Visuo-vestibular mechanisms of bodily self-consciousness

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Abstract

Bodily self-consciousness is linked to multisensory integration and is particularly dependent on vestibular perception providing the brain with the main sensory cues about body motion and location in space. Vestibular and visual inputs are permanently balanced and integrated to encode the most optimal representation of the external world and of the observer in the central nervous system. Vection, an illusory self-motion experience induced only by visual stimuli, illustrates the fact that the visual and the vestibular systems share common neural underpinnings and a similar phenomenology. Optokinetic stimulation inducing vection and direct vestibular stimulation induce whole-body motion sensations that can be used to explore multisensory interactions. A failure in visuo-vestibular integration, artificially induced by the methods of cognitive psychology or in pathological conditions, has also been reported to altered own body perception and bodily self-consciousness. The respective contributions of the vestibular and visual systems to bodily self-consciousness amongst other polymodal sensory mechanisms, and the neural correlates of visuo-vestibular convergence, should be better understood. We first performed a neuroimaging study of brain regions where optokinetic and vestibular stimuli converge, using 7T functional magnetic resonance imaging in individual subjects. We identified three main regions of convergence: (1) the depth of supramarginal gyrus or retroinsular cortex, (2) the surface of supramarginal gyrus at the temporo-parietal junction, (3) and the posterior part of middle temporal gyrus and superior temporal sulcus. Then, we aimed to induce the embodiment of an external fake rubber hand through visuo-tactile conflict - the so-called rubber hand illusion paradigm, and studied how this integration is modulated by vection. Subjects experiencing vection in the direction of the rubber hand mislocalised the position of their real hand towards the rubber hand indicating that visuo-vestibular stimuli can enhance visuo-tactile integration. We also investigated if visuo-proprioceptive and tactile integration in peripersonal space could be dynamically updated based on the congruency of visual and proprioceptive feedback. A pair of rubber hands or feet provided visual feedback. Fake and real limbs were crossed or uncrossed. We showed that sensory cues were integrated in peripersonal space, dynamically reshaped but only for hands. Finally, we investigated a rare case of an illusory own body perception in an epileptic patient suffering from multiple daily disembodiments during seizures. Seizures were associated to a focal cortical microdysplasia juxtaposed to a developmental venous anomaly in the left angular gyrus, a brain region known to be important for visuo-vestibular integration and bodily self-consciousness. Our results characterize the inferior parietal lobule as a crucial structure in merging visual, vestibular, tactile and proprioceptive inputs, allowing the emergence of the global and unified experience of being "I." Multisensory body representation can be reshaped transiently using visual and vestibular signals or in relation to a medical condition affecting the temporo-parietal junction. The integration of visual and vestibular signals, aims to adapt dynamically our internal representations to constant changes occurring in our environment.

Keywords

7T MRI, Bodily self-consciousness, Extrastriate cortex, Functional magnetic resonance imaging, Heautoscopy, Inferior parietal lobule, Multisensory integration, Optokinetic stimulation, Out-of-body experiences, Rubber hand illusion, Temporo parietal junction, Vection, Vestibular system, Visual dominance, Visuo-vestibular

Résumé

La conscience corporelle de soi repose sur l'intégration multisensorielle et particulièrement dépendante de la perception vestibulaire qui fournit au cerveau les indices sensoriels principaux sur le mouvement du corps et de son emplacement dans l'espace. Les informations visuelles et vestibulaires sont en permanence équilibrées et intégrées pour encoder une représentation la plus fidèle possible du monde extérieur et de l'observateur dans le système nerveux central. La vection, expérience de mouvement du corps illusoire induite par des stimuli visuels isolés, illustre bien le fait que le système vestibulaire et la vision partagent des fondements neuronaux communs et une phénoménologie proche. Ainsi, les stimuli optocinétiques induisant une vection et la stimulation vestibulaire directe peuvent induire des sensations de mouvement du corps entier pouvant être utilisées pour étudier les interactions visuo-tactiles. Un échec de l'intégration visuo-vestibulaire, artificiellement provoqué par les méthodes de la psychologie cognitive ou apparaissant dans des états pathologiques, peut conduire à des altérations de l'intégrité corporelle et des troubles de l'appropriation de son propre corps. Parmi le reste du traitement polymodal émanant d'autres modalités sensorielles, les contributions respectives des systèmes visuel et vestibulaire à la conscience de soi corporelle et corrélats neuronaux de la convergence visuo-vestibulaire, sont à préciser. Nous avons cartographié les régions du cerveau où les stimuli optocinétiques et vestibulaires convergent en utilisant l'imagerie par résonance magnétique fonctionnelle à 7 Teslas chez des sujets individuels; nous avons identifié trois principales régions de convergence: (1) la profondeur du gyrus

supramarginal ou cortex rétroinsulaire, (2) la surface du gyrus supramarginal au niveau de la jonction temporo-pariétale, (3) et la partie postérieure du gyrus temporal moyen et du sillon temporal supérieur. Nous avons ensuit cherché à induire l'incorporation dans le schéma corporel d'une fausse main en caoutchouc via un conflit visuo-tactile, communément appelée le paradigme de « l'illusion de la main en caoutchouc », et nous avons étudié comment cette intégration pouvait être modulée par l'utilisation de la vection. Les sujets ressentant une illusion de vection en direction de la main en caoutchouc localisaient par erreur la position de leur vraie main proche du niveau de la main en caoutchouc. Cela signifie que les stimuli visuo-vestibulaires peuvent interagir avec l'intégration visuo-tactile par un effet facilitateur. Nous avons aussi examiné si l'intégration tactile et visuo-proprioceptive dans l'espace péri-personnel pourraient être mises à jour dynamiquement en fonction de la congruence entre le feedback visuel donné par de fausses mains et de faux pieds et la posture réelle des membres, selon que ceux-ci ou les faux membres étaient croisés ou décroisés. Nous avons montré que les signaux sensoriels sont intégrés dans l'espace péri-personnel et que celui-ci peut être dynamiquement remodelé, mais seulement pour les mains. Enfin, nous avons exploré un cas rare d'illusion de la perception du corps chez une jeune patiente épileptique éprouvant des épisodes pluriquotidiens de décorporation pendant les crises, associées à un foyer de micro-dysplasie corticale focale juxtaposée à une anomalie du développement veineux dans le gyrus angulaire gauche, une région capitale dans l'intégration visuo-vestibulaire et la conscience de soi corporelle. Nos résultats plaident pour un rôle clé du lobule pariétal inférieur pour assembler les entrées sensorielles multimodales, afin qu'ils soient intégrés pour permettre l'émergence de l'expérience globale et unifiée du « Je ». La représentation multisensorielle du corps peut être redessinée de façon transitoire en utilisant des signaux visuels et vestibulaires ou en relation avec une pathologie atteignant la jonction temporo-pariétale. L'utilité d'une telle intégration est d'adapter dynamiquement nos représentations internes aux changements permanents de notre environnement.

Mots-clés

Conscience corporelle de soi, Cortex extrastrié, Décorporation, Dominance visuelle, Héautoscopie, Illusion de la main en caoutchouc, Imagerie par résonance magnétique fonctionnelle, Intégration multisensorielle, IRM à 7T, Junction temporo-pariétale, Lobule pariétal inférieur, Stimulation optocinétique, Système vestibulaire , Vection, Visuo-vestibulaire

Contents

Chapter 1 General Introduction

1.1 Bodily self-consciousness as an object of study in neurology

Human consciousness started to be considered as a possible object of scientific study in the last decades (Crick, 1994; Dehaene and Naccache, 2001; Dennett, 2015, 1991). Apparently outside of the span of visual awareness, which was investigated at length, another approach emerged through the systematic study of body perception and self-consciousness, called 'bodily self-consciousness.' How does someone experience the feeling of 'I' (Blanke and Metzinger, 2009)? Three components of bodily self-consciousness have been identified thus far: first-person perspective, self-identification – the feeling of identifying with a body or a body part, and self-location – the place where 'I' feel to be in a spatial referential (Blanke and Metzinger, 2009; Lenggenhager et al., 2007). The feeling of being localised within a physical body or 'embodiment' and the implicit knowledge of body ownership or *somatognosia* can be disturbed in some pathological conditions. Hence, it can lead to autoscopic phenomena such as out-of-body experience (OBE), or its variants, heautoscopy (HAS) and autoscopic hallucination (AH), or illusory presences (Arzy et al., 2006; Blanke and Mohr, 2005; Blanke et al., 2002). OBEs have been triggered by cortical electrical stimulation from the angular gyrus at the right temporo-parietal junction (TPJ) at in one epileptic patient (Blanke et al., 2002). During the OBE, the patient had the illusory feeling of being dissociated from her own body and seeing it from an external visual perspective. Right parieto-temporal lesions are also associated with *somatoparaphrenia,* where body ownership is also impaired (Halligan et al., 1995).

Those patients can either ‘misattribute’ someone else’s body part to themselves, or ‘miss to attribute’ their own body parts to themselves (Aglioti et al., 1996; Bisiach et al., 1991; Bottini et al., 2002). Disorders of bodily self-consciousness include various semiologies such as feeling of presence (Arzy et al., 2006) and many variants of doppelganger’s experiences in very different neurological pathologies (Blanke and Mohr, 2005; Heydrich and Blanke, 2013; Heydrich et al., 2011, 2010; Ionta et al., 2011). Multisensory processing, through the integration of sensory inputs from different modalities, is suspected to be one of the key mechanisms making the global and unitary character of self-consciousness possible, which a healthy human may experience. Interestingly, a strong association seems to exist between illusions concerning the whole body and improper visual perceptions about body parts, such as the patient stimulated by Blanke et al. (2002) who experienced limb elongation and shrinkage sensations. Thus, a failure in multisensory integration may induce changes in limbs sensations and whole body illusions that may be both derived from similar mechanisms (Blanke et al., 2004). Moreover, vestibular sensations during OBEs have been reported (Blanke et al., 2002a; De Ridder et al., 2007; Penfield and Faulk, 1955). To summarize, dissecting the mechanisms of multisensory interactions through illusions or disorders affecting whole body and body limbs may allow a better understanding of bodily self-consciousness. Such studies must focus on the most important sensory signals processed by human bodies, including visual and vestibular systems.

1.2 The importance of vestibular cortex in bodily self-consciousness.

In most mammals, the vestibular system, together with the cochlea, the peripheral sensory organ of the auditory system, constitutes the labyrinth within the inner ear located in the petrous bone. The vestibular system is made of two components: the otoliths (utricle and saccule) and the three semicircular canals (anterior, posterior and horizontal). The otoliths encode linear accelerations and earth's gravitational pull. The semicircular canals encode rotational accelerations. The vestibular system allows body rotation experience (circular motion) - in the three Tait-Bryan axes or yaw, pitch and roll - and translation (linear motion) – along craniocaudal, dorsoventral, mediolateral axes (see Figure 1).

