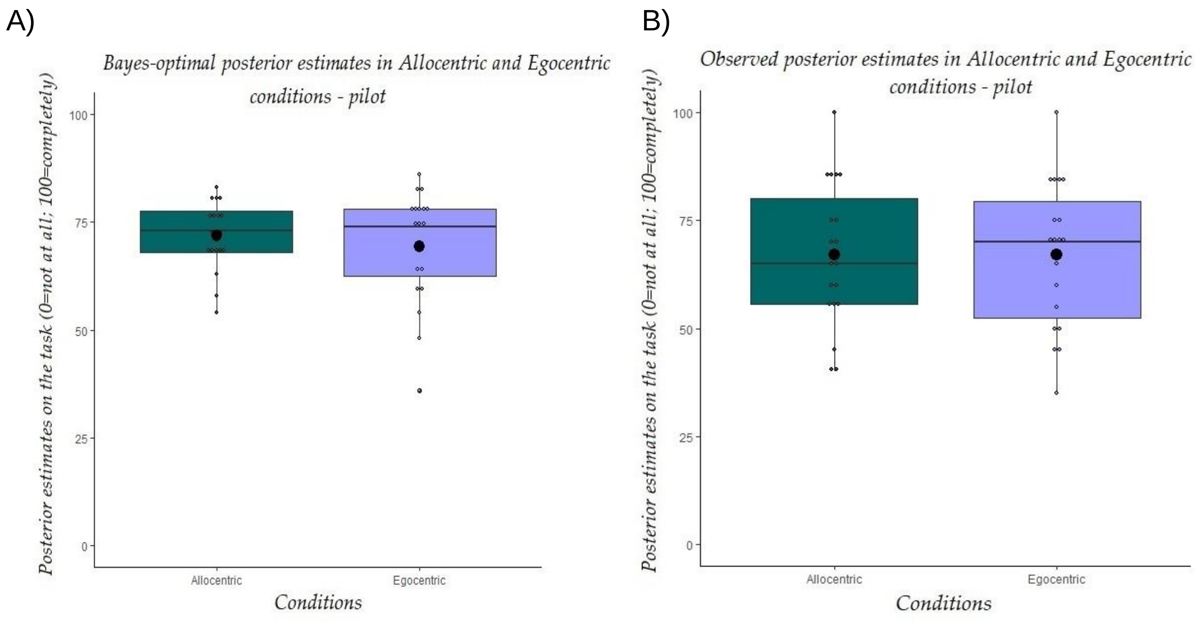


Figure 7.7. A) Bayes-optimal posterior distributions in Allocentric and Egocentric conditions, on a scale from 0-100; B) Actual participants' responses in the posteriors block (in response to the question: "*How well would you be able to remember the distance between 2 points you have just seen?*" ranging from 0="Not at all well" to 100="Completely"). Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR).

In sum, the pilot study showed that participants' prior beliefs on the task were biased towards allocentric trials (i.e. they believe they would be better in allocentric vs egocentric trials before performing the task). However, their performance suggests the contrary: participants' accuracy was higher in egocentric rather than allocentric trials, with no difference in metacognitive awareness. Furthermore, participants' accuracy (regardless of egocentric or allocentric conditions) was predicted by metacognitive awareness and prior estimates. Finally, participants showed a posterior estimates distribution similar to the expected one, given their prior beliefs and their actual performance. The lack of significant findings on metacognitive awareness could be due to the small sample size, so experiment 1 aimed to further expand these findings.

7.3.2. Experiment 1

Priors block

As described above, to investigate the difference between egocentric and allocentric conditions in the priors block of experiment 1, paired-samples t-tests were run on estimates and confidence values. Partially in line with the pilot data, such comparisons revealed a significant difference in both prior estimates and confidence, with allocentric trials being rated as easier than egocentric trials (prior estimates: $t_{(29)}=3.579$, $p = 0.001$, $d= 0.654$; allocentric: M=63.97 , SD=18.13 ; egocentric: M=51.33, SD=17.14; confidence values: $t_{(29)}=3.529$, $p = 0.001$, $d= 0.644$; allocentric: M=65.1 , SD=16.01; egocentric: M=55.13, SD=19.87 – see Figure 7.8 A and B). In line with the pilot data, these findings suggest that participants believed they would perform better in allocentric rather than egocentric trials.

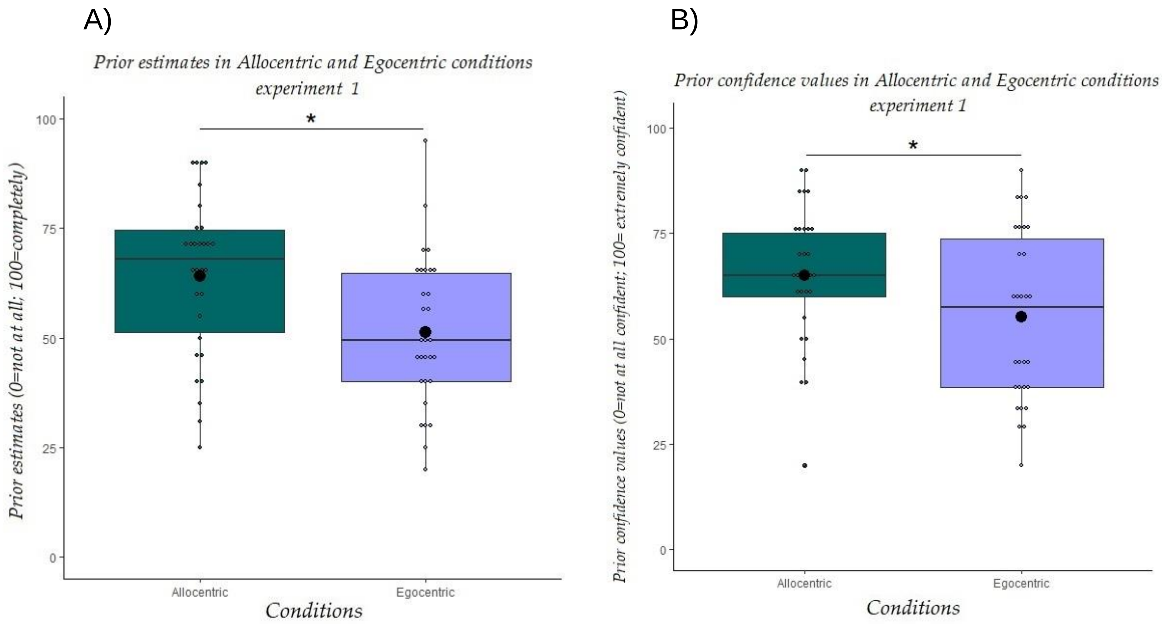


Figure 7.8. Participants' responses in the priors block to the questions A) "*How well would you be able to remember the distance between 2 points you have just seen?*" ranging from 0="Not at all well" to 100="Completely") and B) *"How confident are you in your answer?"* ranging from 0="Not at all confident" to 100="Completely". Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR). *p <0.05

Accuracy and metacognitive awareness - main task

A Wilcoxon-signed rank test (due to violation of normality) between egocentric and allocentric conditions revealed a significant difference, with egocentric trials leading to higher accuracy than allocentric ones (Z=-2.408, p=0.016, *r*=0.439; *Mdn*=0.77, IQR= 0.23; egocentric: *Mdn*=0.83, IQR=0.19 - see Figure 7.9). Again, in line with the pilot data, participants performed better in egocentric rather than allocentric trials, in contrast with their prior beliefs.

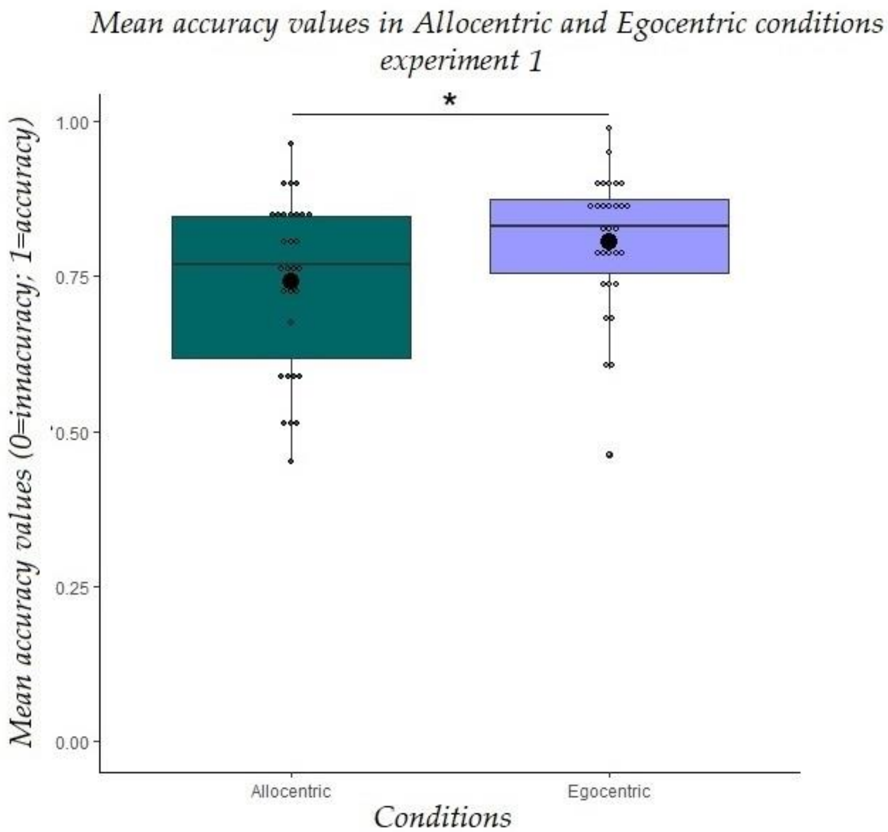


Figure 7.9. Mean accuracy values in egocentric and allocentric conditions. Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR). *p <0.05

The same directional difference was found in metacognitive awareness via a paired-sample t-test ($t_{(29)}$= -2.4569 , p = 0.02, *d*= 0.433; allocentric: M=0.63, SD=0.08; egocentric: M=0.66, SD=0.07 – see Figure 7.10). Participants were able to correctly detect that they performed better in egocentric rather than allocentric trials.

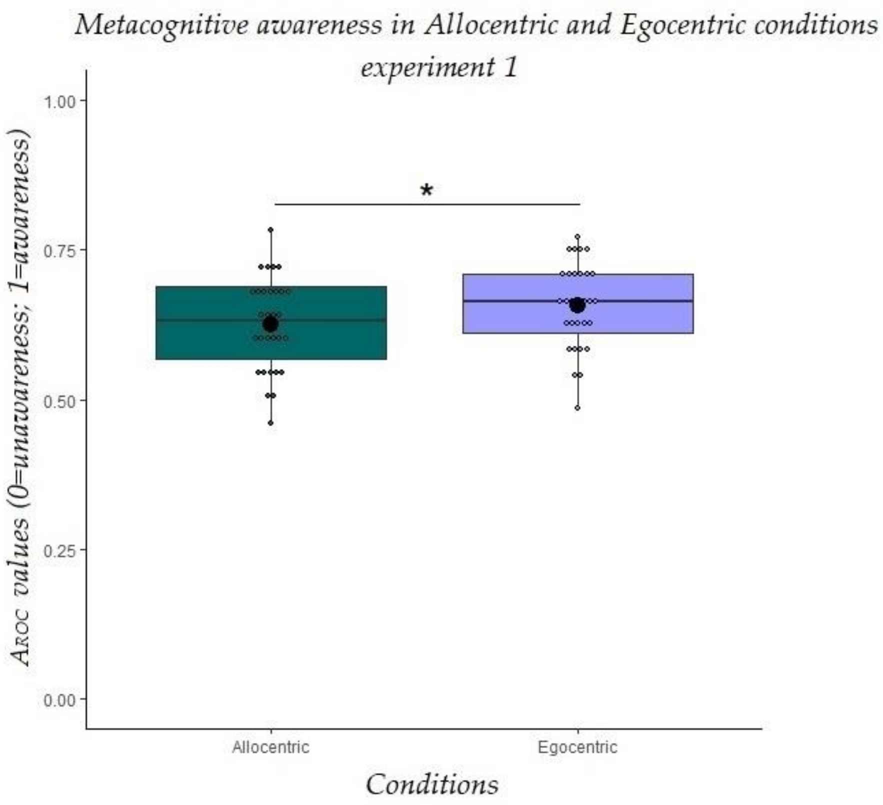


Figure 7.10. Mean A_{ROC} values in egocentric and allocentric conditions. Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR). *p <0.05

A linear mixed model with accuracy as the predicted variable and condition (i.e. egocentric or allocentric), awareness (i.e. A_{ROC} values), priors estimates, questionnaires scores (GSE and IRI perspective taking subscales) and control tasks (Corsi Blocks, Benton JLO, Digit Span) as predictors did not reveal any effects or interaction apart from the intercept. The same was also true for metacognitive awareness values (see Table 7.2.).

Table 7.2. Summary of fixed and random effects of linear mixed models for Accuracy and Metacognitive awareness in experiment 1.

	Accuracy			**Metacognitive awareness**		
Predictors	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*
(Intercept)	-0.58	-1.73 – 0.57	0.328	0.54	0.02 – 1.06	**0.049**
Metacognitive awareness	1.37	-0.24 – 2.98	0.103			

Condition	0.22	-0.21 – 0.65	0.317	0.05	-0.13 – 0.24	0.571
Prior estimates	0.00	-0.01 – 0.01	0.980	-0.00	-0.01 – 0.00	0.350
Corsi blocks	0.01	-0.01 – 0.03	0.446			
Benton JLO	0.01	-0.00 – 0.03	0.092			
Digit span	0.00	-0.01 – 0.01	0.699			
Metacognitive awareness *Condition	-0.28	-0.92 – 0.35	0.383			
Condition*Prior estimates	0.00	-0.00 – 0.00	0.983	-0.00	-0.00 – 0.00	0.841
Metacognitive awareness* Prior estimates	0.00	-0.02 – 0.02	0.936			
Accuracy				0.19	-0.40 – 0.79	0.531
GSE				-0.00	-0.01 – 0.00	0.526
IRI – PT				-0.00	-0.01 – 0.01	0.756
Condition*Accuracy				-0.04	-0.27 – 0.18	0.706
Accuracy*Prior estimates				0.00	-0.00 – 0.01	0.316
Random Effects						
σ^2	0.01			0.00		
τ_{00}	0.00 Participants_			0.00 Participants		
ICC	0.30			0.54		
N	30 Participants_			30 Participants_		
Observations	60			60		
Marginal R^2	0.443			0.340		
Conditional R^2	0.610			0.695		

Bayes-optimal and observed posteriors

In line with the pilot data, no difference was found between allocentric and egocentric trials in the reported posterior estimates nor the Bayes optimal posterior estimates, suggesting that participants updated their beliefs on egocentric trials according to the task they carried out (Bayes-optimal estimates: $t_{(29)}=0.928$, $p = 0.360$, $d= 0.170$; allocentric: M=70.1 , SD=11.19; egocentric: M=68, SD=10.82; Observed estimates: $t_{(29)}=0.987$, $p = 0.331$, $d= 0.180$; allocentric: M=64.53, SD=14.43; egocentric: M=61.63, SD=18.52, figure 7.11A and B). These results suggest that participants updated their egocentric beliefs more, possibly due to the higher metacognition they showed into their performance. Such discrepancy allowed them to correct their priors, hence leading them to believe they would be equally good at both tasks (but not better in egocentric ones).