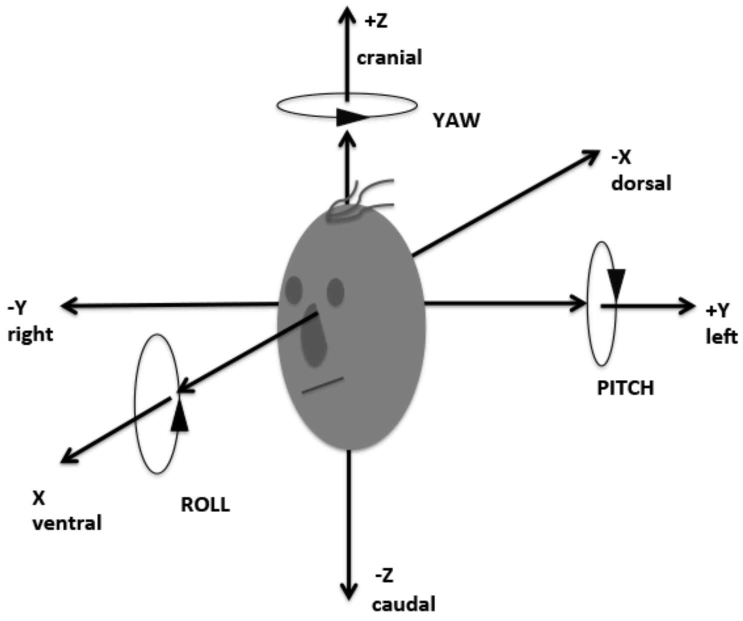

Figure 1. Linear motions and rotations can describe head motion in different axes in rotation and translation. Linear motion is described by its components along front-back (x), left-right (y), and up-down (z) axes. Rotations are named after nautical terms (pitch, roll, and yaw). Copyright Forget Joachim 2015, Inspired from Goldberg et al. (Goldberg and Cullen, 2012).

Vestibular signals contribute to posture and oculomotor control through vestibulo-ocular reflex (Goldberg and Cullen 2012). Vestibular relays are found in many neural structures from the brainstem to the cerebellum, and in the cerebral cortex. They contribute to many cognitive functions (see for reviews Lopez 2015, Lopez and Blanke 2011).

Due to its ontological function of encoding body motion, the vestibular system is challenging to study in laboratory conditions, requiring subjects to remain motionless in the supine position during neuroimaging. The physiological stimulation of the vestibular system under ecological conditions is possible in laboratory conditions and in routine clinical practice, using rotating or translating chair systems, which are not compatible with MRI due to its constraining environment. To achieve vestibular stimulation, diverse methods have been used, including in fMRI, but never tested with ultra-high field MRI above 3T magnetic fields. Two main methods of stimulation have been used: the caloric vestibular stimulation (CVS) and the galvanic vestibular stimulation (GVS). During CVS and GVS, illusory head spinning and body motion are experienced. During CVS, warm or cold water/air is injected in the external auditory canal. The transmission of thermal energy to the inner ear due to the temperature gradient is responsible for convective motion in the endolymph of the semicircular canals, activating the hair cells of the crista ampullaris. GVS (see chapter 2 for details) stimulates the vestibular apparatus using electrical currents through electrodes placed near the mastoid processes. This creates a modulation of hyperpolarization in the vestibular neuroepithelium increasing the firing rate in vestibular afferents to the cathode and decreasing it to the anode. Sensations evoked are stronger with GVS than with CVS because GVS unselectively activates both the otoliths and the semicircular canals (Lopez, 2015).

The vestibular system appears to be particularly important for bodily self-consciousness. Vestibular symptoms are known to accompany many disturbances of bodily self-consciousness (Lenggenhager and Lopez, 2015; Lopez, 2013). The functional and anatomical properties of vestibular neural networks, especially at the cortical level, are still not fully understood both in animals and in humans (Lopez and Blanke, 2011; Lopez, 2015). A core peri-sylvian region in the posterior parietal and insular cortex, including the depth of parietal operculum and the surface of TPJ in inferior parietal lobule (IPL), seems to mediate the processing of vestibular signals (see Figure 2). But the vestibular system is not organised like vision, touch and audition, with the classical hierarchy of a primary sensory cortex with further relays in the associative cortices (Lopez et al., 2012b; Zu Eulenburg et al., 2012). Area OP2 of the parietal operculum may correspond to the human homologue of parieto insular vestibular cortex (PIVC). No proper primary vestibular cortex exists but OP2 (Eickhoff et al., 2006) has the characteristics of a koniocortex (thin and granular) like primary cortices found in cuneus, lingual gyrus, parahippocampal, post central gyrus, and transverse gyrus of Heschl (Arslan, 2001). OP2 may also correspond to an area found by Glasser and Van Essen (Glasser and Van Essen, 2011), showing differential intensity properties in T1- and T2-weighted images. Following the line of interpretation of these authors, those intensity differences are due to particular local intracortical myelination properties, which would fit the classical aspect of a primary sensorial area, like the primary somatosensory cortex or Heschl gyrus, always more hyperintense in T1 weighted sequences than adjacent cortices. Brand et al. (1998) suggest that “all vestibular areas are multisensory.” Other cortical areas seem particularly important for vestibular processing: the inferior parietal lobule *in extenso*, the visual associative areas hMSTd (the anterior part of MT-MST complex in humans, homologue of MSTd in monkeys), the ventral intra parietal area (VIP) or the cingulate sulcus visual area (CSv). All those suspected ‘vestibular cortices’ have been identified using functional magnetic resonance imaging (fMRI) or positron emission tomography (PET) or direct electrical cortical stimulation during clinical investigations for epilepsy (Lopez and Blanke, 2011; Lopez et al., 2012b).

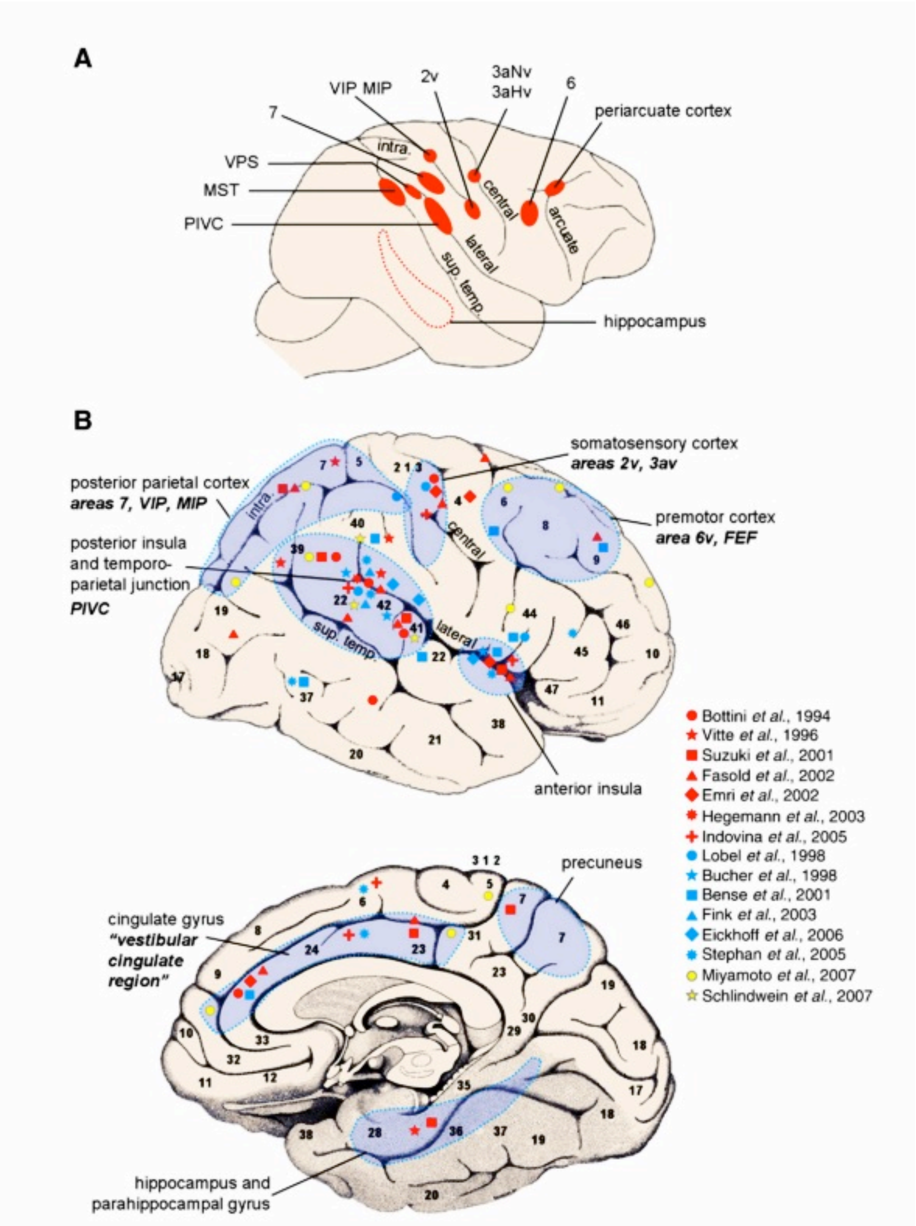

Figure 2. Comparative anatomy of monkey and human vestibular cortex. From Lopez and Blanke (2011). (A) Schematic representation of the vestibular areas in monkeys. Areas 2v, 6v, 7 and 3av (3aHv: 3a-hand-vestibular region, 3aNv: 3a-neck-vestibular region), MIP: medial intraparietal area, MST: medial superior temporal area, PIVC: parieto-insular vestibular cortex, VIP: ventral intraparietal area, VPS: visual posterior sylvian area. Major sulci are represented: arcuate sulcus (arcuate), central sulcus (central), lateral sulcus (lateral), intraparietal sulcus (intra.) and superior temporal sulcus (sup. temp.). Adapted from Sugiuchi et al (Sugiuchi et al., 2005). (B) Vestibular areas in humans revealed by neuroimaging during caloric (red symbols) and galvanic (blue symbols) vestibular stimulation, as well as during short auditory stimulation (yellow symbols). To summarize, right and left cerebral activations are reported on a lateral view of the right hemisphere (modified after Duvernoy, 1999). The supposed homologous vestibular areas reported in animals are indicated in bold letters (FEF: frontal eye fields). The numbers on the cortex refer to the cytoarchitectonic areas defined by Brodmann.

Vestibular cortices must be better mapped and amongst them, important regions for multisensory integration need to be investigated further to understand better the neural correlates of bodily self-consciousness. In TPJ lesions, along angular gyrus (AG) and supramarginal gyrus (SMG), vestibular dysfunctions have been reported and intracranial electrical stimulation at this site also evoked graviceptive sensations and whole-body displacements as well as complex limb transformations (Blanke et al., 2002b; Mazzola et al., 2014; Penfield, 1957). Even if, by the past, vestibular research has not been considered enough by cognitive neuroscientists in the study of neural correlates of consciousness (NCC), many recent works investigated the role of vestibular integration with other polysensory signals in the last decade. Studies focused both on humans (Ferre et al., 2014, 2013, 2010; Ferrè et al., 2013; Lenggenhager et al., 2008; Lopez et al., 2010, 2008b; Pfeiffer et al., 2014, 2013) and on animals. Visual and vestibular inputs were particularly investigated (Angelaki et al., 2011; DeAngelis and Angelaki, 2012; Fetsch et al., 2012, 2011; Ohshiro et al., 2011).

1.3 Multisensory integration: key concepts

As reported by Stein and Stanford (Stein and Stanford, 2008), “For thousands of years science philosophers have been impressed by how effectively the senses work together to enhance the salience of biologically meaningful events. However, they really had no idea how this was accomplished.” Scientists approached the concept of multimodal sensory integration, the so-called “multisensory integration, using various theoretical models. The multisensory integration problem has been classically investigated using the superior colliculus as a model of polysensory integration aiming to the control of eye and head movements (Holmes and Spence, 2005; Miller et al., 2015). Accumulation of multiple sensory evidence also occurs at the cortical level in higher-order association cortices (Ghazanfar and Schroeder, 2006). Three key principles seem to account to multisensory integration: (1) the temporal congruency principle (see also Rowland and Stein, 2014), (2) the spatial congruency principle, (3) the principle of inverse effectiveness (or 'superadditivity'). It means that neuronal responses to stimuli coming from two different sensory modalities have more chance to occur through mutual enhancement if both stimuli come from the same location (1), come at the same time (2) or when at least one of the two stimuli is too weak to excite a single neuron by itself (3). Some models based on divisive normalisation have been proposed. They take into account the integration of sensory evidence by neuronal assemblies (Ohshiro et al., 2011; van Atteveldt et al., 2014). The most recent models based on Bayes theorem (Seilheimer et al., 2014; Vilares and Kording, 2011) have challenged traditional cue combination models (allowing only integration, partial integration or segregation). In Bayesian models, different sensory inputs have a certain amount of variability and the brain has to build a coherent representation of the external world, based on prior knowledge (sensory representations) and likelihood (statistics obtained from the environment). Prior knowledge and likelihood have been shown to be independent parameters (Beierholm et al., 2009). The multisensory assignment problem or "causal inference problem" (Körding et al., 2007) can be addressed through Bayesian models of multisensory integration. The capacity to infer causal structure does not seem to be restricted to conscious cognition (Körding et al 2007) but occurs unconsciously in different aspects of perceptual processes. Body ownership can be viewed as a multisensory assignment problem solved continually in an effortless manner and through multisensory evidence, for body ownership, for body location, and for peripersonal space. This ability may be disrupted temporarily when a subject has to undergo experiments using the methods of cognitive psychology, leading to limit states of bodily self-consciousness and reshaping the integrity of body scheme. This has been shown for example by Guterstam et al. in elegant series of studies where bodily self-consciousness was altered: subjects were either misattributing an external limb to their own body (Guterstam et al., 2011), embodying of volume of empty space as their own hand (Guterstam et al., 2013) or experiencing full disembodiment towards an invisible body (Guterstam et al, 2015). Classical former experiments also showed that a human healthy subject could misattribute a rubber hand as his own body part (Botvinick and Cohen, 1998) and an avatar as his own body (Ehrsson, 2007; Lenggenhager et al., 2007). Perceptual effects of multisensory integration mainly correspond to a decrease of the sensory uncertainty. It happens when multisensory cues are merged as a single percept while we try to localise the source of stimulation. It can lead for example to perceptual illusions ass in the ventriloquism illusion (Alais and Burr, 2004) or in the McGurk effect (McGurk and MacDonald, 1976). Multisensory integration can also diminish reaction times. Hence, the perception of multiple simultaneous or 'optimally' separated in time can be faster than the perception of the same stimuli well separated in space and time. For instance, an optimal level of asynchrony (short delays) in the onsets of a tone and of a light allows detecting them faster than when they are displayed separately (Hershenson, 1962). Similarly, redundant target effects can also be observed, as human subjects will be faster to answer to two simultaneous visual targets than to two separate targets (Ridgway et al., 2008). In our field of interest, i.e.

bodily self-consciousness, visuo-tactile stimuli will trigger faster reaction times than visual or tactile unimodal stimuli (Forster et al., 2002). The enhancement effect seems particularly important for vision and vestibular senses, as readjustment of postures for a new situation while the body is moving is capital, to avoid life threats (for instance, when someone is driving a vehicle). While a fast update of our internal representations of the world seems to be needed, conversely, conscious reports of visual events seem to obey to slow mechanisms occurring in temporal windows of 300 ms (Forget et al., 2010; Sergent and Dehaene, 2004). Vestibular sensations are also reported after long delays of approximately 450 ms in average, following the onset of a vestibular stimulation (Barnett-Cowan and Harris, 2009). The intersensory enhancement processes could occur at different levels of relays of the vestibular before it "reaches" consciousness (Lopez, 2015). Vestibular inputs need visual evidence and proprioceptive evidence to allow fast bodily reactions to the environment, while vestibular inputs seem better to detect transients such as body accelerations, where visual modality alone with proprioception and erroneous top-down predictions may be defective (as in the train illusion, where one can think he is moving while the environment is actually moving).

1.4 Manipulation of embodiment in healthy subjects: multisensory mismatches

Nevertheless, in adulthood, despite of prior learning through multisensory experience, the body schema and the peripersonal space seem to stay flexible enough to be transiently reshaped, at least for some aspects and in certain circumstances. It happens for instance in limit states of perception such as Rubber Hand Illusion

(RHI), Full Body Illusion, vection (see above), train illusions, vestibular and motion aftereffects (motion feeling after body rotation or after optokinetic motion, following a period of habituation and with a sudden stop of the stimulation). We cannot limit definitions to “multisensory integration”. It seems more accurate to speak about “multisensory mechanisms”, as multisensory convergence dos not always lead towards integration. Body disintegration occurs quite easily in laboratory conditions during experimental workup. Environmental conditions continuously alternate when one modality is more effective than the other. Both are balanced to allow an optimal body interaction with its environment. The adaptability to environment (to avoid obstacles for example) might be the evolutionist benefit of such a plasticity of body ownership.

In fact, body ownership can be easily manipulated in healthy humans and a temporary disruption of the physiological multisensory integration can occur through causal interference. Related procedures are the rubber hand illusion (RHI) (Botvinick and Cohen, 1998) or its equivalent for the whole-body in Virtual Reality set-ups (VR), the full body illusion (FBI) (Aspell et al., 2009; Lenggenhager et al., 2007; see also Ehrsson, 2007). RHI and FBI create a mismatch between sensorial modalities, by a manipulation of visual and proprioceptive cues. Those illusions are associated with self-identification to elements external to the physical body, respectively a fake hand in the case of RHI or an avatar in the case of FBI. In the FBI, the subject views his own body from behind displayed in a head-mounted display (a virtual body seen from the back corresponding to a live movie by a camera behind the subject). Thus, when the ‘felt stroking’ on the back of the body is synchronous with the ‘seen stroking’ on the virtual body, the subject has a tendency to self-attribute the virtual body as its own, as a result of visual and tactile congruency and of visual dominance, as vision biases other sensory modalities in crossmodal perceptual tasks (see also Witten and Knudsen, 2005). The touch is illusory felt by the subject at the virtual body location, as if tactile sensations were remapped to the avatar. It also leads to impaired estimation of self-location towards the avatar. Participants show a significantly stronger drift in the direction of the virtual body in the synchronous condition than in the asynchronous condition (see Figure 3).

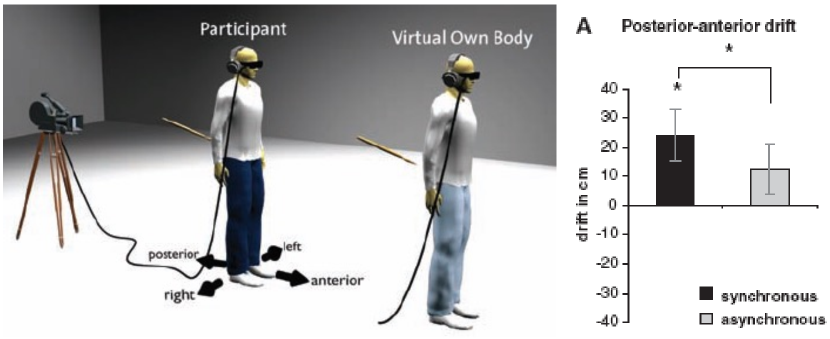

Figure 3. Adaptation of the rubber hand illusion to the entire body: the full body illusion, after Lenggenhager et al. (2007). Experimental setup and proprioceptive drift in cm the synchronous (black) and asynchronous stroking conditions (grey) on the posterior-anterior axis.

Visuo-tactile integration can also be modulated by a stimulation of the vestibular system. The RHI effect can be enhanced with galvanic vestibular stimulation (Lopez et al., 2010). Moreover, the experience of phantom limbs in amputees and paraplegic patients is modulated by CVS (André et al., 2001; Le Chapelain et al., 2001). In healthy humans, vestibular stimulation can impair hand pointing tasks and the reproduction of arm positions (Bresciani et al., 2002; Knox et al., 2006; Mars et al., 2003).

1.5 Vection, a tool to investigate visuo-vestibular interactions and self-motion

Multisensory interactions occur between the visual and vestibular systems. This cross-convergence has been explained by the fact that an organism in motion essentially receives the information from vision and vestibular signals, as well as somatosensory and proprioceptive signals. A typical example of visuo-vestibular interactions is the phenomenon called vection, extensively reported in visual psychophysics literature starting from Ernst Mach in a princeps paper (Mach, 1875) and still studied in contemporary research (Berthoz et al., 1975; Dichgans and Brandt, 1978; Trutoiu et al., 2009). A moving visual scene or an optokinetic stimulus based on an optic flow can induce a sensation of self-motion in the absence of real motion from the subject. Vection is a visually induced illusory self-motion, where bodily self-motion can be felt by the subject, in the direction opposite to the optic flow but on the same axis. Linear upward flow induces downward vection for instance. Vection also leads to postural readjustments (Lestienne et al., 1977). Vection is commonly experienced in daily life, while gazing at the sky and the clouds moving, the water moving in the river stream, or when we are waiting in a train while seeing the train besides starting in opposite direction. The main dilemma to solve for a subject gazing at an optic flow is to rely on an egocentric or on an allocentric referential to decide about his own self-motion: "Is the surrounding environment moving or am I moving?" Visual cues provide important information (together with touch and proprioception) to the brain in order to assess for one's own motion in space at a constant speed motion, when vestibular cues are weak or not present.

Seven functional neuroimaging studies in PET and fMRI investigated vection (Beer et al., 2002; Brandt et al., 1998; Deutschländer et al., 2004; Kleinschmidt et al., 2002; Kovács et al., 2008; Previc et al., 2000; Slobounov et al., 2006). Many other studies focused on coherent optic flow stimulation or optokinetic nystagmus but failed to induce vection or were not interested to induce such illusory self-motion. Inducing vection requires specific criteria including a large peripheral field of view (for linear vection), high velocity stimuli, high visual density of the display, and optimisation by a central fixation. Optokinetic stimuli inducing vection activate a network of motion-sensitive areas such as the anterior portion of the human motion complex (hMSTd or V5a), the TPJ, the dorsomedial cortex or V6 (cuneus and parieto-occipital cortex), and an area of ST and posterior intraparietal cortex (Kleinschmidt et al., 2002). Vection might also correlate with deactivations in the vestibular cortices (retroinsular and parietal-insular regions) and in early motion-sensitive visual areas, supporting the idea of an inhibitory interaction between visual and vestibular systems for motion perception (Brandt et al., 1998; Deutschländer et al., 2004; Kleinschmidt et al., 2002). Kleinschmidt et al (2002) described a direct correlation of vection with cerebellar nodulus activity and Kovacs, Raabe and Greenlee (2008) reported a more intense activity in several regions when they compared vection with object motion perception. Those regions included the right MT, the precuneus and the areas along the dorsal part of the IPS and along the left posterior IPS. The larger cluster of this study was located in the precuneus which is an area activated by optic flow, also activated in visuo-spatial imagery and which has connections with parieto-insular cortical regions (Cavanna and Trimble, 2006). A right paramedian precuneus lesion has also been reported to lead to recurrent illusory linear vection episodes in a patient. Those episodes were reproduced by cortical stimulation at the site lesion and ceased after tumour excision (Wiest et al., 2004). Two associative visual areas seem to receive vestibular afferents in humans: the anterior part of MST (hMST, but not the adjacent area MT) and the cingulate sulcus visual areas CSv, as it has been shown recently in fMRI with using galvanic stimulation (Smith et al., 2012).