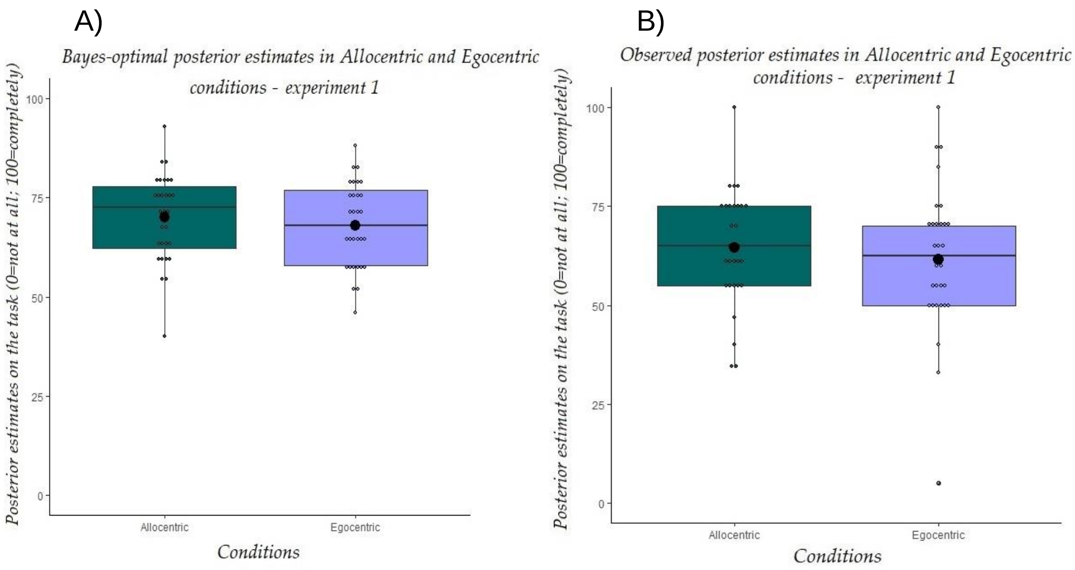


Figure 7.11. A) Bayes-optimal posterior distributions in Allocentric and Egocentric conditions, on a scale from 0-100; B) Actual participants' responses in the posteriors block (in response to the question: "*How well would you be able to remember the distance between 2 points you have just seen?*" ranging from 0="Not at all well" to 100="Completely"). Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR).

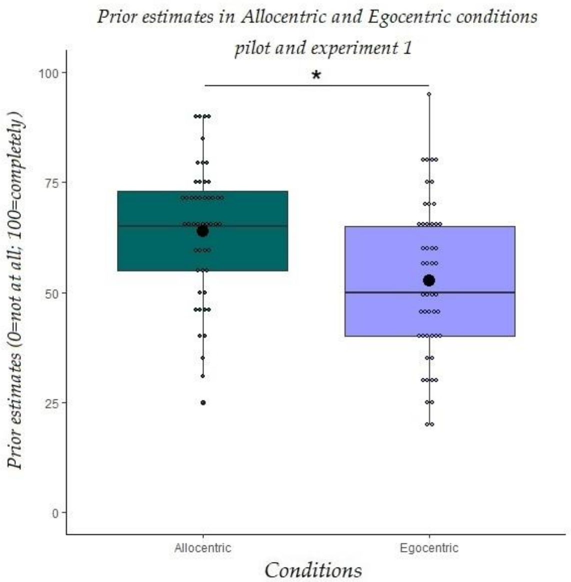
Experiment 1, in line with pilot data, showed that participants' prior beliefs on the task were biased towards allocentric trials (i.e. they believe they would be better in allocentric vs egocentric trials before performing the task). However, their performance again suggests the opposite, with participants' accuracy being higher in egocentric rather than allocentric trials, with the same pattern showed in metacognitive awareness. This suggests that participants were aware of their better performance in egocentric trials. Finally, participants showed a posterior estimates distribution similar to the expected one, given their prior beliefs and their actual performance, i.e. they updated their beliefs according to their performance levels.

7.3.3. Pilot and experiment 1

Priors block

In the merged sample including both pilot and experiment 1, significant differences between allocentric and egocentric conditions were found in both estimates and confidence values. In both instances, and in line with experiment 1, participants rated allocentric trials as easier than egocentric ones (Estimates: $t_{(48)}$=4.330, p <0.001., *d*= 0.619; allocentric: M=63.92, SD=15.47; egocentric: M=52.55, SD=17.99; Confidence: $t_{(48)}$=3.796, p<0.001, *d*= 0.542; allocentric: M=65.33 , SD=14.82; egocentric: M=57.69, SD=18.50 – see figure 7.12. A and B). In line with experiment 1, participants showed higher estimates and confidence in allocentric rather than egocentric trials, thus suggesting that they believed they would perform better in trials relying more on vision than proprioception.

A)



B)

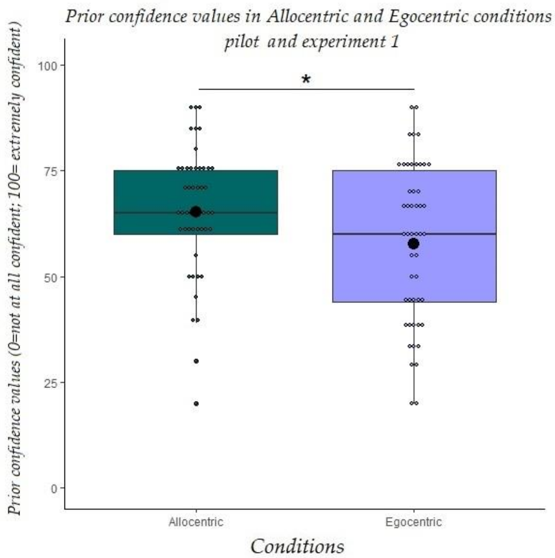


Figure 7.12. Participants' responses in the priors block to the questions A) "*How well would you be able to remember the distance between 2 points you have just seen?*" ranging from 0="Not at all well" to 100="Completely") and B) *"How confident are you in your answer?"* ranging from 0="Not at all confident" to 100="Completely". Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR). *p <0.05

Accuracy and metacognitive awareness - main task

A Wilcoxon paired-samples t-tests between egocentric and allocentric conditions revealed a significant difference, with egocentric trial leading to higher accuracy (Z=-3.500, p<0.0001, *r*=0.639; *Mdn*=0.8, IQR= 0.15; egocentric: *Mdn*=0.84, IQR=0.11 - see Figure 7.13). As for metacognitive awareness, a paired-sample t-test showed the same pattern of differences ($t_{(48)}$=-2.454, p=0.014, *d*=0.311; allocentric: M=0.64, SD=0.08; egocentric: M=0.66, SD=0.07 - Figure 7.14). As for experiment 1, participants performed better in egocentric rather than allocentric trials and were more metacognitively aware of their better performance.

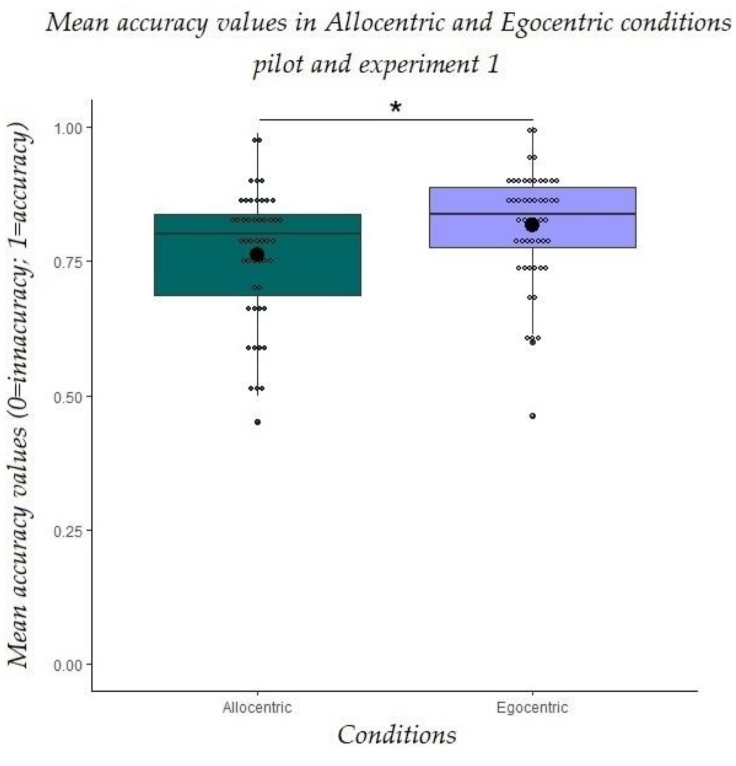


Figure 7.13. Mean accuracy values in egocentric and allocentric conditions. Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR). *p <0.05

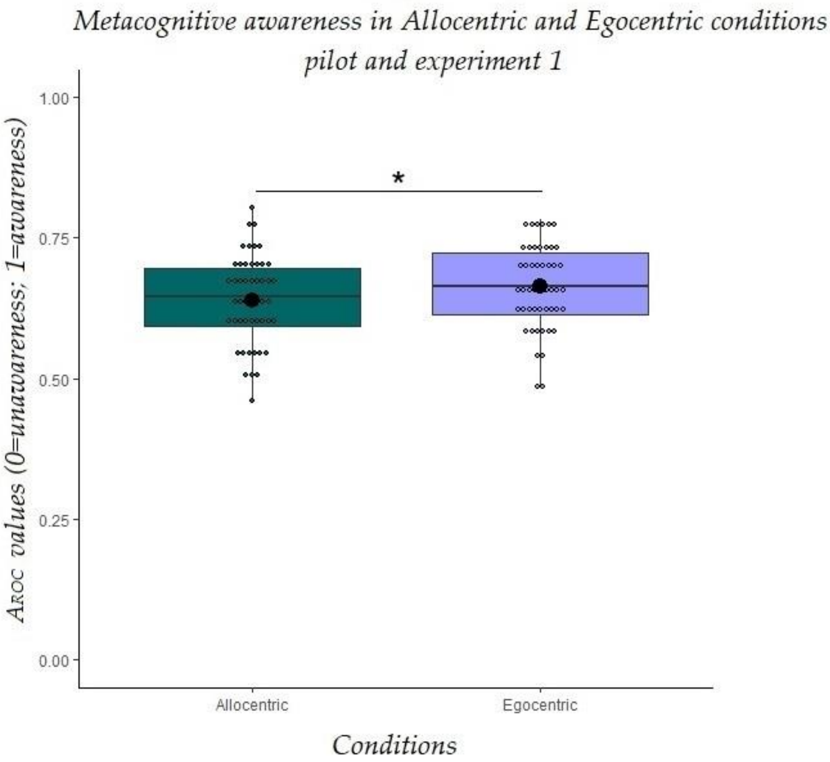


Figure 7.14. Mean AROC values in egocentric and allocentric conditions. Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR). *p <0.05

A linear mixed model with accuracy as the predicted variable and condition (i.e. egocentric or allocentric), awareness (i.e. AROC values), priors estimates and questionnaires scores (GSE and IRI perspective taking subscales) as predictors did not reveal any effects or interaction. The same was also true for metacognitive awareness values (see Table 7.3.).

Table 7.3. Summary of fixed and random effects of linear mixed models for Accuracy and Metacognitive awareness in pilot and experiment 1.

	Accuracy			**Metacognitive awareness**		
Predictors	*Estimates*	*CI*	*p*	*Estimates*	*CI*	*p*
(Intercept)	0.24	-0.50 – 0.97	0.528	0.22	-0.28 – 0.73	0.387
Metacognitive awareness	0.88	-0.24 – 2.00	0.129			
Condition	-0.00	-0.28 – 0.27	0.982	0.11	-0.05 – 0.27	0.169
Prior estimates	-0.00	-0.01 – 0.01	0.957	0.00	-0.00 – 0.01	0.889

Metacognitive awareness* Condition	-0.01	-0.43 – 0.40	0.948			
Condition*Prior estimates	0.00	-0.00 – 0.00	0.430	0.00	-0.00 – 0.00	0.959
Metacognitive awareness* Prior estimates	-0.00	-0.01 – 0.01	0.822			
Accuracy				0.53	-0.05 – 1.11	0.080
GSE				-0.00	-0.01 – 0.00	0.515
IRI – PT				0.00	-0.00 – 0.01	0.797
Condition*Accuracy				-0.13	-0.32 – 0.06	0.190
Accuracy*Prior estimates				0.00	-0.01 – 0.01	0.988
Random Effects						
σ^2	0.00			0.00		
τ_{00}	0.00 Participants			0.00 Participants		
ICC	0.54			0.60		
N	48 Participants			48 Participants		
Observations	96			96		
Marginal R^2	0.320			0.294		
Conditional R^2	0.684			0.716		

Bayes-optimal and observed posteriors

When merging the pilot and experiment 1 data, the same pattern reported in the analysis above was observed, with no difference between egocentric and allocentric conditions (Bayes-optimal estimates: $t_{(48)}$=1.326 , p=0.191, *d*= 0.190; allocentric: M=70.78, SD=9.95; egocentric: M=68.51, SD=11.67; Observed estimates: $t_{(48)}$=0.818, p =0.417, *d*= 0.117; allocentric: M= 65.49 , SD= 15.19 ; egocentric: M= 63.76, SD= 18.02, figure 7.15A and B), suggesting that participants updated their beliefs as expected.

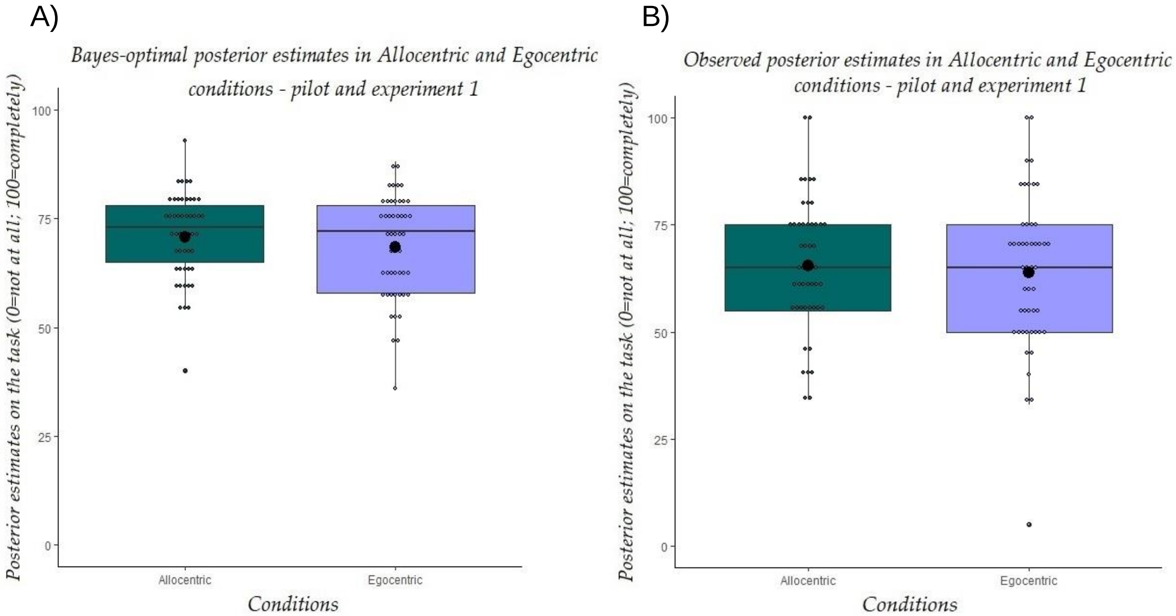


Figure 7.15. A) Bayes-optimal posterior distributions in Allocentric and Egocentric conditions, on a scale from 0-100; B) Actual participants' responses in the posteriors block (in response to the question: "*How well would you be able to remember the distance between 2 points you have just seen?*" ranging from 0="Not at all well" to 100="Completely"). Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR). $p < 0.05$

Combined data for the pilot study and experiment 1, revealed that participants' prior beliefs on the task were that they would perform better in allocentric trials. However, once again, their performance and metacognitive awareness suggests otherwise: participants' accuracy as well as metacognitive awareness were higher in egocentric rather than allocentric trials. Finally, as reported above for experiment 1 as well as the pilot data, participants showed a posterior estimates distribution similar to the expected one, suggesting that they updated their beliefs according to their performance levels and prior beliefs.