1.6 General Overview: investigating visuo-vestibular contributions to bodily self-consciousness

Data from the literature emphasise the concept of a bodily self-consciousness based on multisensory integration and highly linked to vestibular and visual perception. A failure of multisensory integration artificially induced by the methods of cognitive psychology or in pathological conditions can lead to an altered body limb perception, to modified body ownership and even to disembodiment. The contribution of the vestibular system is still to be assessed more extensively amongst other multisensory mechanisms. Vection is a phenomenon for which a functional and anatomical link has been described between visual and vestibular systems. For the study of bodily self-consciousness and bodily perception, optokinetic stimuli or 'optic flow' is a good alternative to direct vestibular stimulation, as it also induces whole-body transformations and may modulate visuo-tactile conflicts observed in classical cognitive psychology paradigms.

On the other hand, the vestibular network description in human remains a major challenge. If we consider it a major contributor to multisensory processing, an extensive knowledge of its anatomy, its function and its interactions with other sensory systems (somatosensory, motor, and proprioceptive) are prerequisites to a better understanding of bodily self-consciousness. Two main obstacles remain: first of all, delivering vestibular stimuli in experimental neuroimaging conditions may be complex but is possible through fMRI using artificial peripheral stimulation with GVS or CVS. Moreover, the characterization of the vestibular cortex imposes a better delineation of the highly folded cortical areas at the TPJ and in the insulo-opercular region to label them accurately and appreciate their respective contribution to the visuo-vestibular integration. It can be achieved by a combination of neuroimaging techniques with high spatial resolution, needing an increased signal-to-noise ratio compared to traditional fMRI at 1.5 or 3T.

This thesis research project was dedicated to the study of visuo-vestibular mechanisms in the healthy human brain and in pathological conditions leading to altered states of bodily self-consciousness. Accordingly to the previous statements, we decided to orientate our work towards two main experimental lines: neuroimaging and cognitive psychology. We approached both healthy people and patients with disturbed embodiment multisensory processing. **In chapter 2** we conducted the main work of this thesis, a functional MRI study of the vestibular network to map the regions of visuo-vestibular convergence in healthy humans. We performed this study with the ultra-high field 7 Tesla MRI EPFL-CIBM machine, and identified the cortical nodes of the vestibular network critical for visuo-vestibular processing. We used galvanic vestibular stimulation within the constraining MR environment to stimulate the vestibular system (Wardman and Fitzpatrick, 2002) and optokinetic stimuli, the visual counterpart of vestibular control during human motion (Warren et al., 2001). **In chapter 3 and 4**, we designed behavioural studies manipulating visual, tactile, proprioceptive and optokinetic stimulations to see how bodily self-consciousness and embodiment of external fake limbs could be modulated by visuo-vestibular signals triggering vection or by visual dominance over somatosensory signals. We used visuo-tactile conflicts based on visual dominance over touch, and tested the respective contribution of visual optokinetic stimuli and visuo-proprioceptive manipulations to assess the weight of those respective sensory inputs to create the body schema and body image. **In chapter 5**, we finally made the link with clinical practice by reporting the case of a patient with a rare disturbance of bodily self-consciousness, based on a mixed semiology between OBE and HAS which was associated with a cortical lesion in a visuo-vestibular multisensory cortex, the left temporo-parietal junction.

Chapter 2 Visuo-vestibular convergence revealed by 7T functional MRI

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Abstract

Visual and vestibular systems interact to encode body motion and location in space. Nevertheless, the existence of cortical areas processing both visual and vestibular signals is unclear. We aimed to identify visuo-vestibular brain regions in the posterior peri-sylvian and extrastriate brain regions using 7T functional magnetic resonance imaging. 11 human subjects received galvanic vestibular stimulation at the mastoid (contrasted to galvanic cutaneous stimulation of the neck) and were exposed to linear coherent motion via an optokinetic visual stimulation (contrasted to a condition with static dots). Visuo-vestibular convergence occurred within a parieto-temporal network and included the (1) retroinsular cortex within the depth of supramarginal gyrus and in the area OP1 of parietal operculum, (2) at the temporo-parietal junction at the surface of the supra marginal gyrus, mainly in areas PF and PFt, and in (3) posterior middle temporal gyrus and superior temporal sulcus extending in extrastriate cortex. Visuo-vestibular convergence in (2) and (3) were found in the majority of subjects while Ri was a less consistently activated across subjects. These data are aligned to recent neurophysiology data in monkeys showing that visuo-vestibular integration does not occur in posterior insula but in its posterior vicinity in the inferior parietal lobule, which incorporated the retroinsular cortex, behind the human analogue of the monkey parieto-insular vestibular cortex. Moreover, we describe a new region of visuo-vestibular convergence in middle temporal gyrus, anterior and superior to the motion-sensitive extrastriate cortex.

Keywords: fMRI, visual, vestibular, convergence, galvanic, 7T

Introduction

The vestibular system encodes rotational and translational accelerations of the head in space, provides important signals about gravity, and contributes to posture and eye movement control. Visual and vestibular systems are complementary in coding self-motion and self-location in daily life (Barry and Burgess, 2014; DeAngelis and Angelaki, 2012). For example, the vestibular system is tuned to high velocity motion while the visual system preferentially encodes low velocity motion in space. In addition, while vestibular receptors are silent during constant velocity motion, visual receptors continue to encode self-motion (Fetsch et al., 2012). As a result, low-velocity coherent visual motion can evoke compelling sensations of self-motion (Berthoz, Pavard, & Young, 1975; Kleinschmidt et al., 2002; Pavard & Berthoz, 1977).

Visuo-vestibular integration has been extensively described in the vestibular nuclei and thalamus of monkeys, cats and rats (Cazin, Precht, & Lannou, 1980; Cullen, Roy, & Sylvestre, 2003; Magnin & Putkonen, 1978; Waespe & Henn, 1980), but there is still scarce description of the mechanisms supporting visuo-vestibular integration in the cortical vestibular network, especially in humans. To date, more than ten cortical regions sensitive to vestibular inputs have been described in animals, including the parieto-insular vestibular cortex (PIVC), primary somatosensory cortex, ventral intraparietal, medial intraparietal and lateral intraparietal areas, medial superior temporal area (MST), the motor and premotor cortex, hippocampus, and several other regions (review in Lopez & Blanke, 2011; Lopez, 2015). Interestingly, visuo-vestibular convergence has been revealed in many of these regions in monkeys, indicating that the vestibular cortex is foremost a cortex underpinning multisensory self-motion perception (Guldin & Grüsser, 1998).

Anatomical investigations into the cortex of several monkey species suggest that the PIVC – located at the junction of the posterior insula, parietal operculum and retroinsular cortex – constitutes the core of the vestibular cortex (Akbarian, Grusser, & Guldin, 1994; Akbarian, Grüsser, & Guldin, 1993; Grüsser, Pause, & Schreiter, 1982, 1990; Grüsser, Pause, Schreiter, et al., 1990; Guldin, & Grüsser, 1998; Guldin, Akbarian, Grüsser, & Grusser, 1992; Guldin, Mirring, & Grüsser, 1993). While electrophysiological studies showed that the PIVC is crucially involved in processing vestibular signals (Chen, DeAngelis, & Angelaki, 2010; Grüsser, Pause, & Schreiter, 1990; Grüsser, Pause, Schreiter, et al., 1990; Liu, Dickman, & Angelaki, 2011; Shinder & Newlands, 2014), these studies provided diverging results regarding the convergence of vestibular and visual signals in PIVC neurons. According to Grüsser and colleagues (Grüsser, Pause, & Schreiter, 1990; Guldin et al., 1992), PIVC neurons in Macaque monkey (*Macaca fascicularis*) respond to body rotation and optic flow rotating around the animal. Other data confirmed this and also reported that PIVC neurons respond to the motion of a visual target (Shinder and Newlands, 2014). In addition, visuo-vestibular integration was reported in an area located posteriorly to the PIVC and referred to as "visual posterior sylvian area" (VPS) (Dicke, Chakraborty, & Thier, 2008; Guldin et al., 1992; Guldin & Grüsser, 1998). By contrast, Chen and colleagues (2010) localised vestibular neurons in rhesus monkeys (*Macaca mulatta*) more posteriorly, "within area Ri (retroinsular) and in the transition zones between S2, Ri and Ig (insular granular field)", and showed that PIVC neurons did not respond to optokinetic stimulation.

In humans, six neuroimaging studies reported brain activations evoked by visual and vestibular stimulation as tested in the same subjects. It is however difficult to directly compare these results as different types of vestibular stimulations have been used (caloric or galvanic vestibular stimulation) as well as different neuroimaging techniques in recent studies using 3T fMRI (Smith, Wall, & Thilo, 2012, Frank, Baumann, Mattingley, & Greenlee, 2014; Billington and Smith, 2015; Della-Justina et al., 2015) and earlier work using PET (Deutschländer et al., 2002) or MEG (Hegemann et al., 2003). Although these studies revealed overlapping visual and vestibular activations in both deep and superficial parts of the posterior Sylvian fissure (Frank et al., 2014; Smith et al., 2012) there is, to date, no detailed anatomical definition of the site of visuo-vestibular convergence in the human PIVC, probably due to diverging nomenclatures and the lack of high spatial resolution in previous neuroimaging studies. Thus, human PIVC has been located in different parts within temporo-parietal cortex: in cytoarchitectonic area OP2 in the parietal operculum (Eickhoff, Weiss, Amunts, Fink, & Zilles, 2006; Lopez & Blanke, 2011; zu Eulenburg et al., 2013; zu Eulenburg, Caspers, Roski, & Eickhoff, 2012), in the posterior insular cortex (Mazzola et al. 2014; Bense et al. 2001), posteriorly to the insula and OP2 in the "retroinsular cortex" (Lopez, Blanke, & Mast, 2012), or in the more superficial "temporo-peri-Sylvian vestibular cortex" widely distributed in the inferior parietal lobule and superior temporal gyrus (Kahane et al., 2003). Thus, it remains unclear which exact region or regions of the human operculo-insular complex and perisylvian area contribute to visuo-vestibular processing. Moreover, functional neuroimaging studies also revealed visuo-vestibular convergence in the extrastriate cortex in MT/MST complex (i.e. hMST), the human homologue of animal MSTd, the anterior part of MT/MST complex (Cardin & Smith, 2010; Frank et al., 2014), as well as in posterior cingulate sulcus (Cardin & Smith, 2010). Although galvanic vestibular stimulation (GVS) activates the posterior part of the middle temporal gyrus (pMTG) and the superior temporal sulcus (pSTS) (upper and anterior to hMST; Lopez et al., 2012; Stephan et al., 2005) visuo-vestibular convergence has not been reported so far in the pMTG and pSTS (note that pMTG and pSTS are part of multisensory cortex activated by to optokinetic stimulation, somatosensory and auditory stimuli (i.e. Beauchamp, 2005).