7.3.4. Experiment 2

Priors block

Paired-samples t-tests revealed a significant difference in the prior estimates, with allocentric trials being rated as easier than egocentric ones ($t_{(29)}$=2.425, p = 0.022, *d*= 0.443; allocentric estimates:

M= 65.17, SD= 16.97; egocentric estimates: M= 57.3, SD= 17.51, figure 7.16A), but no difference in confidence values ($t_{(29)}$=0.863, p = 0.395, *d*= 0.158; allocentric confidence: M= 63.97, SD= 16.75; egocentric confidence: M= 61.7, SD= 13.81, figure 7.16B). As for the pilot and experiment 1, participants believed they would perform better in allocentric (i.e. visually driven) rather than egocentric (i.e. proprioceptive driven) trials.

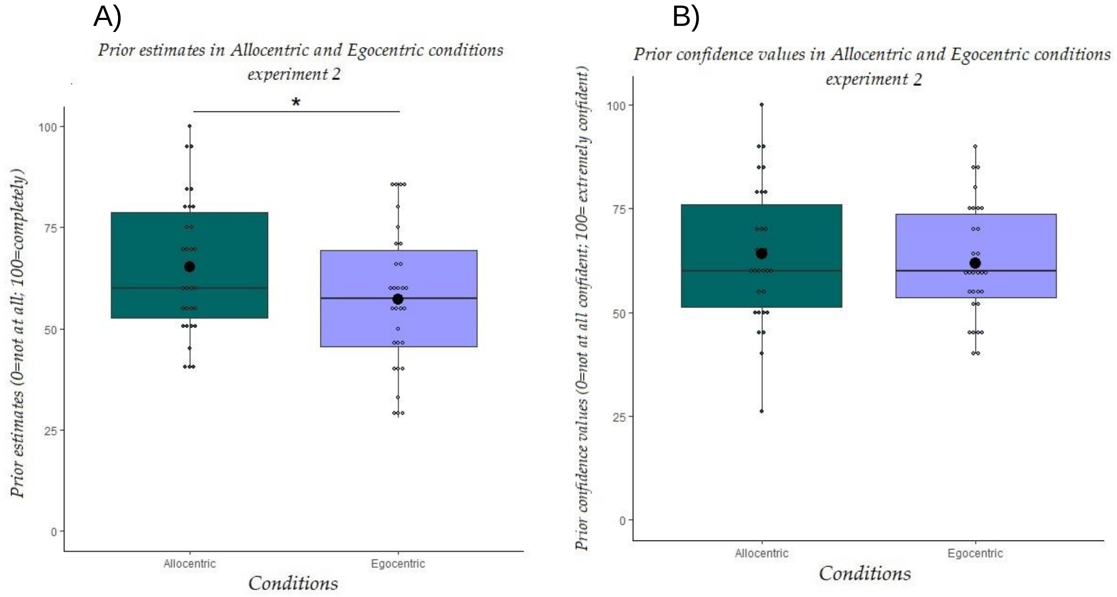


Figure 7.16. Participants' responses in the priors block to the questions A) "*How well would you be able to remember the distance between 2 points you have just seen?*" ranging from 0="Not at all well" to 100="Completely") and B) *"How confident are you in your answer?"* ranging from 0="Not at all confident" to 100="Completely". Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR). *p <0.05

Accuracy and metacognitive awareness – main task

Paired-samples t-tests between egocentric and allocentric conditions in both accuracy (Figure 7.5) and metacognitive awareness (Figure 7.6) did not show any significant difference (Accuracy: $t_{(29)}$= -0.0345, p=0.972, *d*= 0.00; allocentric: M=0.71, SD=0.07; egocentric: M=0.71, SD=0.08; Metacognitive awareness: $t_{(29)}$=0.2959, p=0.769, *d*=0.122; allocentric: M=0.54, SD=0.08; egocentric: M=0.53, SD=0.06 – see Figures 7.17 and 7.18). This finding is in line with the idea that using a staircase procedure equalised performance in order to obtain approximately 70% of correct responses and metacognitive awareness was in line with actual performance (i.e. participants were able to correctly judge lack of differences in their performance).

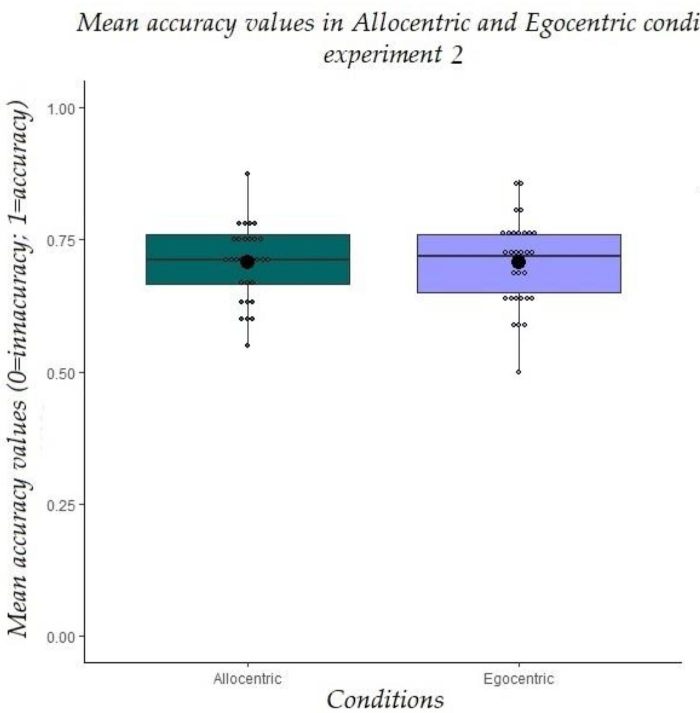


Figure 7.17. Mean accuracy values in egocentric and allocentric conditions. Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR).

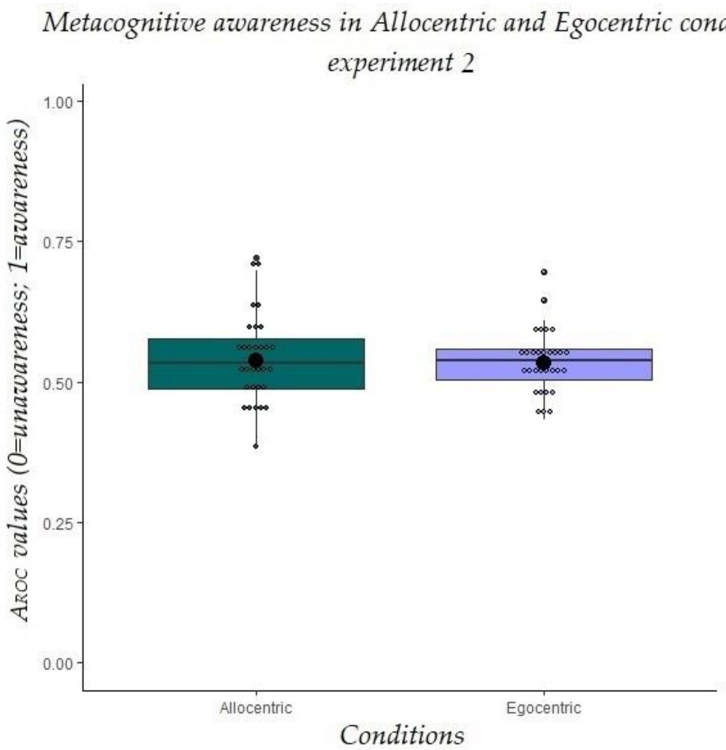


Figure 7.18. Mean A_{ROC} values in egocentric and allocentric conditions. Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR).

A linear mixed model with accuracy as the predicted variable and condition (i.e. egocentric or allocentric), awareness (i.e. A_{ROC} values), priors estimates, questionnaires scores (GSE and IRI perspective taking subscales) and control tasks (Corsi Blocks, Benton JLO, Digit Spant) as predictors did not reveal any effects or interaction. As for metacognitive awareness, the perspective taking subscale of the IRI questionnaire revealed a significant negative predictive effect (see Table 7.4.), suggesting that higher levels of perspective taking may negatively predict individuals' metacognitive awareness.

Table 7.4. Summary of fixed and random effects of linear mixed models for Accuracy and Metacognitive awareness in experiment 2.

	Accuracy			**Metacognitive awareness**		
Predictors	Estimates	CI	p	Estimates	CI	p
(Intercept)	0.82	0.13 – 1.50	**0.026**	0.38	-0.59 – 1.35	0.444
Metacognitive awareness	-0.36	-1.61 – 0.89	0.577			
Condition	-0.08	-0.35 – 0.18	0.541	0.25	-0.09 – 0.59	0.162
Pior estimates	0.00	-0.01 – 0.01	0.725	0.00	-0.01 – 0.01	0.595
Corsi blocks	0.01	-0.02 – 0.03	0.504			
Benton JLO	-0.00	-0.01 – 0.00	0.756			
Digit span	0.00	-0.00 – 0.00	0.671			
Metacognitive awareness* Condition	0.18	-0.34 – 0.70	0.510			
Condition*Priors estimates	-0.00	-0.00 – 0.00	0.877	-0.00	-0.00 – 0.00	0.148
Metacognitive awareness* Prior estimates	-0.00	-0.01 – 0.01	0.815			
Accuracy				0.20	-1.07 – 1.48	0.754
GSE				0.00	-0.00 – 0.00	0.826
IRI – PT				-0.01	-0.02 – -0.00	**0.019**
Condition*Accuracy				-0.22	-0.63 – 0.19	0.296
Accuracy*Prior estimates				0.00	-0.01 – 0.02	0.909
Random Effects						
σ^2	0.00			0.00		
τ_{00}	0.00 Participants			0.00 Participants		
ICC	0.68			0.22		
N	30 Participants_			30 Participants		

Observations	60	60
Marginal R^2	0.039	0.231
Conditional R^2	0.690	0.398

Bayes-optimal and observed posteriors

In line with the hypothesis, when participants' performance was equalised via a staircase procedure, a significant difference between allocentric and egocentric conditions was found in both Bayes-optimal estimates as well as reported posterior estimates. According to Bayes-optimal posterior estimates, participants should have updated their beliefs regarding egocentric trials in order to almost match the allocentric ones (Bayes-optimal estimates: $t_{(29)}$=2.178, p = 0.037, *d*= 0.398; allocentric: M= 68.63, SD= 7.96; egocentric: M= 64.83, SD= 9.10, figure 7.19A). Conversely, when the reported posterior estimates were compared, participants rated egocentric trials as being easier than allocentric ones, thus overcompensating their updating following the main task (observed estimates: $t_{(29)}$=-2.518, p = 0.017, *d*= 0.460; allocentric: M= 65.93, SD=17.69; egocentric: M= 73.63, SD= 16.80, figure 7.17B). These findings suggest that participants updated their egocentric beliefs more even though egocentric and allocentric performance was equalised and participants showed equal metacognitive awareness in the two conditions. This could be explained by the presence of more incorrect priors, so that when asked to express a prospective judgement about future tasks, participants seem to update their prior beliefs in terms of their egocentric priors.

A) B)

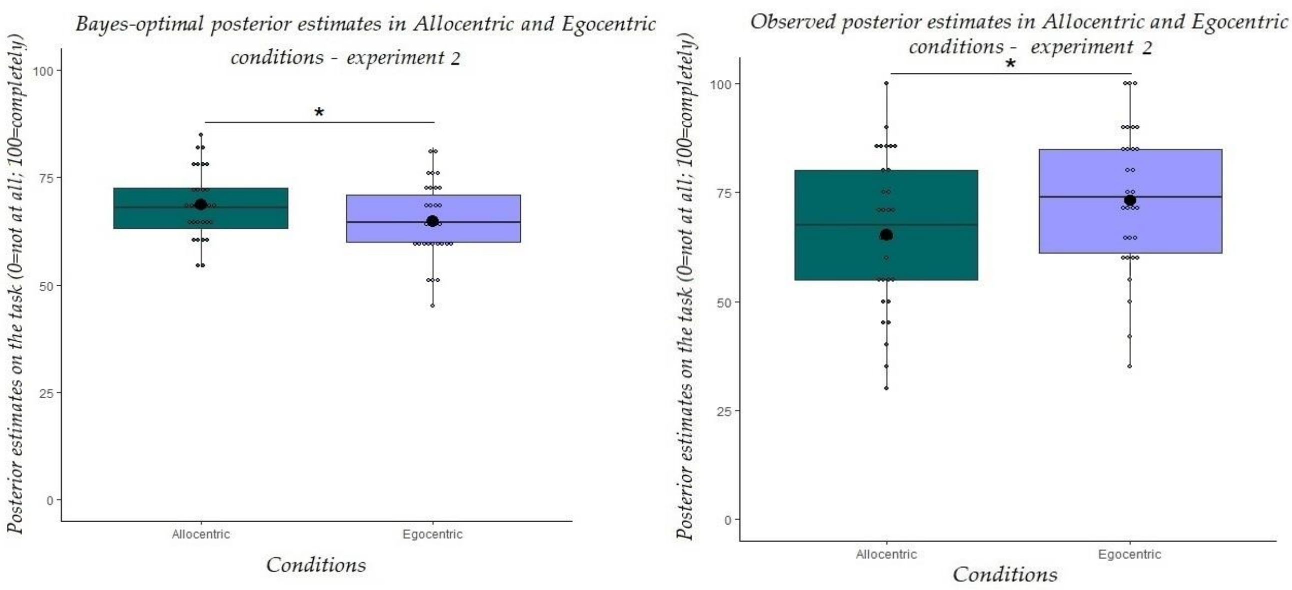


Figure 7.19. A) Bayes-optimal posterior distributions in Allocentric and Egocentric conditions, on a scale from 0-100; B) Actual participants' responses in the posteriors block (in response to the question: "*How well would you be able to remember the distance between 2 points you have just seen?*" ranging from 0="Not at all well" to 100="Completely"). Solid line=median; Black dot= mean; Whiskers: upper whisker = min(max(x), Q_3 + 1.5 * IQR); lower whisker = max(min(x), Q_1 – 1.5 * IQR). p <0.05

Experiment 2, in line with the pilot and experiment 1, confirmed that participants consider allocentric trials easier before performing the task (prior beliefs). When performance is equalised using a staircase procedure, participants show metacognitive abilities in line with their performance whilst doing the task (i.e. their performance did not differ between condition and so did their metacognition). However, when asked to judge how they would perform in the future, if presented with the same task (posterior beliefs), participants showed a bias towards egocentric trials: in the priors block, their estimates were higher for allocentric rather than egocentric trials. In the posteriors block, the reverse is true: participants rate as easier egocentric trials rather than allocentric ones despite the lack of the difference during the task and contrary to the expected posteriors distributions.

7.4. Discussion

The overarching aim of the current study was to identify the role of egocentric and allocentric frames of reference in informing self-awareness. This was done by firstly investigating prior beliefs on one's own ability to perform a perceptual task in egocentric and allocentric frames of reference in healthy volunteers. In all the experiments, participants always rated allocentric trials as being easier than egocentric ones when asked to express a prospective belief in their own perceptual abilities. That is, during the priors block, participants rated allocentric trials as less difficult than egocentric one. Interestingly, whilst no differential hypothesis was put forward regarding differences in prior beliefs, this finding may be explained as participants' belief that visual information could be more reliable than visuo-proprioceptive one. Given that individuals may be more inclined to judge spatial elements using visual inputs (Pasqualotto & Proulx, 2012), rather than using proprioception as a point of reference (when vision is available; Byrne & Henriques, 2013), this result could be due to the unfamiliar nature of the task. Further studies could test whether more ecological solutions (e.g. virtual environment settings) could reduce this potential bias.