Here, we investigated visuo-vestibular convergence in human cortex taking advantage of the ultra-high resolution 7T MRI with its high signal-to-noise ratio allowing BOLD measurements in individual subjects (Dula et al., 2010; Duyn, 2012; van der Zwaag et al., 2009). We compared brain activations evoked by GVS, which is a reliable and safe technique to deliver artificial vestibular stimulation in MRI (Brandt and Dieterich, 1999; Lobel et al., 1998). GVS was contrasted with a control galvanic cutaneous stimulation (GCS), and compared to activations evoked by linear optokinetic stimulation (Saenz, Lewis, Huth, Fine, & Koch, 2008). The high spatial resolution available at 7T (Salomon et al., 2014) allowed us to observe activations in individual subjects, tracking possible inter-individual variability inherent to vestibular stimulation (see for example Bense et al., 2001; Cardin & Smith, 2010; Lopez, Blanke, et al., 2012). To disentangle the respective contribution of small regions in the highly folded region of the inferior parietal lobule, and particularly the cortices including parietal operculum, supramarginal gyrus and posterior insula, the detected regions of visuo-vestibular convergence were precisely mapped according to cytoarchitectonic subdivisions of the inferior parietal lobule using cytoarchitectonic atlases of the parietal and occipital lobe (Triarhou, 2013; Von Economo and Koskinas, 2008) as well as probabilistic cytoarchitectonic mapping (Caspers et al., 2013, 2008; Eickhoff et al., 2005; Eickhoff et al., 2006a; Eickhoff et al., 2006; Kurth et al., 2010)

Materials and methods

Subjects

Twelve subjects participated to the study, of which one had to be excluded due to failure of the galvanic vestibular stimulation during fMRI scanning. The remaining eleven subjects (7 males; mean age ± standard deviation: 26.2 ± 5.1 years) were all right-handed, had normal or corrected-to-normal vision, and gave written informed consent to participate in the study. All procedures received the approval of the Ethics Committee of the Faculty of Biology and Medicine of the University of Lausanne and the study was conducted in accordance with the Declaration of Helsinki.

Experimental setup for sensory stimulations

Galvanic vestibular stimulation and galvanic cutaneous stimulation

GVS and GCS were applied using a bipolar, binaural configuration. A stimulator (Model Grass S48, Astor-Med Inc., West Warwick, RI, USA) delivered a square wave pulse through an isolation unit (Model Grass SIU5), a constant current stimulus unit (Model Grass CCU1), and a switch box to alternate current polarity between the electrodes. Two pairs of rubber carbon electrodes (4 × 5 cm) embedded in a sponge saturated with water were attached to the subject's head. For GVS, the electrodes were placed on the skin over the mastoid processes. For GCS, the electrodes were placed on the left and right side of the neck, 5 cm below the GVS electrodes. GCS was used to evoke tactile sensations mimicking those evoked by GVS, without inducing vestibular stimulation (Lenggenhager et al., 2008). The firing rate of vestibular afferents is known to increase on the cathodal side and decrease on the anodal side (Goldberg et al., 1984). Accordingly, right GVS and GCS refer to right cathodal stimulations, whereas left GVS and GCS refer to left cathodal stimulations.

In the pre-scan testing phase, GVS voltage was adapted for each subject: while the subject was sitting with eyes closed outside of the scanning room, the current intensity was progressively increased until the subject reported a vestibular sensation as strong as possible without being uncomfortable or painful. For GCS, the current intensity was progressively increased until the subject reported the same intensity of tactile and/or heat sensation as during GVS. Before the beginning of the GVS and GCS runs, while the subject was lying inside the bore, the intensity of the GVS and

GCS was controlled to ensure that vestibular and tactile sensations were not modified by head position and fixation in the MRI coil. Individual thresholds were confirmed once the subject was placed supine inside the scanner. All subject reported identical cutaneous sensations for GVS and GCS stimulation. The current intensity used for GVS (mean ± SD: 2.5 ± 1.2 mA) did not differ from that used for GCS (mean ± SD: 2.0 ± 1.1 mA; paired-sampled t-tests: $p = 0.14$).

The stimulation protocol was controlled using E-prime (Psychology Software Tools, Inc.) and included two functional runs, one providing GVS and the other GCS. Each of the two runs consisted of 10 blocks of right cathodal stimulation and 10 blocks of left cathodal stimulation, delivered in a random order. Each block consisted of 5 pulses of 1500 ms with inter-stimulus intervals of 500 ms (for a total duration of 10 s per block), followed by 20 s of rest. In total, the duration of each run was 8 min. Subjects were asked to keep their eyes closed during GVS and GCS runs.

Optokinetic stimulation

We used an optokinetic stimulation, that does not evoke vection, originally designed to localise the MT+/V5 complex (Saenz, Lewis, Huth, Fine, & Koch, 2008). The stimulus consisted of 300 white dots located within a circular field of view, moving coherently on a black background, with a velocity of 8 °/s, radially inward or outward with a reversal of the direction of motion every 800 ms. Random dot arrays subtended ±12° of visual angle from a central fixation point. Individual dots

(50 displayed in total in each frame) subtended 1°. Subjects were instructed to fixate a red dot at the centre of the visual field for the entire duration of the run. Stimulation blocks were made of periods of moving dots of 12 s alternatively moving forward or backward separated by 18 s during which the dots remained stationary, used as a baseline condition. The functional run included 8 repetitions of the stimulation-rest blocks, starting with the moving one, resulting in a total duration of 4 minutes. Visual stimuli were generated using MATLAB (The MathWorks Inc.) and the Psychophysics Toolbox (www.psychtoolbox.org) and projected onto a rear-projection screen visible from the scanner bore via a mirror mounted on the head coil.

MRI data acquisition

Images were acquired on a short-bore 7T scanner (Siemens Medical, Germany) equipped with a 32-channel Rx / 1-channel Tx rf-coil (Nova Medical, Cleveland, USA) (Salomon et al., 2014). Functional images were acquired using a sinusoidal readout EPI sequence and comprised 46 transverse slices, placed in order to cover the insula, the temporo-parietal junction and visual associative areas, with an in-plane resolution of 1.5×1.5 mm^2 (slice thickness = 1.5 mm, no gap). The matrix size was 140 × 140, field of view = 210 mm, TE = 26 ms, TR = 2.5 s, GRAPPA = 3. Each GVS and GCS functional run comprised 200 volumes and the optokinetic functional run 96 volumes. An anatomical volume was acquired using the MP2RAGE sequence (Marques et al., 2010) at $1 \times 1 \times 1$ mm^3 resolution (TE = 2.63 ms, TR = 7.2 ms, TI_1 = 0.9 s, TI_2 = 3.2 s, TR_{MPRAGE} = 5 s). To perform the coregistration between functional and anatomical volumes, a whole brain EPI with 80 slices was also acquired (in-plane resolution of 1.5 × 1.5 mm^2, TR = 4350 ms, TE = 26 ms, slice thickness = 1.5 mm, no gap, matrix size 140 × 140).

Functional MRI data analysis and anatomical landmarks

Pre-processing and analysis were conducted with SPM8 (Wellcome Department of Cognitive Neurology, London, UK). Functional volumes were spatially realigned to the first volume acquired, and smoothed with an isotropic Gaussian kernel (FWHM = 2 mm). Blocks of left and right GVS stimulation and blocks of visual stimulation were statistically analysed using the General Linear Model using the canonical hemodynamic response function (HRF) and its time derivative as basis functions. A high-pass filter was applied to remove slow signal drifts with a period longer than 256 s in the case of GVS and GCS and longer than 60 s in the case of visual stimuli.

The MP2RAGE volume was coregistered to the whole brain EPI image by means of rigid body transformation and both were coregistered to the mean EPI functional volume. All the fMRI analysis was conducted in the individual subject space (i.e. in the space of individual functional acquisitions) and, for visualization purposes, these results were then normalized to the MNI standard brain and resampled at a resolution of 1 × 1 × 1 mm^3. To this end, the transformed structural images were first segmented into grey matter, white matter and cerebrospinal fluid using SPM8 and then transformed into the MNI (Montreal Neurological Institute) space using the Diffeomorphic Anatomical Registration Through Exponentiated Lie algebra (DARTEL) tool (Ashburner, 2007).

Vestibular regions were identified as those brain areas showing higher activation for GVS than GCS for the right and left stimulation separately and results were masked inclusively by the GVS activation in order to keep only GVS-activated regions. To identify visual motion areas, the optic flow was contrasted to the static images. We were interested to look at true positive voxels (i.e. the conjunction of visual and vestibular activations). To this end, conjunction maps were computed with a threshold of $p < 0.005^2 = p < 2.5\ e^{-5}$, uncorrected for multiple comparisons. Corresponding to a threshold of $p < 0.005$, uncorrected for multiple comparisons, for single modality t-maps, respectively right and left GVS-GCS and visual motion-static images.

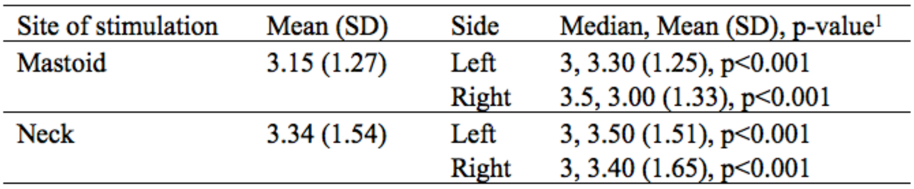
After normalization of the results to the MNI template brain, activations were allocated to probabilistic cytoarchitectonic maps of the parietal operculum, posterior insula, and temporo-occipital cortex using the SPM Anatomy toolbox based on Jülich/Düsseldorf group data (Caspers et al., 2006, 2008; Eickhoff, Schleicher, Zilles, & Amunts, 2006; Eickhoff, Weiss, et al., 2006; Eickhoff et al., 2007) and anatomic atlases of human brain for regions not yet marked in the Anatomy toolbox (Duvernoy, 1999; Von Economo and Koskinas 1925 and 2008, Triarhou 2013). Von Economo and Koskinas (Koskinas, 1925; Von Economo, 2009) attributed a nomenclature where the first capital letter corresponds to the lobe (F = frontal, P = parietal, Oc = occipital, T = temporal), and the second capital letter corresponds to a subpart of the lobe. A third letter may index another subdivision. Inferior parietal cortex is then composed of 5 subregions in supramarginal gyrus (PF: rostral main inferior parietal area or 'area supramarginalis'; PFcm: 'columnata magnocellularis' subregion of PF; PFm: 'magnocellularis' subregion of PF; PFop: 'tenuicorticalis opercularis' subregion of PF; PFt: 'tenuicorticalis' subregion of PF) and 2 regions in angular gyrus or 'area angularis' or PG, the caudal main inferior parietal area (PGa: anterior; PGp: posterior). For extrastriate regions, we do not use original Von Economo nomenclature. In fact, area Oam or area 16 in Fleschig Atlas (Flechsig, 1920) , at the junction between BA37 and anterior BA19, has been originally described by Von Economo and Koskinas (1925) as corresponding to MT+ but was discarded by further research (Malikovic et al., 2007; see also page 1037 Paxinos and Mai, 2004). We prefer here the nomenclature of Malikovic et al., 2007 used by Anatomy Toolbox. The letter 'h' corresponds to 'human', 'Oc' to occipital cortex, and area is numbered as 5, "when moving laterally from the primary visual cortex" (Malikovic et al., 2007). Parietal operculum is corresponding to functionally defined region SII and is subdivided into OP1, 2, 3 and 4 (Caspers et al., 2006; Eickhoff et al., 2006a). Posterior medial temporal lobe regions are not defined in the Anatomy toolbox, except for the medial part of PH (see above), corresponding to fusiform gyrus (Fg1 and Fg2). Correspondence between Brodmann and Von Economo and Koskinas atlases have been schematized (Caspers, 2015) Brodmann area 37 (BA37) is a heterogeneous brain region corresponding to a part of lateral occipital cortex, including hOc5 and of part of posterior medial temporal gyrus. The anterior and superior part of BA37 corresponds to posterior middle temporal region still considered as part of parietal lobe called PH in Von Economo and Koskinas (Von Economo and Koskinas, 1925; see also figure 27.13 in Paxinos and Mai, 2004). PH is considered as paratemporalis 'homotypical' cortex in Smith Atlas (1907) and as temporal by Campbell atlas (1905) (page 768, comparison of classification schemes of the human cortex, in Paxinos, 2012) or as area parietalis basalis by Von Economo and

Koskinas atlas (Paxinos, 2012). PH is subdivided into PH (main region), PHo (area parietalis basalis limes occipitalis), PHt (temporalis) and PHp (parietalis).