Participants' accuracy and metacognitive awareness were explored via a perceptual task including encoding of stimuli in egocentric and allocentric frames of reference both with and without a staircase procedure to equalise performance. In the pilot study and in experiment 1, participants' performance was better when stimuli were encoded egocentrically rather than allocentrically. This finding is in line with participants' metacognitive judgements: their ability to discern whether they performed better allocentrically or egocentrically followed their actual performance. Whilst this is an unexpected finding, it suggests that participants are metacognitively able to monitor their own performance (Fleming & Daw, 2017) during a task (i.e. "online"). In experiment 2, when performance was equalised, no difference in accuracy was found, in line with the hypothesis. This was unexpectedly corroborated by participants' metacognitive awareness: no difference was found between egocentric and allocentric conditions. The results of experiment 2 suggest that the metacognitive differences found in the pilot and in experiment 1 could be due to the actual differences in participants' performance rather than signifying a metacognitive discrepancy between stimuli perceived in egocentric and allocentric

FoRs. In the pilot study only, a linear mixed model revealed that participants' awareness positively predicted their accuracy at the net of all other factors. Prior estimates were also found to be predictive of accuracy: both allocentric prior estimates and allocentric accuracy were aligned, whilst egocentric accuracy was higher than participants' priors estimates. These results suggest a good online monitoring ability in spatial tasks (Stevens & Carlson, 2016; Yeung & Summerfield, 2012), despite a discrepancy between accuracy and awareness during the task and prior beliefs on the same task.

Finally, belief updating abilities were investigated by computing a Bayes-optimal posterior distribution (given prior estimates and actual performance) as well as by directly asking participants to express a judgement on how well they thought they would be able to perform the same task again in the future (prospective belief). Interestingly, participants showed higher updating in their egocentric beliefs in all the three experiments. Whilst in pilot and experiment 1 Bayes-optimal posteriors were in line with participants' reported posteriors, in experiment 2, in which no difference in performance nor metacognitive awareness was found, participants reported posteriors were higher for egocentric rather than allocentric trials. Furthermore, reported posteriors were in the opposite direction in comparison with Bayes-optimal ones: whilst Bayes-optimal distributions revealed a higher expected updating in allocentric rather than egocentric trials, participants' reported posteriors showed the opposite pattern. Thus, participants seem to be less able to correctly update their beliefs when judging their own prospective performance in egocentric rather than allocentric conditions. This is in line with the idea that participants are better in retrospective rather than prospective judgements (Siedlecka et al., 2016); however, rather than being a generalised inability to judge their own actions prospectively, the findings of the current study may be linked to the specificity of a body-centred vs a world-centred processing. This corroborates the idea of an egocentric bias in updating beliefs related to one's own self in a prospective, rather than online fashion. This finding is in line with the suggested explanation of anosognosic patients' behaviour: such inability to correctly update egocentric prior beliefs may underlie the difficulty in disengaging from the 1st person perspective found in anosognosia (Besharati et al., 2016; Fotopoulou et al., 2008; Vocat et al., 2013). This lack of transferred knowledge from a good ability to monitor one's own performance online to a biased prospective judgement may provide an explanatory framework for AHP patients' behaviour.

This study also had some methodological limitation. Firstly, due to the nature of the apparatus, the experimenter had to manually position participants' hand on the graphic tablet. This may have led to small errors, impacting on egocentric trials. However, in order to ensure accuracy, the experimenter was visually guided by the cursor, which was moving according to participants' hand. Moreover, the finding that participants performed better in egocentric rather than allocentric condition does not seem to suggest disadvantages during egocentric trials. Secondly, the length of the task may have impacted on participants' responses. To avoid excessive fatigue, the experimenter ensured that participants had at least one break in the middle of the task as well as multiple breaks according to participants' needs. Thirdly, even though better model fitting procedures have been developed to analyse metacognitive awareness (e.g. Fleming, 2017), the current data-set did not allow for such fitting due to the non-parametric characteristic of the distributions. Hence, A_{ROC} analysis, which allowed for non-parametric metacognition data to be analysed, was used. Additionally, it could be argued that an additional difference, potentially undermining the experimental manipulation, exists between egocentric and allocentric trials: while participants are only exposed to visual stimuli during allocentric trials, in egocentric ones the integration of visual as well as proprioceptive signals is needed in order to estimate the distance between participants' own hand and the visual cue. Nevertheless, this unisensory versus multisensory difference is intrinsic to allocentric versus egocentric processing: allocentric judgements rely, by definition, on the relationship between elements of the surroundings that are visually perceived, whereas egocentric processing involves judgements of self-positioning in respect to environmental cues (which can often been perceived visually). Finally, egocentric trials entail a transformation from a screen-based, two-dimensional percept (i.e. the circle) to a three-dimensional point of reference (i.e. one's own hand). Whilst it was not possible to test whether such difference impacted on the perception of the stimuli, participants performed better in the egocentric, rather than allocentric trials, thus ruling out the possibility of an increased difficulty for egocentric but not allocentric conditions. Future studies could employ a virtual reality paradigm in order to equalise the perception of all different stimuli in a three-dimensional space.

In conclusion, the current study showed that participants believed that they would better perform a task when stimuli are presented allocentrically rather than egocentrically. However, their actual performance, as well as their metacognitive monitoring, was better in egocentric trials when performance was not equalised. When adopting a staircase procedure, participants showed an inability to update their beliefs according to their actual performance: such egocentric bias may be at the heart of failures in belief updating in clinical conditions, such as anosognosia for hemiplegia.

Chapter 8

General discussion

8.1. Introduction

The aim of this thesis was to explore the way individuals combine different sensory signals in order to achieve a sense of bodily awareness. Through neuromodulation, behavioural as well as neuropsychological studies, this thesis gained insight into the way we form and maintain our sense of self. The first aim was to assess the contribution of the vestibular system in weighting different sensory modalities according to their contextual relevance. Specifically, the focus of the first two experimental chapters (Chapters 2-3) was on the role of two, often understudied, sensory modalities in multisensory integration: the vestibular system and interoception. In Chapter 4, the specific contribution of vestibular stimulation to proprioception, visuo-spatial perception as well as body representation was explored, in order to rule out alternative hypotheses for the findings of the studies reported in Chapters 2 and 3. The second aim was to establish how multisensory integration processes contribute to different facets of the bodily self (namely ownership, motor awareness and agency) following brain damage, in order to better understand the underlying mechanisms in healthy subjects. Thus, in Chapter 5, ownership feelings, agency and motor awareness in patients with right-sided fronto-parietal stroke and left-side paralysis were investigated, to assess the role of vision and proprioception in body ownership as well as investigating the relationship between ownership, motor awareness and agency. The third aim was to explore the possibility that different visual perspectives could contribute to body ownership and motor awareness in patients with disorders of the self (AHP and DSO). As such, in Chapter 6, a task employing different visual perspectives (i.e. 1st, 3rd and their integration) was used to assess the influence of perspective taking on the bodily self. Finally, the fourth aim was to investigate the role of different spatial reference frames in awareness of healthy individuals' perceptual choices. In the last experimental chapter (Chapter 7), the possibility that individuals may be poorer in monitoring their own performance on a task when stimuli are perceived in a body-centred, egocentric way, was examined and compared to a world-centred, allocentric one, in order to gain a better understanding of the processes underlying self-awareness. The overall findings of these experimental chapters, as well as suggestions for future research, will be discussed and reviewed in this final chapter, together with methodological considerations, potential limitations and clinical implications.

8.2. Summary of main findings and future directions

To explore the first aim of the current thesis, i.e. that the vestibular system weights different sensory modalities according to the context in which they are experienced, three different studies were devised. In Chapter 2, a study using GVS in a Rubber Hand Illusion paradigm with touch delivered either affectively (i.e. in a CT-optimal fashion) or neutrally (i.e. in a non-CT-optimal one) has been presented. The aim of this study was twofold: 1) to investigate the role of vestibular stimulation in multisensory integration and 2) to explore the possibility of a joint modulation of vestibular and interoceptive systems in multisensory integration. Findings were in line with the predictions: specifically, vestibular stimulation of the right hemisphere led to greater proprioceptive drifts in comparison with the other two GVS configurations. Furthermore, interoceptive signals (i.e. affective touch), coupled with vestibular stimulation, strengthened such effect, leading to a further enhancement of vision over proprioception. In Chapter 3, a GVS and adapted RHI paradigm, looked at replicating findings from the previous study (i.e. that LGVS favours vision over proprioception) and investigate the role of vestibular stimulation in modulating 1) different epistemic aspects of touch (i.e. seen vs felt) and 2) specifically, affective touch (with felt affective touch enhancing proprioception over vision more than neutral touch and vice-versa when touch was seen). Findings from the first study were successfully replicated, i.e. LGVS led to greater proprioceptive drifts in visual only conditions. Moreover, when touch was only felt on participant's hand but not seen on the rubber hand, proprioceptive cues were weighted more than visual ones (i.e. proprioceptive drifts were lower), whilst the opposite was true when touch was seen but not felt (regardless of whether the touch was affective or neutral). Finally, in a control study (Chapter 4), alternative explanations for the findings presented in the first two experimental chapters were explored via a set of three control conditions. Specifically, the hypothesis that these findings may be explained by a modulation of multisensory integration following LGVS, was challenged by three alternative possibilities: 1) that LGVS reduces the weight of proprioceptive signals; 2) that LGVS induces a shift in space on the horizontal plane and 3) that LGVS effects are not related to the position in space of the object to be embodied. Results were in line with the originally hypothesis: LGVS did not influence proprioception or spatial perception per se. However, the visual capture findings reported in Chapters 2 and 3 were not successfully replicated: no changes in proprioceptive drifts were found in either the bio-mechanically possible or impossible position following LGVS. Nevertheless, the idea, posited by Ferrè and colleagues (2015), that vestibular signals may weight sensory modalities according to the context, still holds true even when taking into account alternative hypotheses, such as downregulation of proprioceptive signals or shifts in the visuo-spatial lateral plane, which do not seem to be able to explain the role of vestibular signals during multisensory integration on their own. Taken together, the findings of the first three experimental chapters pointed to a weighting role of the vestibular system during multisensory integration: that is, vestibular signals differently balance sensory modalities in order to reduce perceptual ambiguity.

The second aim of this thesis was to investigate multisensory integration processes contributing to ownership, motor awareness and agency in patients with right-sided stroke, in order to shed light on the underlying mechanisms involved in bodily awareness in healthy subjects. In Chapter 5, via a bed-side Rubber Hand Illusion paradigm, ownership, agency and motor awareness were investigated by asking patients to, firstly, look at a motionless rubber hand and rate their ownership feelings of it. Secondly, patients were asked to try to move whilst being provided with visual feedback that was either congruent with their motor intentions (i.e. the hand was moved by the experimenter) or incongruent with them (i.e. the rubber hand remained still) and then asked whether they detected any movement. Thirdly, AHP patients were asked whether they felt agency over detected movements and such responses, together with ownership values in the different conditions (i.e. baseline, movement, no movement), were used to investigate whether agency was modulated by ownership (and vice-versa). In terms of the first aim, findings from previous studies (Martinaud et al., 2017) were successfully replicated: the majority of right hemisphere patients automatically embodied a motionless rubber hand, with vision overriding proprioception. As for the second aim, in line with predictions, patients with Anosognosia for Hemiplegia (i.e. AHP) were more likely than controls to report occurrence of movement in the intention-incongruent condition (i.e. lack of movement). Finally, the exploratory analysis of the relationship between agency and ownership revealed that even when AHP patients do not experience agency over a detected movement, this does not impact ownership feelings. On the other hand, patients who never felt agency over detected movements also showed lack of ownership, thus suggesting the presence of a relationship with an unclear direction. Specifically, ownership seems to be less influenced than agency by changes in the external environment, thus suggesting a key role of visual dominance over other sensory modalities in establishing feelings of ownership but not agency.

The third aim of this thesis was to explore whether using different visual perspectives (i.e. 1st, 3rd and their integration) would lead to an improvement in ownership feelings (Disturbed Sensation of limb Ownership, i.e. DSO, patients) and motor awareness (in AHP patients). To do so, a bed-side paradigm involving the use of a mirror (with or without blocking direct view with a clipboard) was implemented (Chapter 6), together with a set of questions investigating ownership and motor awareness. In relation to the latter, patients were asked to state whether they could move, both before and after having attempted a movement (whilst looking at their arm either directly or in a mirror). In AHP and DSO patients, using mirrors to manipulate visual perspectives temporarily reinstated ownership feelings (in 3rd and integrated perspectives) but not motor awareness. This finding might be explained as a lack of "online" monitoring abilities in AHP patients, which leads to a failure in integrating sensory information leading to self-awareness.

The fourth aim of this thesis was to investigate self-awareness in healthy subjects following presentation of stimuli in different frames of reference (Chapter 7). Subjects were asked to perform a perceptual choice and then to rate their confidence in such choice. Accuracy, confidence ratings and prior/posterior beliefs on participants' hypothesised performance were collected and analysed to assess their awareness in their own responses following presentation of stimuli in egocentric (i.e. body-centred) or allocentric (i.e. world-centred) reference frames. In line with the evidence reported in AHP patients, healthy subjects showed lower awareness of their own performance (when judged prospectively) only when information was perceived in a body-centred (i.e. egocentric) fashion compared to a world-centred, allocentric one. These findings point towards an egocentric bias in individuals' awareness of their own actions.

The results of the different experimental studies, as well as suggestions for future research, will be discussed in further details, and in relation to their aims, in the next four paragraphs.

8.2.1. The role of the vestibular system in balancing sensory conflict and informing body representation

The study of multisensory integration and the bodily self has been increasingly departing from classic views of the body as experienced exteroceptively (e.g. via vision; Folegatti, de Vignemont, Pavani, Rossetti, & Farne, 2009; Holmes, Crozier, & Spence, 2004; Pavani, Spence, & Driver, 2000; van Beers, Wolpert, & Haggard, 2002). The abovementioned studies focused on the extent to which vision would dominate over other sensory modalities in sensory conflictual situations. Recently, more integrative views started to encompass vestibular (Ferre, Berlot, et al., 2015; Lenggenhager & Lopez, 2015; Lopez, Lenggenhager, & Blanke, 2010) and interoceptive systems (Crucianelli, Krahe, Jenkinson, & Fotopoulou, 2017; Crucianelli, Metcalf, Fotopoulou, & Jenkinson, 2013; Lloyd, Gillis, Lewis, Farrell, & Morrison, 2013; Suzuki, Garfinkel, Critchley, & Seth, 2013; van Stralen et al., 2014) as key sensory modalities contributing to multisensory integration and body representation. Nevertheless, the relationship between these different sensory modalities on determining the way individuals perceive their body as their own has not been clearly identified. Two existing studies that used the Rubber Hand Illusion paradigm (Botvinick & Cohen, 1998) investigated how the vestibular system modulates multisensory integration, with findings pointing to conflicting explanations. Lopez and colleagues (2010) suggested that vestibular stimulation of the right hemisphere enhances vision over proprioception, thus leading to an increased illusion of ownership of a rubber hand. Conversely, Ferrè and colleagues (2015) showed the opposite, with brief bursts of vestibular stimulation enhancing proprioception over vision (via decreasing proprioceptive drifts). Whilst there are some methodological differences that could potentially account for such discrepancy (see section 2.4. Discussion, Chapter 2), both studies indicated a regulatory role of the vestibular system in multisensory integration. However, neither of these studies, nor others in the literature, investigated the possibility of a vestibular modulation of multisensory integration, including interoceptive signals.