Subjective reports

At the end of the experiment, subjects filled in a questionnaire (from Lopez et al., 2010) to report the effects of GVS and GCS (irrespective of the cathode location). Subjects rated the intensity of their body translations and rotations induced by the electrical stimulation, the perception of motion during optokinetic stimulation, and the skin sensation on a 7-point Likert scale ranging from 0 (no feeling at all) to 6 (very strong feeling). Axes of rotation and translation were reported according to a body-centred reference frame, not with respect to gravity.

The intensity of tactile sensation experienced during GVS and GCS is reported in Table 1. All ratings were significantly different from zero ($p < 0.001$), indicating that a tactile perception was induced by GVS and GCS. No difference between the intensity of tactile sensation was observed between GVS and GCS ($p = 0.7$), neither between right and left stimulation ($p = 0.5$).

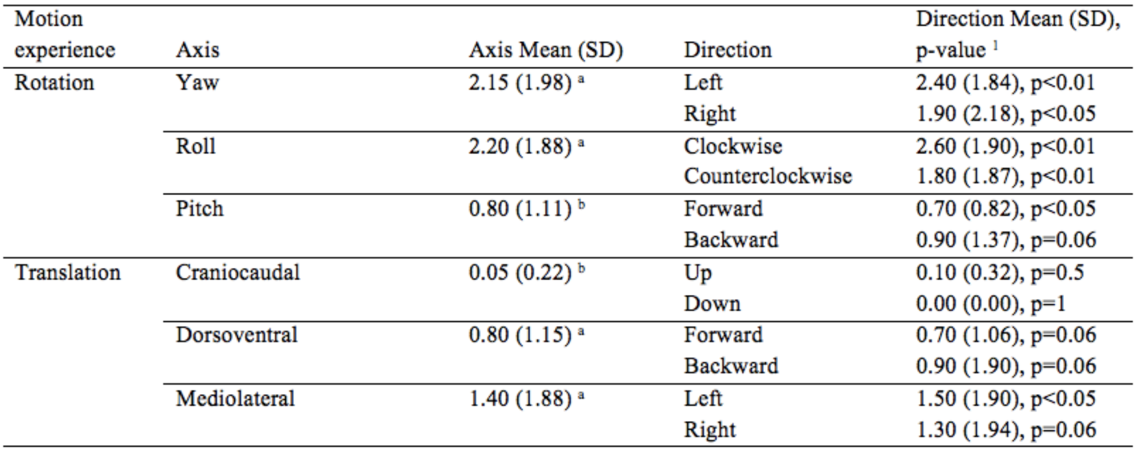


Site of stimulation	Mean (SD)	Side	Median, Mean (SD), p-value[1]
Mastoid	3.15 (1.27)	Left	3, 3.30 (1.25), p<0.001
		Right	3.5, 3.00 (1.33), p<0.001
Neck	3.34 (1.54)	Left	3, 3.50 (1.51), p<0.001
		Right	3, 3.40 (1.65), p<0.001

[1] p-values based on the sign test on one sample set.

Table 1. Skin percepts

Table 2 summarizes the intensity of self-motion perception during GVS and GCS. No subject reported vestibular sensation outside GVS stimulation. Subjects reported sensations of body rotation only around the yaw and pitch axes or sensations of body translation only along the mediolateral axis. A Mann-Whitney test indicated significantly stronger sensations of body rotation than translation ($U = 1178.5$, $p < 0.0001$). Sign-tests computed on each direction of rotation showed that GVS induced a significant perception of body rotation observed along all axes, except along the pitch axis in the backward direction (see Table 2 for the statistical values). Sign-tests computed on each direction of translation showed that the only significant perception of body translation observed during GVS was in the left direction along the mediolateral axis (see Table 2 for the statistical values).



Motion experience	Axis	Axis Mean (SD)	Direction	Direction Mean (SD), p-value [1]
Rotation	Yaw	2.15 (1.98) ^{a}	Left	2.40 (1.84), $p<0.01$
			Right	1.90 (2.18), $p<0.05$
	Roll	2.20 (1.88) ^{a}	Clockwise	2.60 (1.90), $p<0.01$
			Counterclockwise	1.80 (1.87), $p<0.01$
	Pitch	0.80 (1.11) ^{b}	Forward	0.70 (0.82), $p<0.05$
			Backward	0.90 (1.37), $p=0.06$
Translation	Craniocaudal	0.05 (0.22) ^{b}	Up	0.10 (0.32), $p=0.5$
			Down	0.00 (0.00), $p=1$
	Dorsoventral	0.80 (1.15) ^{a}	Forward	0.70 (1.06), $p=0.06$
			Backward	0.90 (1.90), $p=0.06$
	Mediolateral	1.40 (1.88) ^{a}	Left	1.50 (1.90), $p<0.05$
			Right	1.30 (1.94), $p=0.06$

[1] p-values are based on the sign test on the one sample set.

[2] The letters for each axis category are linked to the result of the Mann-Whitney test for each motion experience (rotation/translation). Group a is significantly different from group b ($\alpha<0.05$)

Table 2. Body percepts

Results

Functional MRI data

Visuo-vestibular convergence

We identified three main loci of visuo-vestibular convergence in the retroinsular cortex (Ri), at the temporo-parietal junction (TPJ) and in the posterior part of the medial temporal gyrus and superior temporal sulcus (pMTG-STS). Visuo-vestibular convergence is illustrated for three representative subjects in Figures 1, 2 and 3. Pooling right and left cathodal stimulations, we observed that the majority of the subjects showed visuo-vestibular convergence in the bilateral TPJ and pMTG-STS, and to lesser extent in Ri. For TPJ, ten out of eleven subjects showed visuo-vestibular convergence. Among those, seven subjects showed bilateral TPJ convergence, two showed right TPJ convergence, and one showed left TPJ convergence. For pMTG-STS, nine subjects showed visuo-vestibular convergence. Seven subjects showed bilateral pMTG-STS convergence, one showed right pMTG-STS convergence and one showed left pMTG-STS convergence. For Ri, six subjects showed visuo-vestibular convergence. Two subjects showed bilateral Ri convergence, three subjects showed right Ri convergence, and one showed left Ri convergence.

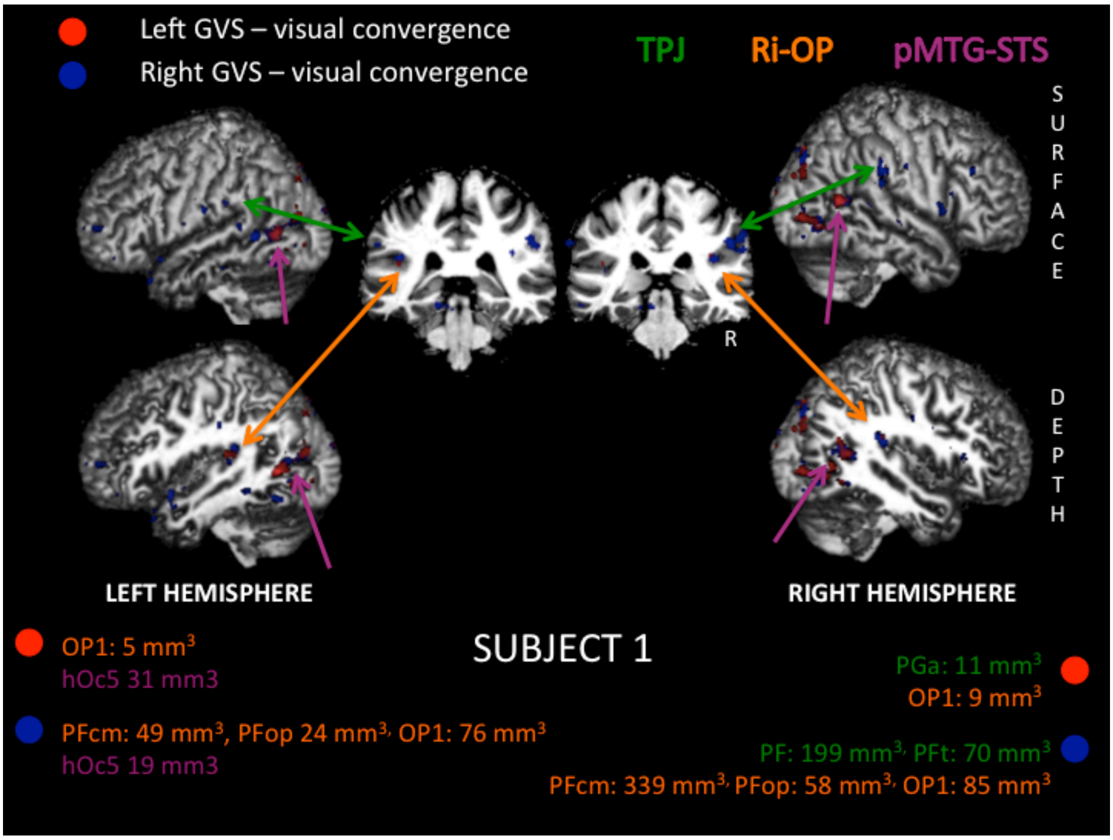


Figure 1. Representative subjects: subject 1. We can see deep and superficial convergence in perisylvian areas, respectively in Ri and parietal operculum, and also at TPJ along supramarginal gyrus in more posterior and superficial parts of IPL called PF and PFt. pMTG and pSTS convergence extends on left side to hOc5 (hMSTd), lower and more posteriorly. In this subject, we find mostly anterior convergence, explaining why cytoarchitectonic areas in the depth are still implying OP1 with PFcm, PFt and PFop both in the depth and at the surface, and PF at the surface.

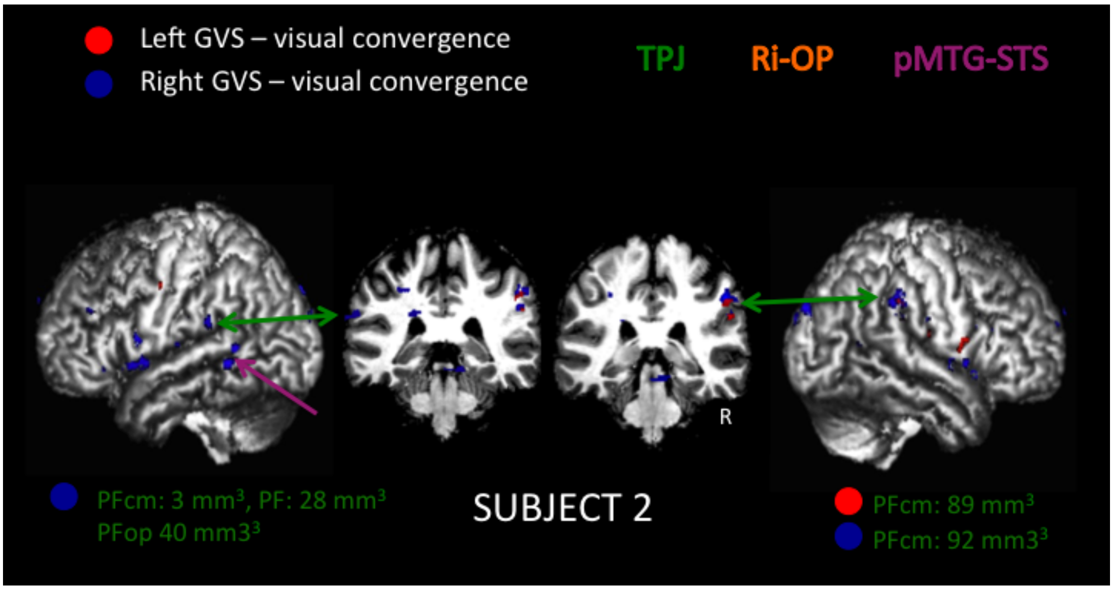


Figure 2. Representative subjects: subject 2. We can see mostly small loci of convergence at the surface of TPJ. Cytoarchitectonic analyses show activation of PF and PFop mainly on right side. PF is always at the surface while PFop is also more at the surface at this localization according to Caspers 2008. It shows how PFcm and PFop can be classified in some subjects as superficial (TPJ) and in some others as in the depth as “Ri” as PFcm is mostly in the depth. In left side, most of the convergence are more posterior that on right side and seem to belong mostly to PFcm.