As argued in Chapter 2, vestibular and interoceptive systems share functional and neuroanatomical features that would underlie their role in the mechanisms leading to a coherent sense of bodily self (e.g. Lopez, 2016). Hence, the first two studies of the current thesis aimed to explore the relationship between vestibular and interoceptive systems, with the idea that the right-hemisphere vestibular network would modulate different sensory modalities, including interoception, according to the context. In the first study, this was done via stimulation of the vestibular nerves using galvanic vestibular stimulation (i.e. LGVS, RGVS and Sham) in an RHI paradigm implementing a visual only condition as well as tactile ones, with affective (i.e. CT-optimal, interoceptive) or neutral touch delivered both synchronously and asynchronously. Findings revealed that participants showed an enhancement of vision over proprioception during LGVS (i.e. greater proprioceptive drifts) in visual only conditions (i.e. with no touch applied), and beyond any general GVS effects. This result is in line with Lopez and colleagues (2010) and suggests that stimulation of the right-vestibular network may enhance vision over proprioception, thus leading to a greater proprioceptive displacement of participants' own hand. Moreover, when touch was delivered in synchrony on both the participant's and rubber hand, proprioceptive drifts were greater following LGVS, in line with the visual only conditions. Finally, in LGVS synchronous conditions only, affective, CT-optimal touch led to a further increase in the weighting of visual signals, increasing proprioceptive drifts in comparison with neutral touch. This latter result points towards a vestibular modulation of interoceptive (via stimulation of C-tactile fibres) as well as exteroceptive modalities during multisensory integration: when there is a conflict between different sensory modalities (i.e. vision, touch and proprioception), stimulation of the right vestibular network, enhances vision over proprioception in order to solve such conflict, with affective touch further strengthening such effect.

Nevertheless, in this first study, it was not possible to conclude whether the enhancement of vision over proprioception during synchronous affective touch was due to its *felt* (from within) or *seen* (vicarious) properties or their combination. As detailed in Chapter 3, affective touch elicits the same neural activation and subjective responses of pleasantness when felt as well as when observed on someone else's skin (Morrison, Bjornsdotter, & Olausson, 2011b). Hence, in Chapter 3, two studies were devised in order to shed light on the relationship between the vestibular system and different epistemic aspects of touch (felt vs seen), and specifically affective touch, in multisensory integration. To do so, in two separate experiments, participants underwent GVS while either receiving CT-optimal (affective) or non-CT optimal (neutral) touch on their own hand only (experiment 1) or seeing touch being delivered on the rubber hand only (experiment 2) at a CT-optimal or non-CT-optimal velocity. Furthermore, in order to replicate the findings of the first study, i.e. that LGVS enhances vision over proprioception in visual only conditions, two additional conditions with no touch involved were devised. During these conditions, participants were asked to look at the rubber hand, similarly to what happened in the first condition of Study 1 (but for 30 instead of 15 seconds). In terms of replicating the finding of the first study, LGVS enhanced vision over proprioception in visual only conditions in comparison with the other GVS configurations. Furthermore, findings related to the tactile conditions were partially in line with the hypotheses: stimulation of the right vestibular network enhanced proprioception over vision when touch was felt but not seen, and vision over proprioception when touch was seen but not felt (i.e. proprioceptive drifts were smaller following touch felt but not seen and greater when touch was seen but not felt). However, this was not specific to the affectivity of touch (i.e. both felt and seen touch equally contributed to the aforementioned effects, regardless of their affectivity), thus suggesting a relationship between vestibular modulation of different epistemic, but not affective, types of touch.

Taken together, these results suggest a role of the vestibular system in balancing different sensory modalities during sensory conflict (i.e. when there is a mismatch between visual, proprioceptive and tactile information). Specifically, and in agreement with neuroimaging findings, suggesting an overlap between the vestibular and multisensory integration networks (Lopez et al., 2012; zu Eulenburg et al., 2012), vestibular signals in the right temporo-parietal and insular areas may influence the weighting of different sensory inputs according to their contextual relevance. Such balancing role of the vestibular system can be explained in terms of a weighting mechanism, implemented to solve ambiguous perceptual situations (e.g. in the RHI, this would translate into an increased weight of visual signals over proprioceptive ones, leading to embodiment of the rubber hand). On the other hand, the relationship between vestibular and interoceptive systems may be less straightforward: one possibility is that both felt and seen components of affective touch are needed in order to modulate multisensory integration (Filippetti et al., 2019) and this hypothesis should be addressed in future research.

Importantly, the above-mentioned results could also be explained by alternative mechanisms, such as a downregulation of proprioceptive signals (i.e. a hypoactivation of somatosensory areas which might make proprioceptive signals less reliable) and visuo-spatial shifts towards the left side on the horizontal plane. In Chapter 4, such possibilities were explored in a new study, which also included additional control conditions, aimed at clarifying whether the observed enhancement of vision over proprioception was specific to a plausible body representation or to a lower-level multisensory integration process. In one condition, the rubber hand was positioned in a biomechanically possible fashion, whereas in a second condition the hand was in a biomechanically impossible position. Results did not show differences between the three GVS configurations in either proprioceptive drifts (during proprioceptive only conditions) nor visuo-spatial judgements. Findings from this study showed that neither a downregulation of proprioceptive signals nor a shift on the horizontal plane could be used as alternative explanations to previous results on their own. That is, the idea that the vestibular system acts as a balancing factor at the multisensory integration level was not ruled out by simpler, lower-level mechanisms. On the other hand, in this final neuromodulation study, previous results related to visual capture of proprioception have not been replicated, i.e. LGVS did not increase proprioceptive drifts when the hand was positioned in a biomechanically plausible position, and there was no difference in proprioceptive drifts following the two conditions (biomechanically possible or impossible) in LGVS. As explained in detail in Chapter 4, this might be due to either lack of power or to the fact that such weighting mechanism influenced by vestibular signals might operate at lower-level of multisensory integration preceding body representation. Put simply, instead of acting on a higher level of the body representation hierarchy, vestibular signals may inform the integration of different sensory signals even when they are not related to the representation of biomechanically plausible body parts. Future studies could shed light on whether using different objects, rather than different positions, has an impact on visual dominance over proprioception during vestibular stimulation, in order to establish whether the nature of the object (i.e. a body part vs an object), rather than its position only, would influence visual capture of proprioception.

The lack of subjective embodiment in all these experiments suggests that the top-down (i.e. from higher-order cognition to perception) regulation involved in embodiment (i.e. in *feeling* that this body is mine) may not be influenced by the vestibular system. Contrary to the findings of Lopez and colleagues (2010), none of the neuromodulation studies presented in this dissertation pointed to an involvement of LGVS in enhancing ownership feelings as measured via self-reported questionnaires. This is, per se, consistent with the established dissociation between different measures during the RHI, which may tap into different aspects of the bodily self: embodiment feelings and proprioceptive drifts in the RHI have been found to dissociate in several studies (Abdulkarim & Ehrsson, 2016; Makin et al., 2008; Rohde et al., 2011) and this is in line with the abovementioned idea that vestibular signals may act at a lower-level of multisensory integration. Future research may disentangle such differences in previous research, by testing different tools to measure embodiment during vestibular stimulation.

To summarise, the findings of the first three experimental chapters of this thesis suggested that vestibular signals contribute to multisensory integration processes involved in body ownership by weighting the contribution of different sensory signals according to the context in which they arise. In the next section, neuropsychological data on multisensory integration and bodily awareness will be discussed, with the aim of shedding further light on the processes underlying body representation in individuals with a compromised bodily self.

8.2.2. The compromised bodily self: body ownership, self-awareness and agency in right-hemisphere stroke patients

Anosognosia for Hemiplegia (Babinski, 1914; Vossel et al., 2013; Fotopoulou, 2014) and Disturbed Sensations of limb Ownership (i.e. DSO; Baier and Karnath, 2008; Gerstmann, 1942) offer a window of insight into several facets of the bodily self, such as body ownership (e.g. Martinaud et al., 2017; van Stralen, van Zandvoort, Kappelle, & Dijkerman, 2013; Zeller, Gross, Bartsch, Johansen-Berg, & Classen, 2011), motor awareness (e.g. Fotopoulou et al., 2008) and agency (e.g. Haggard, 2005). Given that, in healthy subjects, it is not possible to fully explore such aspects (as the sense of bodily self is an always-present aspect of self-consciousness), neuropsychological patients with focal disorders of the self have the potential of aiding our understanding of mechanisms underlying the maintenance of a sense of self.

As such, the second main aim of this thesis was to firstly, building upon existing findings, explore the possibility of a dominance of vision over proprioception in right-hemisphere stroke patients, regardless of their clinical presentation (i.e. with or without DSO), versus age-matched controls. The study presented in Chapter 5 implemented a bedside RHI paradigm in order to explore body ownership, motor awareness and agency (and their relationship) in right hemisphere stroke patients. Patients were asked to look at a motionless rubber hand and rate their feelings of ownership of it. Results showed that 70% of the sample was visually captured by the rubber hand, stating the hand was their own, thus confirming previous findings that the majority of right-hemisphere stroke patients show Visual Capture of Ownership (i.e. VoC; Martinaud et al., 2017) when presented with a motionless rubber hand. The percentage of VoC feelings was significantly higher in the patient population when compared with age-matched controls, thus ruling out the possibility that VoC may be due to normal ageing processing leading to increased malleability of body representation (Marotta et al., 2018). This mechanism of visual dominance over proprioception may be the result of a compromised multisensory integration following lesions in the right fronto-parietal areas. Nevertheless, lesion mapping analysis did not reveal any significant pattern of lesion associated with this phenomenon, contrary to previous results (Martinaud et al., 2017). Further studies are needed to disentangle such discrepancy.

Secondly, the extent to which motor intentions shape awareness of one's own movement (and related feelings of agency over such movements) was investigated in anosognosic patients. Previous studies (Fotopoulou et al., 2008) suggested that AHP patients tend to detect movements even when there is none and attribute agency over such movement to themselves, due to the dominance of motor intentions over sensory feedback. To test this, patients were asked to try and perform a movement and were presented with either an intention-congruent movement of the rubber hand (i.e. the rubber hand moved) or an intention-incongruent one (i.e. the rubber hand did not move). As predicted, AHP patients tended to report a movement occurring even when there was no movement of the rubber hand. However, this was not necessarily linked to a sense of agency (i.e. a sense of being in control of one's own actions) over such movement: AHP patients felt significantly higher agency only when the rubber hand actually moved and not when it remained motionless. That is, they detected a movement (which occurred) and felt that they were the ones responsible for it, whereas hemiplegic controls still detected the movement but did not attribute it to themselves. These results are partially in line with the hypotheses: according to previous studies (Fotopoulou et al., 2008), a sense of agency in intention-incongruent conditions was also expected, given AHP patients tendency to disregard visual feedback and rely on their motor expectations (Fotopoulou, 2014). One possibility is that motor intentions may influence motor awareness but they may not influence the sense of agency. Further studies should explore this possibility by replicating and expanding the full protocol of Fotopoulou and colleagues (2008), in order to include conditions coupling motor intentions with explicitly externally generated movements.

Finally, the relationship between ownership and agency feelings was investigated. The lack of agreement on such relationship in the literature did not allow for clear directional predictions. While Kalckert and Ehrsson (2012) posit that ownership and agency are two dissociated facets of the self, more recent work suggests that one may influence the other, with research indicating that ownership shapes agency (Burin et al., 2019) or vice-versa (Asai, 2016; Tsakiris, Prabhu, & Haggard, 2006). Findings from the current study are partially in line with the idea of a dissociation between agency and ownership, with agency changing according to contextual information (in this case, presence or absence of movement) and ownership being more stable, regardless of the visual feedback. This could be explained as ownership feelings requiring additional top-down information to arise (as argued in the previous section), whilst agency may depend on lower-level multisensory integration mechanisms. Further studies could investigate whether there is a true dissociation between ownership and agency or whether they are different steps of a hierarchical model of body representation.

To summarise, the study reported in Chapter 5 found that right-hemisphere stroke patients exhibit an exaggerated dominance of visual information over other sensory signals during multisensory integration, which leads to strong feelings of ownership for a seen rubber hand. This finding is similar to what happens in healthy subjects following vestibular stimulation of the right vestibular network, where the weighing of visual information is enhanced over proprioception. A possible explanation for VoC effects is that somatosensation is deemed unreliable as a result of lesions in multisensory integration areas that normally lead to a coherent sense of body ownership (e.g. frontal operculum; Ehrsson et al., 2005). However, in the current study, lesion mapping analysis did not lead to significant results due to the implementation of stricter analysis criteria. It was hypothesised (as in Martinaud et al., 2017) that VoC would be associated with lesions in fronto-parietal areas (and, specifically, the frontal operculum), which are crucial in establishment of feelings of ownership in healthy subjects (Ehrsson, Holmes, & Passingham, 2005; Ehrsson, Spence, & Passingham, 2004). Future studies are needed to shed light on the neural correlates of VoC. In terms of motor awareness and agency, anosognosic patients present with a dominance of motor intention over sensory feedback, which does not necessarily translate to feeling agency over detected movements. Accordingly, the relationship between agency and ownership points towards a more bottom-up process leading to agency and a more top-down one needed to maintain ownership.

8.2.3. Perspective-taking in AHP and DSO: can integrating 1st and 3rd person perspectives influence motor awareness and ownership?

As detailed in Chapter 6, the third main aim of this thesis was to investigate the possibility that manipulations of visual perspectives could influence motor awareness and ownership in patients with Anosognosia for Hemiplegia (AHP) and Disturbed Sensations of limb Ownership (DSO). AHP and DSO might arise as a result of a compromised first-person (i.e. as experienced directly) representation of the body, despite an intact third-person one (i.e. as seen from the outside). Although patients seem to be able to regain awareness of their motor deficits (AHP) as well as ownership of their paralysed limb (DSO) while looking at themselves via a 3rd person-perspective (in video-replays or mirrors, respectively), they may not be able to integrate this information into their current body representation in every-day life (Besharati et al, 2014; Fotopoulou et al., 2009; Fotopoulou et al., 2011). In line with this evidence, the prediction was that asking patients to observe their own arm in a mirror (i.e. introducing a 3rd person-perspective) would temporarily remit dis-ownership feelings but that it might not be as effective in reinstating awareness due to its "online" nature (i.e. entailing the presence of motor intentions during self-observation) vs the offline one of videos (i.e. self-observation whilst not trying to actively move). In order to explore this hypothesis, a bed-side paradigm involving the use of a mirror was devised. Patients were asked whether they felt ownership of their own hand. Then, they were asked whether they could move it (before and after attempting a movement). These questions were asked while patients were looking either at their own hand directly (1st person-perspective); their own hand in a mirror, with direct view not obstructed (integration of 1st and 3rd perspectives); and their hand in a mirror with direct view being blocked (3rd person-perspective).

It was found that, contrary to predictions, AHP patients' awareness improved after the failure of the attempted movement, regardless of the type of view (mirror vs direct). In terms ownership, 4/7 DSO patients regained ownership while viewing their own arm in the mirror in comparison with the direct view. These results suggest that integration of 1st and 3rd person perspective did not reinstate awareness but improved ownership feelings, with no specific effects of 3rd person-perspective conditions only on either awareness or ownership. In terms of anosognosic patients' motor awareness, these findings could be linked to the "online" nature of the task: when patients are confronted with a movement whilst performing it, their motor intentions may override visual feedback (similarly to what has been observed and discussed in Chapter 5 and in the section above). However, when they are shown clips of themselves trying to perform a movement in an "offline" fashion (i.e. when they are not actively trying to move), their awareness improves (Besharati et al, 2014; Fotopoulou et al., 2009). Future research could employ both offline (i.e. video-replays) and online (i.e. mirrors) methods to allow for a direct comparison. Ideally, this should be done in a between-subjects design, given the possibility that video-replays may reinstate awareness after the first view.

In terms of ownership feelings, the findings of this study are consistent with previous research (Fotopoulou et al., 2011; Jenkinson et al., 2013) indicating that using mirrors temporarily reinstate ownership in DSO patients. This result, and its lack of lasting effects, may be due to a dissociation in DSO patients between their direct experience of their own body versus their body as experienced from outside (Fotopoulou et al., 2011). The ability of DSO patients to effectively use information coming from their 3rd person-perspective when confronted with it, whilst being unable to use it to inform their current body representation, may result from an impaired integration of different spatial perspectives. However, contrary to AHP, DSO patients do not present with concurrent conflicting information (i.e. motor intentions) when presented with their arm in the mirror and are thus able to use such information to temporarily gain ownership of their own arm. Future studies could test whether targeted interventions, with repeated mirror sessions, could facilitate such integration, thus improving ownership feelings. More broadly, findings from the current study seem to suggest that both AHP and DSO patients present with a failure in integrating incoming sensory feedback informing their body representation.

8.2.4. Influence of egocentric and allocentric frames of reference on metacognition in healthy individuals: evidence for an egocentric bias?

In the final chapter of this thesis (Chapter 7), the aim was to assess metacognitive abilities in healthy subjects following presentation of stimuli in different frames of reference. This was achieved via devising a novel experimental paradigm, during which participants were presented with stimuli positioned either egocentrically or allocentrically and were subsequently asked to make a perceptual choice between two alternatives (with one of them being the correct response) and express their confidence on such choice. Before this main task, participants were also presented with a short block assessing their belief regarding how well they would perform the task before starting it (prior beliefs) as well as a final short block assessing their prospective belief in case they were asked to perform the same task again in the future (posterior beliefs).

Findings from the studies presented in Chapter 5 and Chapter 6 point to a failure, in AHP patients, to correctly interpret, and properly integrate, information coming from their own body (as perceived directly by them). This may be linked to a broader impairment in monitoring their own performance when it is presented to them in an egocentric (i.e. based on the perceiver) fashion. However, no study to date explored how healthy subjects' awareness of their own actions is modulated by different spatial frames of reference (i.e. an egocentric versus allocentric, world-based one). If an egocentric bias is present in healthy subjects, this may provide an explanation for the mechanisms sub-serving lack of awareness in AHP, as well as improving our understanding of conscious awareness processes.

In terms of prior beliefs, participants always rated allocentric trials as being easier than egocentric ones. Even though no directional prediction was made in regard to the priors, this finding is in line with the idea that participants may intuitively find visual information more reliable than visuo-proprioceptive one, given their spatial judgements are normally guided by visual inputs in everyday life (Byrne & Henriques, 2013; Pasqualotto & Proulx, 2012). Future studies could explore whether more ecological paradigms (e.g. virtual reality ones) could increase the reliability of visuo-proprioceptive signals, thus equalising the perceived difficulty of the task from the beginning.

In the main task, lower awareness was expected following processing of stimuli in the egocentric, rather than allocentric, reference frame. This prediction was, however, not supported: on the contrary, participants were more accurate and also more metacognitively aware when presented with egocentric rather than allocentric signals. Moreover, when task difficulty was matched for both egocentric and allocentric conditions (and thus accuracy was equal), no metacognitive difference was found, suggesting that participants had overall good “online” monitoring abilities regardless of the spatial reference frame in which stimuli were perceived. However, and in line with the hypothesis, participants showed a lack of belief updating specific to the egocentric frame of reference: that is, when judging their prospective abilities, participants seem to believe that they would perform significantly better in egocentric tasks even when this was not corroborated by the actual performance (and when it was, significantly more than expected).

Thus, this final study, indicates that healthy participants may present with an egocentric bias in belief updating, which is specific to one’s own abilities in a prospective, rather than online, fashion (Siedlecka et al., 2016). Furthermore, this could provide a working framework for explaining anosognosic patients’ behaviour, which could stem from patients’ inability to update prior beliefs about their own body as perceived egocentrically (i.e. their paralysis) (Besharati et al., 2016; Fotopoulou et al., 2008; Vocat et al., 2013).

8.3. Methodological considerations and potential limitations

This dissertation aimed to explore how combining different sensory signals allow individuals to achieve a sense of bodily awareness using a variety of techniques, ranging from neuromodulation to neuropsychological studies. As such, it presents with some methodological issues as well as potential limitations. While specific issues have been discussed in each experimental chapter in detail, in the following section more general methodological issues will be considered.

8.3.1. Galvanic vestibular stimulation and the Rubber Hand Illusion

Galvanic Vestibular Stimulation (i.e. GVS) has been proven to be an effective tool in both research as well as clinical environments (Utz et al., 2011). Nevertheless, its usage entails some intrinsic methodological constraints. Some of GVS methodological issues are linked to the specific machine used in the abovementioned experiments (NeuroConn Direct Current stimulator, neuroCare Group GmbH, München, Germany). This device, instead of being compatible with a remote, computerised control mechanism, works with a simple on/off button, leading to a reduced experimental control. Furthermore, a fixed intensity of 1 mA was implemented throughout the four experiments reported in chapter 2-4. This was done in order to allow comparability between different GVS configurations as well as replicability in the patients' population using established safe parameters (Utz et al., 2011). However, suprathreshold stimulation (i.e. a stimulation calibrated on each subject's own vestibular sensation threshold, used as the minimum stimulation intensity), allows for increased control over vestibular feelings (i.e. researchers can be sure the subject felt noticeable vestibular sensations). One of the counterindications of using suprathreshold stimulation (e.g. Lopez et al., 2010) is that it has the potential risk of reducing the placebo effect of Sham conditions due to the fact that suprathreshold stimulation leads to stronger feelings of dizziness, motion sickness and vertigo in comparison with lower intensities. Thus, in line with previous research indicating that a fixed intensity of 1 mA leads to identifiable vestibular feelings without necessarily compromising the role of Sham (Wilkinson et al., 2010; Kerkhoff et al., 2011; Schmidt et al., 2013a, 2013b; Ferrè et al., 2013a, 2013b; Ferrè et al., 2015), this intensity was used to ensure maximum comparability between LGVS, RGVS and Sham configurations.

Nevertheless, while the majority of the subjects in all the GVS experiments presented in the current thesis identified Sham as a vestibular stimulation, approximately 1/3 of each sample did not.

Even though this may suggest that the role of Sham as a placebo intervention may not be as efficient as expected, differences in judgements were also present for LGVS and RGVS, with part of the subjects not being able to recognise them as vestibular stimulations. Due to the unfamiliar nature of this type of stimulation, it is possible that subjects may not have been entirely able to distinguish between the sensations elicited by the different types of stimulation (i.e. they may have been more focused on the itchiness and skin-related effects of the stimulation rather than the vestibular ones), thus not necessarily ruling out Sham as a reliable control condition.

Furthermore, as discussed in section 3.4, Discussion, Chapter 3, this GVS device did not allow for fully blinded procedures. As a countermeasure for the fact that the experimenter administering the GVS could not be blind to the stimulation delivered, data were collected by different fully-trained experimenters (studies in Chapter 3 and Chapter 4), all under the supervision of the main experimenter (who was the only one participating in the study design), to decrease experimenter's bias.

Throughout the thesis, and in line with neuroimaging findings (Bense et al., 2000; Eickhoff et al., 2006; Kammermeier et al., 2017; Lopez et al., 2012 Stephan et al., 2005; zu Eulenburg et al., 2012), work was carried out under the assumption that following left-anodal/right-cathodal (i.e. LGVS) stimulation, areas of the right vestibular network would be activated, whereas the opposite configuration (right-anodal/left-cathodal, i.e. RGVS) would activate areas of the vestibular networks bilaterally. However, no neuroimaging technique was used during the experiments reported in this dissertation, thus not allowing for a definitive conclusion in terms of functional activation in response to GVS. Whilst it was not possible to implement the paradigms used in the first three experimental chapters in an fMRI environment, due to their length and the attempt to maintain ecological validity, EEG measures could have been used. Nevertheless, given vestibular stimulation may induce dizziness and vertigo, it was frequently not possible to ask participants to maintain their head perfectly still. On the other hand, implementing a chin-rest wouldn't have allowed participants to look at the rubber hand for the required time without causing distress and fatigue. Hence, these tasks, as devised, were not ideally suitable for neuroimaging recording with classic EEG devices. Future research, based on these preliminary behavioural and neuromodulation findings, could however decrease testing time (by, for instance, eliminating RGVS and comparing only LGVS vs Sham) and employ newer EEG devices (which have a better signal-to-noise ratio even when in motion; e.g. Versatile EEG 32, Bitbrain) coupled with GVS.

In terms of the combined usage of GVS and the Rubber Hand Illusion (i.e. RHI), there are some methodological considerations to discuss. Firstly, in all the GVS experiments presented in the current thesis, participants were always right-handed, with the rubber and stimulated hand used during the experiments always being the left one. This was done in order to explore the relationship between vestibular stimulation of the right vestibular network and a lateralised right-hemisphere network for bodily awareness (e.g. Cappa et al., 1987; Bisiach et al., 1991; Ferrè et al., 2015; Naito et al., 2005; Tsakiris et al., 2007; Tsakiris, 2010). This decision, however, could be interpreted as a potential limitation: the findings of the experimental studies presented in Chapters 2-4 may not expand to the right hand (i.e. instead of representing a change in bodily awareness they might be limited to the left hand) or to the rest of the body. Nevertheless, as detailed in section 2.4. Discussion, Chapter 2, previous research has shown that when the RHI is performed on the right hand, functional activation is present in both right and left hemispheres (Ehrsson et al. 2004; Gentile et al., 2013). This would corroborate the hypothesis that the findings reported in this thesis may extend to both limbs. Future research could confirm this possibility by replicating these findings on the right hand as well as on the whole body (e.g. via full body illusions; Ehrsson, 2007).

Secondly, in all the experiments presented, visual only conditions were always administered first in each experimental block (while, for instance, the other conditions were either randomised or counterbalanced). This decision was driven by the interest in investigating whether healthy participants, when exposed to the rubber hand during vestibular stimulation of the right vestibular network, would integrate vision and proprioception in favour of vision (prior to any tactile stimulation and any related carry-over effects). Thus, this condition had to precede the tactile conditions in each block to avoid any touch (3-way integration) and cumulative effects influencing this 2-way integration. Similarly, in Chapter 4, proprioceptive only conditions were always preceding any further multisensory condition involving vision of the rubber hand. Whilst this may have led to order effects, in Chapter 3 the presence of two different visual only conditions provided evidence that this was not the case (as both conditions led to comparable outcomes).

8.3.2. Affective touch and embodiment

In Chapter 2 and Chapter 3, in order to explore the combined effects of vestibular and interoceptive systems, slow, affective touch, delivered at a velocity of 3 cm/s was employed and compared with fast, neutral touch (at 18 cm/s). Whilst manual delivery of affective touch by trained experimenters could be seen as a disadvantage, as discussed in Chapter 2(section 2.2. Materials and methods), research employing this technique showed consistent results in terms of perceived pleasantness and highlighted the increase in experimenter's control of pressure and velocity when touch was delivered manually in comparison with a robotic hand (Crucianelli et al., 2013 and Krahé et al., 2016; Triscoli et al., 2012).

On the contrary, in the current study, findings on heightened embodiment following CT-optimal touch (Crucianelli et al., 2013; 2017; Lloyds et al., 2014) were not replicated in any of the GVS configurations (including Sham). As argued in Chapters 2 and 3 (sections 2.4. Discussion and 3.4, Discussion), this result might be due to methodological differences: whilst in Crucianelli and colleagues' studies, a baseline measure of embodiment was taken before each condition, thus allowing for a procedure similar to the proprioceptive drift one (i.e. taking into account participants' baseline at the beginning of the experimental condition and then comparing it with a post-condition measurement), in the experiments presented in this thesis this was not a possibility. The reason was twofold: firstly, one of the aims was to investigate the effects of vestibular stimulation on vision alone. Thus, taking a visual only baseline each time would have undermined this aim, as it would not have been feasible to take all the measurements twice in each of the conditions of the experimental block. Secondly, and in line with the latter point, implementing GVS in all its configurations in one session meant having two 20-minutes breaks in between each block plus the time needed to carry out the experimental blocks. Adding a baseline in each condition would have considerably increased testing time, thus making each experiment too long for participants and therefore decreasing data reliability.

8.3.3. Studying the bodily self in right-hemisphere stroke patients

In Chapter 5 and Chapter 6, neuropsychological studies with right-hemisphere stroke patients were presented. Carrying out studies in this specific patients' population entails a number of constraints and limitations that do not apply to healthy subject research.

Firstly, recruiting patients in different hospital sites (in the current case, six different wards across London) has several potential limitations. Whilst the majority of these sites have an established interconnected referral pathway (i.e. patients are admitted in the acute wards and then discharged in a rehabilitation ward among the six mentioned above), some of them do not, and patients who are often admitted in central London are then discharged to local hospitals outside the city. Not having access to these sites precludes the possibility to finish assessments and testing: in several occasions, patients started the recruitment process only to drop out before being able to take part in any of the experimental tasks. Furthermore, whilst some of these wards have on-site research nurses/qualified research staff referring patients for their recruitment in active research studies, others rely on the researchers screening the wards themselves. This leads to a considerable chance of losing patients: even when in a team, being able to successfully screen every hospital every week still did not ensure recruitment of all suitable patients. Given that a patient might stay for one or two days in an acute ward and then be discharged elsewhere more locally, researchers might lose this referral entirely if the hospital has not been checked for more than two days (e.g. if the discharge happened during the weekend).

Secondly, discharge to different locations, worsening of the patient's condition, as well as patients' own schedule (e.g. physiotherapy sessions, family visits), often translate into missing data: a patient might have completed a part of the assessments and experimental protocols but not all of them. To overcome this issue, patients with incomplete data sets regarding experimental protocols have not been included in the analysis; nevertheless, the loss of these patients' contribution to the experimental protocols as well as missing data on the neuropsychological assessments remain an open issue.

The above links to another key factor in testing stroke patients: fatigue. On the top of the fatigue related to the condition, especially in the acute and subacute phases (Groot, Phillips, & Eskes, 2003), there is also the issue of age, with the majority of stroke patients being part of the elderly population and being, therefore, more easily tired than younger patients. Whilst there has been a worrying increase in the occurrence of strokes before the age of 55 (Kissela et al., 2012), testing elderly is an inevitable direct consequence of investigating bodily awareness in stroke patients.

Finally, as detailed in Chapter 5 and Chapter 6, patients were grouped according to well-established assessments and clinical observations. However, whilst relaxing grouping criteria (i.e. including, in the DSO group, patients who did not necessarily score in line with the Cutting's questionnaire at the beginning of the testing session but showed clinical indications of dis-ownership during it) is in line with more recent definitions of bodily awareness disorders (e.g. Jenkinson et al., 2018), it also entails some difficulties in properly capturing the phenomenon of interest. A patient with a subtle form of asomatognosia (e.g. a patient reporting low levels of ownership of her own limbs) presents with milder feelings of dis-ownership in comparison with a somatoparaphrenic patient. Accordingly, an anosognosic patient detecting lack of movement following a direct question about her disability may present with different clinical symptoms in comparison with a patient with strong denial of paralysis following confrontation (i.e. a failure in attempting a movement). Whilst the assessments used in the current dissertation are well-known and widely employed (e.g. Moro et al., 2016), a stricter sub-categorisation of patients could have provided further insight into the different presentations of unawareness and dis-ownership. Nevertheless, doing so would have dramatically reduced the sample size.