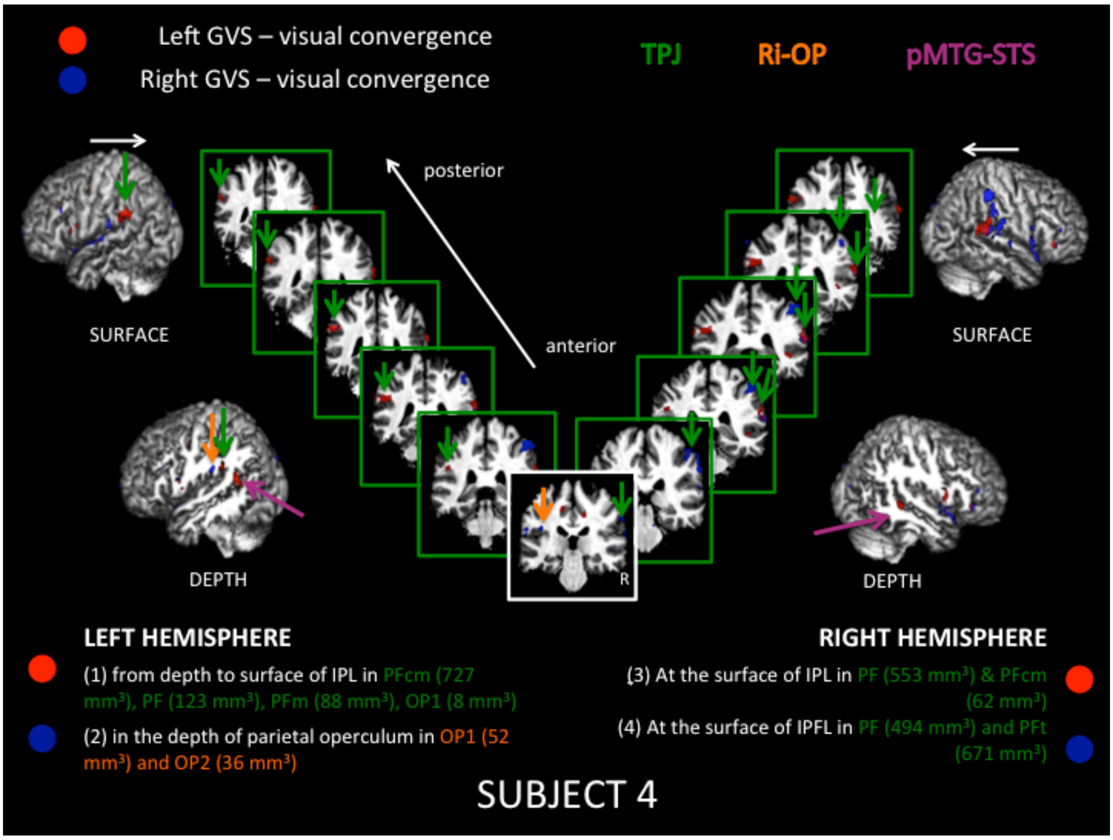


Figure 3. Representative subjects: subject 4. The most anterior convergence on left hemisphere corresponds to parietal opercular regions OP1 and OP2, while the biggest component of convergence appears to follow a gradient from anterior to posterior and from depth to surface along z axis, corresponding massively to PFcm anatomy anteriorly and to PF and PFm posteriorly, illustrating again why some loci of convergence can be sometimes assessed as Ri or as TPJ while they are in continuity, anterior part in the depth and posterior part at the surface. On right hemisphere, activations are at the surface and generally more posterior than on left side, explaining why they are classified as posterior PFcm for a small part and in majority within PF and upper PFt (superficial) at the surface of IPL.

Figure 4 summarizes the centre of each subject's visuo-vestibular convergence locus on an inflated brain. Although we describe three locations of visuo-vestibular convergence, we note that anatomically, especially in the right hemisphere, convergences in individual subjects seem to be distributed along the SMG from the depth to the surface and from the anterior to posterior sites in functionally defined regions called here Ri and TPJ.

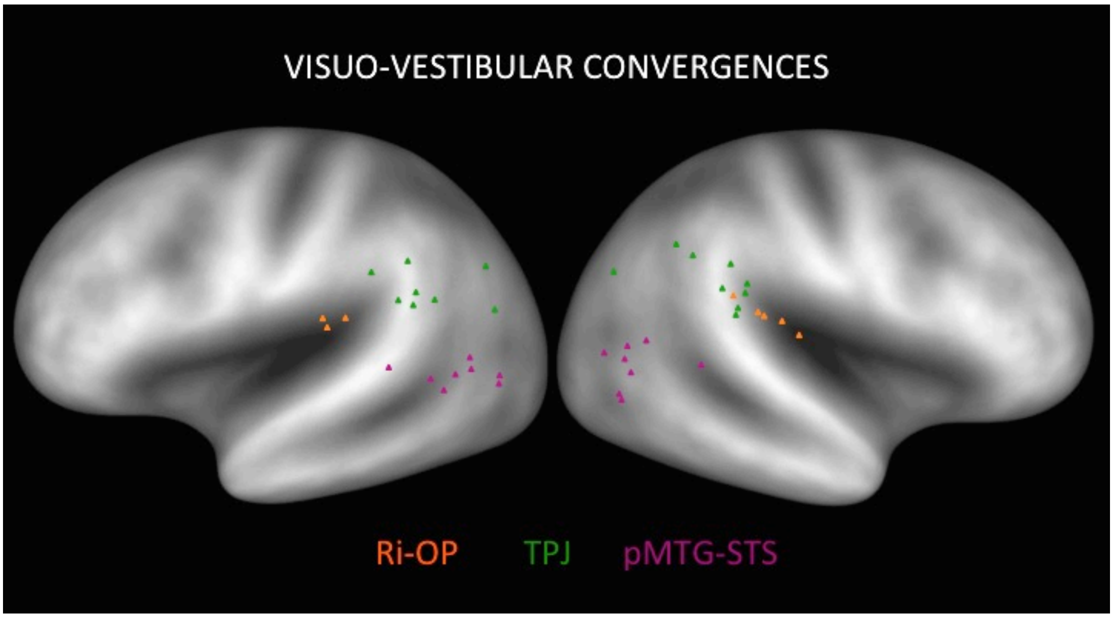


Figure 4. Summary of visuo-vestibular convergences where we projected on a generic inflated brain, the centre of each locus of convergence of each individual subject. A continuum of activations from the depth of Ri and OP to the surface of TPJ can be observed, mainly on right side. A second hub of convergence is observed centred in posterior MTG region, extending in lower bank of posterior STS and projecting on hMSTd or hOc5 in 4/ 8 subjects showing convergence in pMTG-STS.

Overlap with cytoarchitectonic probabilistic maps

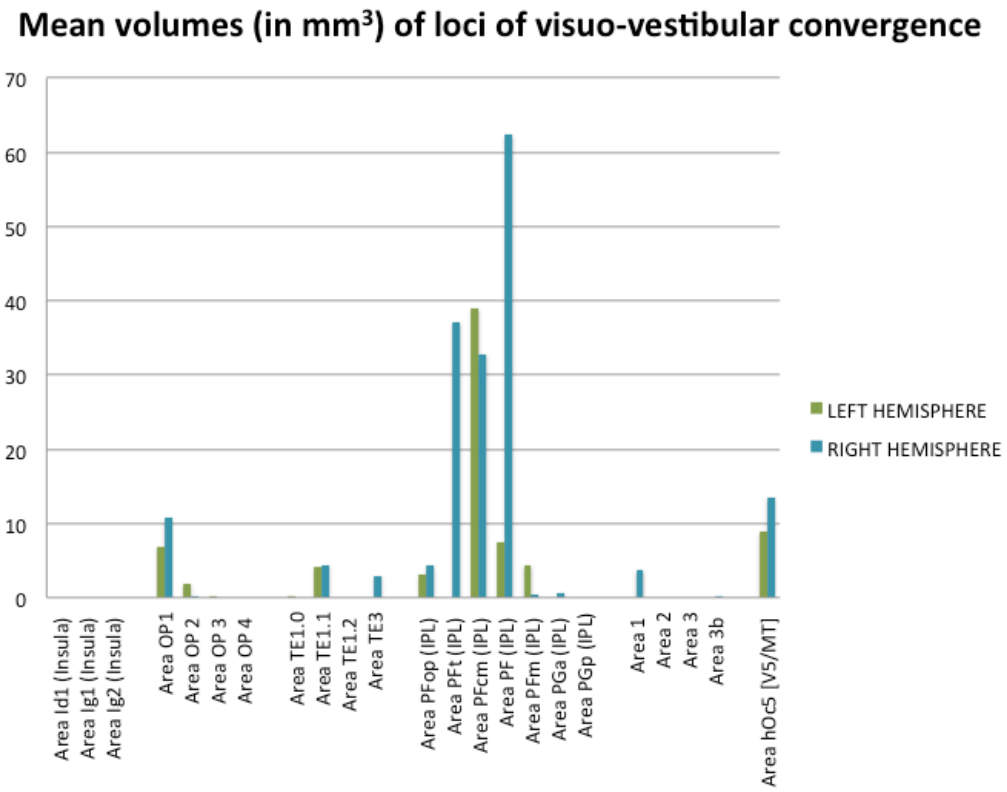


Figure 5. Mean brain volumes of visuo-vestibular convergence, classified by hemisphere and cytoarchitectonic region of IPL, parietal operculum and extrastriate cortex. We gather convergence due to Right and Left GVS. We can see that the small volumes of hOc5 activated contrast while very reproductive convergence was assessed within pMTG, but upper and anterior to hOc5 (=hMSTd) and not mapped by cytoarchitectonic maps. We also notice more important convergence in the non-dominant hemisphere (right). Our data advocate for a continuum of activations between depth and surface along the anatomy of mainly PFcm, which could correspond to the so-called retroinsular cortex, behind and upper parietal opercular region OP1. Other subdivisions of IPL are also activated and mainly PF and PFt, at the surface, also following an anatomy from depth to surface, front to back, in what we call here temporo-parietal junction, projecting actually on the surface of supramarginal cortex and anterior part of angular gyrus.