8.3.4. <u>Lesion mapping analysis</u>

In terms of lesion analysis, several methodological constraints can impact the validity and significance of the results. First of all, in the majority of cases, lesion-mapping methods employ binary criteria of symptoms classification (i.e. either presence or absence). In the current studies, this was avoided (whenever possible) by employing a continuum (e.g. scales to define strength of ownership feelings on a 0-10 scale) rather than a categorical classification (e.g. ownership/dis-ownership)

(Sperber & Karnath, 2018). Secondly, the time point at which scans were obtained could also vary from patient to patient as well as from ward to ward. Time is a key factor in brain remapping following lesions, with differences in lesion size and presentation between acute, subacute and chronic phases of recovery (Vocat, Staub, Stroppini, & Vuilleumier, 2010). In order to reduce potential misleading data due to such variability, all the available scans from each patient were used to guide the drawings (from those performed in the acute phase to the last ones done before discharge; Karnath & Rorden, 2012). The type of scans used varied from hospital to hospital, with some wards being able to provide MRI scans while others only used CT scans for clinical purposes. Whilst being useful in guiding lesion drawing, CT scans may be of lower resolution quality in comparison with MRI scans (Lezak, Howieson, Loring, Hannay, & Fischer, 2004). Furthermore, while MRI scans are more precise in detecting ischaemic strokes, CT-scans are more sensitive to haemorrhagic strokes (Sperber & Karnath, 2018). In the current thesis both patients with ischaemic and haemorrhagic strokes were recruited and both types of scan implemented when possible to guide lesion drawings. Finally, in terms of statistical analysis, in the current thesis a conservative method correcting for multiple comparisons was employed in order to avoid false positives (i.e. permutations). Furthermore, only voxels damaged in at least the 10% of the patients were included in order to increase power (de Haan & Karnath, 2018). However, given the relatively small sample size and the variety of lesions' presentation of the current studies, such strict criteria may have been too conservative. Future research, with targeted neuroimaging protocols targeting different lesion types (i.e. CT for haemorrhagic and MRI for ischaemic strokes) and an increased sample size could be better suited to investigate the neural correlates of the bodily self in this population.

8.3.5. Metacognition: experimenter errors and length

The study reported in Chapter 7 also presented some technical and methodological issues. First of all, due to practical considerations, the experimenter manually positioned participants' hand on the graphic tablet before each trial. Whilst this was done to avoid participants' actively positioning themselves, it could have led to small errors in positioning participants before egocentric trials. While other studies employed robot hands to carry out passive movements (e.g. Phantom robots; Symmons, Richardson, Wuillemin, & VanDoorn, 2005), this was not possible in the current set-up, as there was not enough physical space to allow robot-guided positioning on the graphic tablet, whilst maintaining the monitor sufficiently close to participants' actual hand position. As the latter was an important component of this study, ensuring ecological validity of stimuli presentation, manual positioning was chosen as the best option. To overcome this limitation, the experimenter was visually guided by a cursor while positioning participant's hand, in order to increase accuracy.

Secondly, the high number of trials used in this task may have led to participants' fatigue and response set. However, studies in the metacognition literature suggest to employ at least 50 trials per condition to ensure statistical power and model fitting (e.g. Fleming, 2017). As a countermeasure, the experimenter allowed participants to take multiple breaks whenever needed on the top of the embedded break in the middle of the experiment.

8.4. Clinical implications

The experimental studies of this dissertation varied in terms of methodology as well as target populations tested (healthy subjects versus right-hemisphere stroke patients). As such, they present several areas of applicability and potential implications for clinical advances.

The neuromodulation studies presented in Chapters 2-3, aimed at defining the role of vestibular and interoceptive systems in multisensory integration and body representation, may have applications for treating different clinical conditions. For instance, vestibular stimulation, without concurrent tactile manipulations, has already been proven effective in improving unilateral neglect (Saj, Honoré, & Rousseaux, 2006), anosognosia for hemiplegia and somatoparaphrenia (Bisiach et al., 1991; Cappa, Sterzi, Vallar, & Bisiach, 1987). Importantly, vestibular stimulation reduced pain-related feeling in healthy subjects (Ferre, Haggard, Bottini, & Iannetti, 2015) as well as chronic pain in a stroke patient (Spitoni et al., 2016). Hence, one potential implication of the studies presented in this thesis is the use of galvanic vestibular stimulation in treating chronic pain, which currently lacks effective treatment options (Turk, 2002; Turk & Okifuji, 2002). Using GVS, coupled with asymmetric tactile stimulation on a rubber hand (i.e. touch seen but not felt), could shifts patients' attention away from their own body by focusing it on affectively positive visual experiences, thus reducing pain salience. Whilst this possibility has not been tested in the current thesis, it could open the door for viable feasibility studies in pain research.

The studies reported in Chapters 5-6, investigating bodily awareness mechanisms in right-hemisphere stroke populations, also provided insight into possible rehabilitative avenues. Importantly, despite recent advances in understanding disorders of the self following right-hemisphere stroke, there is no established form of therapy to reinstate awareness in AHP or ownership in DSO. Crucially, although most AHP and DSO patients recover spontaneously after days or weeks from the onset (Vocat et al., 2010), their prognosis is usually worse compared to the rest of the stroke population (Jehkonen, Laihosalo, & Kettunen, 2006; Jenkinson, Preston, & Ellis, 2011), because these complex disorders of bodily awareness negatively impact patients' willingness to engage in rehabilitative activities (Gasquoine, 2016) and lead to hazardous behaviours (e.g. trying to get out of bed without help; Moro et al., 2011). Hence, the use of mirrors in DSO and video replays in AHP could open new avenues in rehabilitating AHP and DSO with simple bedside manipulations of visual perspective: as shown in Chapter 6, feelings of dis-ownership were reduced following view of patients own arm in the mirror. Even though in the current study mirrors did not have any effect on awareness, these findings corroborate the idea that using video-replays may be an effective treatment option (Besharati et al., 2014; Fotopoulou et al., 2009).

Finally, the last experimental chapter provided valuable insight into the role of spatial reference frames in belief updating. This could be the basis for a working theoretical framework explaining anosognosic patients' compromised ability to generalise information on their own body when viewed from their own point of view (given that they are able to point it out in others or in themselves during video replays; Besharati et al., 2014; Marcel et al., 2004; Fotopoulou et al., 2009). Furthermore, this egocentric bias (or lack thereof) could also be involved in explaining other clinical conditions, such as anosognosia in Alzheimer's disease (Serino and Riva, 2017) as well as mental health pathologies (such as eating disorders; Riva, 2012).

8.5. Conclusions

In conclusion, the current thesis explored different facets of the bodily self, namely body ownership, self-awareness and agency, via a series of behavioural, neuromodulation and neuropsychological studies. In healthy subjects, an enhancement of vision over proprioception has been found during vestibular stimulation of the right hemisphere, interpreted as a balancing mechanism modulating perceptual ambiguity during sensory conflict. Following a stroke in the right fronto-parietal areas, such dynamic updating of one's own body is compromised, resulting in a pathological dominance of vision over proprioception (leading to feelings of ownership of a rubber hand) and in an impairment of self-awareness as well as feelings of agency. Finally, awareness of one's own choices may be influenced by the context in which stimuli are perceived: when the environment is experienced in an egocentric, bodily-centred, fashion (as opposed to an allocentric, world-centred one), individuals show poorer abilities in updating beliefs regarding their own actions. The overall findings of this thesis suggest that the way we represent our own body is dynamically updated according to contextual and spatial changes and that such updating, regulated via vestibular signals, is influenced by both exteroceptive as well as interoceptive modalities.

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Appendices

Appendix 1

Embodiment Questionnaire (Longo et al., 2008)

An adapted version of Longo and colleagues (2008) embodiment questionnaire, including 9 statements, was implemented.

Participants answered the questionnaire using a 7-points Likert scale, ranging from -3 ('Strongly disagree') to +3 ('Strongly agree') with 0 being 'Neither agree nor disagree'.

During the block…

Ownership (1-5):

1. …it seemed like I was looking directly at my own hand, rather than at a rubber hand.
2. …it seemed like the rubber hand began to resemble my real hand.
3. …it seemed like the rubber hand belonged to me.
4. …it seemed like the rubber hand was my hand.
5. …it seemed like the rubber hand was part of my body.

Location (6-8):

6. …it seemed like the rubber hand was in the location where my hand was.
7. …it seemed like my hand was in the location where the rubber hand was.
8. …it seemed like the touch I felt was caused by the brush touching the rubber hand.

Affect (9):

9. … I found the overall experience enjoyable.

Adapted from the original ("I found that experience interesting")

Appendix 2

1. Results

1.1. Outliers

Three participants were excluded from the final analyses. One did not perceive the pleasantness of the touch as intended, i.e. she reported fast touch as more pleasant than slow touch, another participant was excluded because he couldn't follow instructions and one participant was more than 2SD away from the group mean across most LGVS and Sham conditions.

1.2. Ownership and location

2.2.2. Ownership - Hemispheric specific effects

Visual capture conditions

We conducted a paired sample *t*-test to compare feelings of ownership after observation of the rubber hand without tactile stimulation following LGVS versus RGVS. We did not find any significant difference between the conditions (t_{22}=-.115, p=.909, *d*=-.034).

Stroking conditions

A 2 (stimulation: LGVS and RGVS) x 2 (stroking synchrony: synchronous and asynchronous) x 2 (stroking velocities: slow and fast) repeated measures ANOVA revealed a main effect of Synchrony ($F_{(1,22)}$=28.295, p<.000, η_p^2=.563) but not Stimulation ($F_{(1,22)}$=2.389, p=.136, η_p^2=.098) or Velocity ($F_{(1,22)}$=2.708, p=.114, η_p^2=.110) and none of the interactions was significant Stimulation*Synchrony, $F_{(1,22)}$=.948 p=.341, η_p^2=.041; Stimulation*Velocity, $F_{(1,22)}$=.409, p=.529, η_p^2=.018; Synchrony*Velocity, $F_{(1,22)}$=1.189, p=.287, η_p^2=.051; Stimulation*Synchrony*Velocity, $F_{(1,22)}$=.335, p=.568, η_p^2=.015).

2.2.3. Ownership - Non-hemispheric specific effects

Visual capture conditions

We did not find a generic effect of GVS on ownership values after visual exposure to the rubber hand; a paired sample t-test comparing the average of the two stimulations ((LGVS+RGVS)/2) with Sham was not significant (t_{22}=.787, p=.439, d=0.23).

Stroking conditions

A 2 (stimulation: (LGVS+RGVS)/2 and Sham) x 2 (stroking synchrony: synchronous and asynchronous) x 2 (stroking velocities: slow and fast) repeated measures ANOVA revealed main effects of Synchrony ($F_{(1,22)}$=25.236, p=.000, η_p^2=.534) and Velocity ($F_{(1,22)}$=5.268, p=.032, η_p^2=.193) but not Stimulation ($F_{(1,22)}$=3.545, p=.073, η_p^2=.139). No significant interactions were found (Stimulation*Synchrony, $F_{(1,22)}$=.083 p=.776, η_p^2=.004; Stimulation*Velocity, $F_{(1,22)}$=.001, p=.981, η_p^2=.000; Synchrony*Velocity, $F_{(1,22)}$=.042, p=.839, η_p^2=.002; Stimulation*Synchrony*Velocity, $F_{(1,22)}$=2.093, p=.162, η_p^2=.087). These results indicate that felt ownership was higher during synchronous conditions and when the velocity of stroking was faster.

<u>2.2.4. Location - Hemispheric specific effects</u>

Visual capture conditions

A paired sample *t*-test comparing felt location in LGVS versus RGVS was not significant (t_{22}=.00, p=1.00, *d*=000), suggesting that we did not find any difference between the two vestibular stimulations following visual only conditions in felt location.

Stroking conditions

We conducted a 2 (stimulation: LGVS and RGVS) x 2 (stroking synchrony: synchronous and asynchronous) x 2 (stroking velocities: slow and fast) repeated measures ANOVA that showed a main effect of Synchrony ($F_{(1,22)}$=28.990, p<.000, η_p^2=.569) but not Stimulation ($F_{(1,22)}$=.256, p=.618, η_p^2=.011) or Velocity ($F_{(1,22)}$=1.995, p=.172, η_p^2=.083). These findings suggest that the only factor influencing the felt location was the synchrony of stroking, with synchronous conditions leading to higher values. None of the interactions was significant (Stimulation*Synchrony, $F_{(1,22)}$=.678 p=.419, η_p^2=.030;

Stimulation*Velocity, $F_{(1,22)}$=3.22, p=.086, η_p^2=.128; Synchrony*Velocity, $F_{(1,22)}$=1.131, p=.299, η_p^2=.049; Stimulation*Synchrony*Velocity, $F_{(1,22)}$=.127, p=.725, η_p^2=.006).

2.2.5. Location - Non-hemispheric specific effects

Visual capture conditions

A paired sample t-test comparing the average of the two stimulations ((LGVS+RGVS)/2) with Sham was not significant (t_{22}=.239, p=.813, *d*=.072), indicating that we did not find any generic arousal effects due to GVS on felt location following visual only conditions.

Stroking conditions

A 2 (stimulation: LGVS+RGVS)/2 and Sham) x 2 (stroking synchrony: synchronous and asynchronous) x 2 (stroking velocities: slow and fast) repeated measures ANOVA revealed main effects of Synchrony ($F_{(1,22)}$=25.747, p<.000, η_p^2=.539) and Stimulation ($F_{(1,22)}$=7.167, p=.014, η_p^2=.246), but not Velocity ($F_{(1,22)}$=2.788, p=.109, η_p^2=.112), suggesting that felt location was influenced by synchrony, with synchronous conditions leading to higher values, and stimulation, with Sham contributing to an increased subjective experience of the illusion. None of the interactions was significant (Stimulation*Synchrony, $F_{(1,22)}$=.288 p=.597, η_p^2=.013; Stimulation*Velocity, $F_{(1,22)}$=.247, p=.624, η_p^2=.011; Synchrony*Velocity, $F_{(1,22)}$=.069, p=.796, η_p^2=.003; Stimulation*Synchrony*Velocity, $F_{(1,22)}$=1.083, p=.309, η_p^2=.047).

Table 1. Descriptive statistics of embodiment questionnaire's single items values in the different conditions.

	Ownership					*Location*		
	1. …it seemed like I was looking directly at my own hand, rather than at a rubber hand.	*2. …it seemed like the rubber hand began to resemble my real hand.*	*3…it seemed like the rubber hand belonged to me.*	*4.…it seemed like the rubber hand was my hand.*	*5…it seemed like the rubber hand was part of my body.*	*6. …it seemed like the rubber hand was in the location where my hand was.*	*7. …it seemed like my hand was in the location where the rubber hand was.*	*8. …it seemed like the touch I felt was caused by the brush touching the rubber hand.*
	Mean *(SD)*	Mean *(SD)*	Mean *(SD)*	Mean *(SD)*	Mean *(SD)*	Mean *(SD)*	Mean *(SD)*	Mean *(SD)*
LGVS								
VC	-0.39 *(2.02)*	-0.69 *(1.87)*	-0.69 *(1.79)*	-0.69 *(1.94)*	-0.43 *(1.67)*	-0.91 *(1.75)*	-0.74 *(1.81)*	-
SST	0.48 *(1.7)*	0.74 *(1.5)*	0.74 *(1.42)*	0.78 *(1.59)*	0.83 *(1.58)*	-0.43 *(1.9)*	0.39 *(1.95)*	1.13 *(1.49)*
SFT	1.04 *(1.58)*	1.09 *(1.44)*	1.09 *(1.31)*	1.13 *(1.45)*	0.91 *(1.59)*	0.13 *(1.91)*	0.69 *(1.89)*	1.56 *(1.53)*
AST	-0.43 *(1.9)*	-0.56 *(1.72)*	-0.56 *(1.67)*	-0.52 *(1.73)*	-0.52 *(1.65)*	-1 *(1.59)*	-0.65 *(1.8)*	-1.39 *(1.53)*
AFT	-0.04 *(1.64)*	-0.26 *(1.72)*	-0.26 *(1.54)*	-0.26 *(1.66)*	-0.43 *(1.62)*	-0.87 *(1.63)*	-0.52 *(1.85)*	-0.83 *(1.72)*
RGVS								
VC	-0.61 *(1.92)*	-0.61 *(1.83)*	-0.61 *(1.8)*	-0.65 *(1.75)*	-0.39 *(1.67)*	-1.09 *(1.7)*	-0.74 *(1.86)*	-
SST	0.22 *(1.83)*	0.35 *(1.59)*	0.35 *(1.69)*	0.48 *(1.78)*	0.26 *(1.89)*	-0.22 *(1.7)*	0.17 *(2.08)*	1.22 *(1.54)*
SFT	0.61 *(1.59)*	0.69 *(1.59)*	0.69 *(1.66)*	0.83 *(1.75)*	0.61 *(1.59)*	-0.04 *(1.79)*	0.35 *(1.94)*	1.09 *(1.53)*
AST	-0.52 *(1.53)*	-0.56 *(1.82)*	-0.56 *(1.7)*	-0.65 *(1.61)*	-0.61 *(1.5)*	-0.87 *(1.63)*	-0.56 *(1.73)*	-1.17 *(1.64)*
AFT	-0.43 *(1.56)*	-0.56 *(1.73)*	-0.56 *(1.75)*	-0.65 *(1.52)*	-0.48 *(1.65)*	-0.96 *(1.69)*	-0.56 *(1.65)*	-1.13 *(1.6)*
Sham								
VC	-0.17 *(2.06)*	-0.26 *(1.88)*	-0.26 *(1.84)*	-0.35 *(1.8)*	-0.3 *(1.84)*	-0.91 *(1.78)*	-0.78 *(1.9)*	-
SST	0.96 *(1.58)*	0.91 *(1.34)*	0.91 *(1.44)*	0.87 *(1.71)*	1 *(1.51)*	0.13 *(1.87)*	0.56 *(1.78)*	1.52 *(1.5)*
SFT	0.74 *(1.74)*	1.17 *(1.46)*	1.17 *(1.43)*	1.04 *(1.58)*	1.09 *(1.34)*	0.3 *(1.87)*	0.52 *(1.75)*	1.43 *(1.56)*
AST	-0.56 *(2.06)*	-0.39 *(1.9)*	-0.39 *(1.72)*	-0.39 *(1.78)*	-0.3 *(1.79)*	-0.65 *(1.9)*	-0.48 *(1.93)*	-0.78 *(2.07)*
AFT	-0.13 *(1.6)*	0.08 *(1.65)*	0.08 *(1.62)*	-0.13 *(1.71)*	0.04 *(1.46)*	-0.35 *(1.75)*	-0.35 *(1.58)*	-0.56 *(1.65)*
L+R/2								

VC	-0.5 *(1.78)*	-0.65 *(1.58)*	-0.65 *(1.58)*	-0.67*(1.61)*	-0.41 *(1.5)*	-1 *(1.52)*	-0.74 *(1.72)*	-
SST	0.35 *(1.58)*	0.54 *(1.42)*	0.54 *(1.39)*	0.63 *(1.49)*	0.54 *(1.58)*	-0.33 *(1.58)*	0.28 *(1.87)*	1.17 *(1.36)*
SFT	0.83 *(1.4)*	0.89 *(1.44)*	0.89 *(1.37)*	0.98 *(1.55)*	0.76 *(1.45)*	0.04 *(1.78)*	0.52 *(1.83)*	1.33 *(1.45)*
AST	-0.48 *(1.6)*	-0.56 *(1.65)*	-0.56 *(1.52)*	-0.59 *(1.49)*	-0.56 *(1.51)*	-0.93 *(1.49)*	-0.61 *(1.67)*	-1.28 *(1.49)*
AFT	-0.24 *(1.44)*	-0.41 *(1.52)*	-0.41 *(1.43)*	-0.46 *(1.48)*	-0.46 *(1.43)*	-0.91 *(1.51)*	-0.54 *(1.57)*	-0.98 *(1.5)*

VC= visual capture; SST= synchronous slow touch; SFT= synchronous fast touch; AST= asynchronous slow touch;
AFT= asynchronous fast touch

1.3. Affective component

Affective aspects of the rubber hand illusion were investigated by analysing participants' responses to one of the questionnaire's statement (i.e. "I found the overall experience enjoyable"). The procedure is the same used in the analyses reported above.

1.3.1. Hemispheric specific effects

Visual capture conditions

A paired sample t-test between LGVS and RGVS did not show any significant difference between the conditions (t_{22}=.127, p=.900, *d*=.038), suggesting that we did not find any GVS specific effect on affective aspects of embodiment during visual exposure to the rubber hand.

Stroking conditions

A 2 (stimulation: LGVS and RGVS) x 2 (stroking synchrony: synchronous and asynchronous) x 2 (stroking velocities: slow and fast) repeated measures ANOVA was conducted. We found a main effect of Synchrony ($F_{(1,22)}$=16.656, p=.000, η_p^2=.431), indicating that synchronous conditions led to higher levels of affective aspects. Stimulation ($F_{(1,22)}$=.156, p=.696, η_p^2=.007), Velocity ($F_{(1,22)}$=.513, p=.481, η_p^2=.023) nor none of the interactions (Stimulation*Synchrony, $F_{(1,22)}$=1.416 p=.247, η_p^2=.060; Stimulation*Velocity, $F_{(1,22)}$=.035, p=.854, η_p^2=.002; Synchrony*Velocity, $F_{(1,22)}$=1.034, p=.320, η_p^2=.045; Stimulation*synchrony*velocity, $F_{(1,22)}$=1.289, p=.269, η_p^2=.055) were significant. The results highlight that affective aspects of embodiment were not linked to GVS polarity and were only influenced by the synchrony of stroking.

1.3.2. Non-hemispheric specific effects

Visual capture conditions

A paired sample t-test between (LGVS+RGVS)/2 and Sham did not reveal significant differences between the conditions (t_{22}=1.141, p=.266, *d*=.344), thus suggesting that in the current study we did not find a generic arousal effect of vestibular stimulation on the affective aspect of visual capture.

Stroking conditions

A 2 (stimulation: (LGVS+RGVS)/2 and Sham) x 2 (stroking synchrony: synchronous and asynchronous) x 2 (stroking velocities: slow and fast) repeated measures ANOVA highlighted a main effect of Synchrony ($F_{(1,22)}$=22.138, p=.000, η_p^2=.502), with synchronous conditions leading to an increase in the affective component, while Stimulation ($F_{(1,22)}$=.007, p=0.936, η_p^2=.000) and Velocity ($F_{(1,22)}$=.000, p=1.000, η_p^2=.000) as well as all the interactions (Stimulation*Synchrony, $F_{(1,22)}$=.2.616 p=.120, η_p^2=.106; Stimulation*Velocity, $F_{(1,22)}$=1.043, p=.318, η_p^2=.045; Synchrony*Velocity, $F_{(1,22)}$=1.645, p=.213, η_p^2=.070; Stimulation*synchrony*velocity, $F_{(1,22)}$=.105, p=.749, η_p^2=.005) did not reach the significance level. Again, this analysis revealed that there was no generic effect of GVS on the affective component and that the only factor influencing participants' answers was the synchrony of stroking.

2.6 Non parametric analysis

2.6.1. Data analysis

Main effects of Stimulation, synchrony and stroking CT-optimality were analysed by calculating the average of the proprioceptive drifts or questionnaire values obtained in each of the vestibular stimulations regardless of synchrony and CT-optimality. The same procedure was followed in order to check for main effects of synchrony and CT-optimality.

2-way interactions (Stimulation*synchrony, Stimulation*CT-optimality and Synchrony*Ct-optimality) were obtained by averaging the conditions related to the factor not of interest in the comparison (for instance, CT-optimality when investigating Stimulation* Synchrony) and by subtracting one level of the factor of interest from the other one (in the case of Stimulation*Synchrony, the subtraction has been performed between LGVS synchronous and asynchronous conditions and the result has then been compared with the equivalent subtraction in RGVS). The results were then analysed via a Wilcoxon signed rank test.

3-ways interactions followed a similar approach: we subtracted synchronous and asynchronous slow, CT-optimal touch and synchronous and asynchronous fast, non CT-optimal touch separately, we then calculated their difference, and finally analysed the effect of vestibular stimulation via a Wilcoxon signed rank test.

The findings detailed below are in line with the parametric results reported in the manuscript and we refer you to section 3 of the manuscript for any additional interpretation of these findings.

<u>2.6.2. Proprioceptive drift</u>

All the proprioceptive drift distributions are normally distributed (except for 2 of them: Sham Synchronous non CT-optimal touch, K-S: $D(23)=.183$, $p=0.045$ and The average of LGVS and RGVS Synchronous non CT-optimal touch, , K-S: $D(23)=.209$, $p=0.011$).

Visual capture conditions:

A Wilcoxon signed rank test was used to compare proprioceptive drift after observation of the rubber hand without tactile stimulation. We found that LGVS led to greater proprioceptive drift than RGVS ($Z=-3.088$, $p<0.01$, LGVS: Mdn= 2.30; RGVS: Mdn= 0.40), whereas the comparison between Sham and the average of LGVS and RGVS was not significant (Z=.730, p=.456 Sham: Mdn=0.60; (LGVS+RGVS)/2: Mdn=1.35)

LGVS vs RGVS – stroking conditions

In line with the parametric analysis reported in the manuscript, a Wilcoxon signed rank test revealed a main effect of synchrony (Z=-3.498, p<0.01, Synchronous: Mdn=1.37; Asynchronous: Mdn=0.97) but not CT-optimality (Z=-1.521, p=0.128, CT-optimal: Mdn= 1.87; non CT-optimal: Mdn= 1.10) or stimulation (Z=-0.639, p=0.523, LGVS: Mdn=1.80; RGVS: Mdn=1.32).

In line with the parametric analysis reported in the manuscript, a Wilcoxon signed rank test revealed a significant interaction between stimulation and synchrony (Z=-2.555, p=0.01) and Stimulation, synchrony, CT-optimality (Z=-2.023, p=0.043) but no other significant interaction (Stimulation*CT-optimality: Z=-.779, p=.436, and Synchrony*Ct-optimality: Z=-1.536, p=.124). To explore the nature of the above, significant, 3-way interaction, we conducted two additional sets of comparisons using Wilcoxon signed rank test on LGVS and RGVS separately, examining main effects and interactions of synchrony and velocity.

In line with the parametric analysis reported in the manuscript, when analysing LGVS and RGVS separately we found a main effect of Synchrony of stroking in LGVS (Z=-3.985, p=<0.01 Synchronous: Mdn=2.50; Asynchronous: Mdn=0.35) but no main effect of CT-optimality (Z=-1.689, p=.091; CT-optimal: Mdn=1.90; non CT-optimal: Mdn=1.00) and no main effect of either synchrony or CT-optimality in RGVS (synchrony: Z=-1.506, p=.132; Synchronous: Mdn=0.85; Asynchronous: Mdn=1.00; CT-optimality: Z=-0.585, p=.559; CT-optimal: Mdn=1.00; non CT-optimal: Mdn=1.25). As expected, we found a significant interaction between Synchrony and CT-optimality in LGVS (Z=-2.632, p<0.01), but not in RGVS (Z=.104, p=.917).

The significant 2-way interaction between synchrony and CT-optimality found in LGVS conditions was further analysed using post-hoc Wilcoxon signed rank test (Bonferroni corrected, α = 0.025) to compare CT-optimal, slow touch and non-CT-optimal, fast touch in synchronous and asynchronous conditions separately. In line with the results reported in the manuscript, synchronous slow touch led to significantly higher proprioceptive drift than synchronous fast touch (synchronous CT-optimal, slow touch: Mdn=3.50, synchronous non CT-optimal, fast touch: Mdn=1.50; Z=-2.602, p<0.01), while the difference between the two asynchronous conditions was not significant (asynchronous CT-optimal, slow touch: Mdn=0.30; asynchronous non CT-optimal, fast touch: Mdn=0.50; Z=.536, p=.592).

Sham vs (LGVS+RGVS)/2 – stroking conditions

A Wilcoxon signed rank test revealed a main effect of stimulation (Z=4.167, p<0.01, Sham: Mdn=1.40; (LGVS+RGVS)/2: Mdn=4.43), synchrony (Z=-4.061, p<0.01, Synchronous: Mdn=1.43; Asynchronous: Mdn=0.83) and CT-optimality (Z=-1.992, p=0.046, CT-optimal: Mdn=1.45; non CT-optimal: Mdn=0.85). The main effect of CT-optimality, that was approaching significance (p=0.053) in the parametric analysis reported in the main manuscript, is within the parameters for statistical significance in the non parametric ones (p=0.046). As expected, a Wilcoxon signed rank test revealed no significant interaction (Stimulation*Synchrony: Z=0.730, p=0.456; Stimulation*CT-optimality: Z=0.046., p=0.964; Synchrony*CT-optimality: Z=-0.503, p=0.615. and Stimulation*synchrony*CT-optimality: Z=-0.806, p=0.420,).

2.6.3. Questionnaire values

Almost all the questionnaire scores distributions are normally distributed (except for 4/20 of them: Sham Synchronous non CT-optimal touch, K-S: D(23)=.186, p=0.038, Sham Asynchronous non CT-optimal touch, K-S: D(23)=.184, p=0.043, LGVS Synchronous CT-optimal touch, K-S: D(23)=.197, p=0.021 and the average of LGVS and RGVS Synchronous non CT-optimal touch, K-S: D(23)=.215, p=0.007).

Visual capture conditions

A Wilcoxon signed rank test was used to compare questionnaire values obtained after observation of the rubber hand without tactile stimulation. In line with the parametric data reported in the manuscript, we did not find a significant different in either LGVS vs RGVS or Sham vs the average of LGVS and RGVS (LGVS vs RGVS: Z=0.262, p=794, LGVS: Mdn=-0.43 ; RGVS: Mdn=-0.71 ; Sham vs (LGVS+RGVS)/2: Z=-0.448 p=.654; Sham: Mdn=-0.57, L+R/2: Mdn=-0.71).

LGVS vs RGVS – stroking conditions

A Wilcoxon signed rank test revealed a main effect of synchrony (Z=-4.107, p<0.01, Synchronous: Mdn=0.72; Asynchronous: Mdn=-0.78) but no stimulation (Z=-1.591, p=0.112, LGVS: Mdn=0.06; RGVS: Mdn=-0.06) nor CT-optimality (Z=1.530, p=0.126, CT-optimal: Mdn=-0.16; non CT-optimal: Mdn=0.28). In line with the parametric analysis reported in the manuscript, a Wilcoxon signed rank test revealed no significant interaction (Stimulation*Synchrony: Z=-0.894, p=371; Stimulation*CT-optimality: Z=1.608, p=0.108; Synchrony*CT-optimality: Z=1.289, p=0.197 and Stimulation*synchrony*CT-optimality: Z=-0.452, p=0.651).

Sham vs (LGVS+RGVS)/2 – stroking conditions

A Wilcoxon signed rank test revealed a main effect of stimulation (Z=-2.221, p=0.026, Sham: Mdn=0.44; (LGVS+RGVS)/2: Mdn=0.03), synchrony (Z=-4.198, p<0.01, Synchronous: Mdn=0.95; Asynchronous: Mdn=-0.48), and CT-optimality (Z=2.099, p=0.036, CT-optimal: Mdn=0.13; non CT-optimal: Mdn=0.33). As expected, a Wilcoxon signed rank test revealed no significant interaction (Stimulation*Synchrony: Z=0.341, p=0.733; Stimulation*CT-optimality: Z=-0.198, p=0.843; Synchrony*CT-optimality: Z=-1.020, p=0.308. and Stimulation*synchrony*CT-optimality: Z=-1.050, p=0.294).