We used the SPM Anatomy Toolbox (Eickhoff et al., 2005) to determine the cytoarchitectonic brain areas of the Ri and TPJ activations described above. This analysis was carried out for 10 subjects (this analysis could not be done for subject 7 because he showed a wide activation pattern extending over the entire area, making it impossible to separate the contribution of different subregions). Figure 5 shows the average volume of activation allocated to each cytoarchitectonic region, separately for each hemisphere (pooling activations due to right and left cathodal stimulation). The present analysis revealed that Ri activations were mostly located in cytoarchitectonic areas PFcm and OP1. TPJ activations were mostly located in areas PF and PFt of the supramarginal gyrus, and less consistently in areas PFop, PFm and PGa. Visuo-vestibular convergence in TPJ was not consistently allocated to OP2. Modest contributions of TPJ activations were found in superior temporal regions of the region temporalis propria (TE1.0, TE1.1, TE1.2, TE3) (Morosan et al., 2001; Zilles, 2004) and primary sensory cortex (area 1) (Geyer et al., 2000) and there was no visuo-vestibular convergence in the dysgranular insular area Id1, granular insular areas Ig1 and Ig2, and area PGp of angular gyrus. Activation labelled here as pMTG-STS was effectively centred on the posterior MTG and the lower bank of posterior STS and did not match any probability map available in the Anatomy toolbox, except in 4 subjects where this activation extended also downward and posteriorly into the cytoarchitectonic region hOc5 of occipital cortex functionally identified as the putative human homologue of V5/MT+ (Dumoulin et al., 2000; Malikovic et al., 2007; Wilms et al., 2005).

Discussion

We provide a detailed anatomical analysis of visuo-vestibular convergence in the human brain using a single subject approach and 7 Tesla MRI. Visuo-vestibular convergence was evident in three main regions centred on the inferior parietal lobule: (1) Retroinsular activation in the depth of the posterior part of the lateral fissure, allocated to cytoarchitectonic area PFcm of the SMG. (2) A superficial region at the temporo-parietal junction in areas PF and PFt corresponding to superficial parts of SMG. (3) The posterior aspect of the middle temporal gyrus, extending to the posterior STS, sometimes also extending downwards and posteriorly to the cytoarchitectonic area hOc5 which may be fit the definition of human v5/MT+ (Malikovic et al., 2007). In the following part, we discuss each activation site separately with respect to different anatomical and functional classifications of the human vestibular cortex as well as electrophysiological data in non-human primates.

Retroinsular and opercular activations

Visuo-vestibular convergence was found in the depth of the posterior Sylvian fissure, within medial aspects of the IPL (areas PFcm, PFop) and marginally within OP1. This localization is in agreement with the results of two recent meta-analytic definitions of the human vestibular cortex that localised the core region of vestibular cortex in area OP2 (Zu Eulenburg et al., 2012) or in areas OP2 and Ri (Lopez et al., 2012). This is also agreeing anatomically with the findings of a recent fMRI study analysing visuo-vestibular convergence (Frank et al., 2014) reporting a bimodal region in an area termed PIC (for ‘posterior insula cortex’). This region was defined in reference to a visual motion sensitive area described previously at the posterior border of the insula (Claeys et al., 2003). Frank et al. (2014) reported large intersubject variability in the location of PIC, in agreement with a partial variability reported in the present study. Moreover, the location of visuo-vestibular convergence that was found in our study is also close to the retroinsular activations observed in response to optic flow stimulations in Cardin and Smith (2010) and in responses to visuo-vestibular convergences in Billington and Smith (2014).

However, no study (Frank et al., 2014; Cardin and Smith, 2010) analysed activations with respect to cytoarchitectonic areas. Results from the present study therefore add that visuo-vestibular convergence in the posterior Sylvian fissure involved mostly area PFcm, to a smaller extent area PFop, and marginally involved OP1 Accordingly, we propose that the retroinsular responses to optic flow and vestibular stimulation reported in the present study and previous investigations (Cardin and Smith, 2010; Frank et al., 2014) correspond to area PFcm of the supramarginal gyrus, behind the PIVC. PFcm has been shown to be involved also in speech and hand motor execution (Heim et al., 2012) but more studies need to be performed using cytoarchitectonic maps to map what are the exact functions allocated to respective subparts of SMG. A significant gender difference is known as PFcm seem to be significantly wider in males subjects (Caspers et al 2008). In addition, we propose that Ri may partly correspond to cytoarchitectonic region PFcm. Ri is not well defined in humans (Bense et al., 2001a; Eickhoff et al., 2006b) and it has been shown to be involved in vestibular processing and the perception of gravitational motion (Indovina et al., 2005; for review see Lacquaniti et al., 2013). Ri has been shown to be a multisensory region, integrating signals from tactile and muscular proprioceptive receptors (Bottini et al., 2005, 2001), a finding consistent with electrophysiological investigations in monkeys (Robinson and Burton, 1980a, 1980b;

see also for insular cortex organization (Evrard and Craig, 2015; Evrard et al., 2014). Ri has been clearly defined functionally as the region behind the posterior insula, and behind the areas OP2 and OP1; the only cortical region at this location is the deeper part of SMG or PFcm, which thus may be necessarily, be the anatomical correlate of Ri.

Interestingly, we did not find visuo-vestibular convergence in the granular (Ig1, Ig2) and dysgranular (Id1) insular cortex. This finding is in contrast with earlier hypotheses about the implication of the posterior insular cortex in vestibular processing as demonstrated by previous GVS and CVS studies (Bense et al., 2001a; Dieterich and Brandt, 2001; Emri et al., 2003; Lopez et al., 2012; zu Eulenburg et al., 2013, 2012) and intracranial stimulation investigations (Mazzola et al., 2014). However, the present data are in agreement with more recent visuo-vestibular investigations and electrophysiological recordings in macaque PIVC showing that visuo-vestibular integration does not occur in PIVC, but rather takes place in more posterior regions, adjacent to the insular cortex (Chen et al., 2011; Liu and Angelaki, 2009; Shinder and Newlands, 2014). Hence, our present data do not confirm the existence of visuo-vestibular integration in the posterior insula as seminally posited by Grüsser and colleagues (Grüsser et al., 1990b, 1982; Guldin et al., 1992), but concord with the extensive observations by Angelaki and co-workers (Chen et al., 2011; Liu and Angelaki, 2009; Shinder and Newlands, 2014).

Inferior parietal lobule, superficial part

Another region in the inferior parietal lobule showed visuo-vestibular convergence, in particular the superficial parts of IPL. Importantly, this region also showed strongest and most consistent activations across subjects. Cytoarchitectonic allocation showed that the IPL included areas PF and PFt and to a smaller extent area PFm and PGa. Anatomically, these IPL regions involve mostly the supramarginal gyrus, but also involve adjacent parts of the angular gyrus in PGa (i.e. respectively Brodmann areas 40 for PF and PFt and BA 39 for PGa). PFt has been suggested to be involved in the mirror neuron system as the human analogue of monkeys' PF (Peeters et al., 2013) but again more past functional studies using fMRI should be reinterpreted under the light of cytoarchitectonic maps allowing a more detailed anatomical mapping. Intracranial stimulation studies in epileptic patients are compatible with vestibular responses in this region and have demonstrated that the focal stimulation of both gyri may evoke conscious sensations that the body is spinning (Kahane et al., 2003) or translating (Blanke et al., 2002). Previous studies using CVS and GVS also consistently reported activations of these regions with SMG and anterior parts of the AG (Bense et al., 2001a; Stephan et al., 2005; review in Lopez and Blanke 2011). Interestingly, SMG and AG are key regions for the embodied experience of self-location (Ionta et al., 2011) and various neurological conditions in these regions may disturb the sense of self-location (for example: Blanke, Landis, Spinelli, & Seeck, 2004; Blanke, Ortigue, Landis, & Seeck, 2002b; Heydrich, Dieguez, Grunwald, Seeck, & Blanke, 2010; Heydrich, Lopez, Seeck, & Blanke, 2011; Heydrich & Blanke, 2013).

We note that there is an anatomical distribution along the same sulcus between the activations in the superficial aspect of the IPL and the retroinsular activations in the depth of the Sylvian fissure. This likely reflects the complex anatomical folded organization of the IPL, with cytoarchitectonic subregions of IPL organised from the surface (i.e. PF) to the depth of the IPL (i.e. PFcm) (Caspers, 2015; Caspers et al., 2008) (see Figure 5) who all seem to respond to vestibular and visual stimuli.

Posterior middle temporal cortex and superior temporal sulcus

Partially consistent with previous data analyzing GVS-induced (Billington and Smith, 2015; Frank et al., 2014; Smith et al., 2012; Stephan et al., 2005) or CVS-induced brain activations in humans (Wang et al., 2008) and electrophysiological studies in monkeys (Gu et al., 2008, 2007), we also observed visuo-vestibular convergence within cytoarchitectonic area hOc5 as in Malikovic et al., 2007). However, we found an overlap of the individually defined regions of activation with hOc5 in only half of our subjects who exhibited wider responses in pMTG region. The activation in pMTG extended dorsally and posteriorly to reach the anterior and superior parts of hOc5, that is extrastriate cortex, and where only small volumes were allocated while the volume was centred on pMTG. In agreement with human (Smith et al., 2012) and animal research (Bremmer et al., 1999; Chen et al., 2008; Gu et al., 2008, 2007; Takahashi et al., 2007), these data may suggest that only the anterior part of MT-MST complex (likely hMST), was activated in the present subjects in whom an overlap was found with extrastriate cortex.

To our knowledge, this is the first study to report visuo-vestibular convergence in pMTG and pSTS. Only one previous work reported that GVS activates pMTG (Stephan et al., 2005) but no visuo-vestibular convergence was explored in this work. Nevertheless, this mapping as hOc5 in our study should be taken with caution as the anatomy of the sulcation in the region as well as the functional localization of MT+ is highly variable from one subject to another (Malikovic et al., 2007). We can thus speculate that this component of visuo-vestibular convergence in pMTG and pSTS has been reported as extrastriate loci of convergence on a functional basis, as MT or MST. As suggested by Saenz and colleagues (Saenz et al., 2008), " the probable human homologue of visual motion-responsive macaque areas MT and MST, is typically located posterior to the intersection of the lateral occipital sulcus (LOS) and the inferior temporal sulcus (ITS). However, identifying human MT+ by anatomical landmarks and/or stereotaxic coordinates alone is problematic because of significant anatomical variability between individuals (Dumoulin et al., 2000; Zeki et al., 1993) and because of its proximity to polysensory temporal lobe regions (Beauchamp et al., 2004). As a result, the location of MT+ is normally defined functionally, by its response to moving visual stimuli (Dumoulin et al., 2000; Tootell et al., 1995)."

In original description from Von Economo and Koskinas (1925), cytoarchitectonic region 'Oam' was speculated as being MT+ but it was discarded by further research (see page 1037 in Zilles, 2004). If hOc5 seems to be the best candidate to fit the definition of V5/MT+, but the anterior part of MT-MST complex still needs to be localised with more accuracy in further studies. We speculate here that our activations more anterior to hOc5 (MT+), in pMTG, i.e. corresponding to cytoarchitectonic baso-parietal regions PH and its subdivisions PHo, PHt, and

PHp, may partially correspond to the anterior part of MT-MST complex: the human homologue of MST of hMST. It may explain why hOc5 is not activated in all subjects and why when it is activated, only small brain volumes in this area are concerned (Zilles et al., 2015). Nevertheless, this could be better explored using different stimuli preferred by MST, an area that does not show retinotopy, and sensitive to optic flows stimulating peripheral field of views (Cheng et al., 1995; Huk et al., 2002). The precise location of what was claimed to be hMST in previous studies (Billington and Smith, 2015; Smith et al., 2012), responding to vestibular and visual inputs, should be compared by further studies on the same basis of cytoarchitectonic atlases in individual subjects 7T fMRI studies to compare coordinates of hMST and regions anteriorly and upper than hOc5 in Von Economo's PH region, the lateral and posterior part of middle temporal gyrus.

Several studies reported pSTS and pMTG as brain regions activated by optokinetic stimuli (Beer et al., 2009; Gilaie-Dotan et al., 2013a, 2013b; Grosbras et al., 2012; Grossman et al., 2000; Grossman and Blake, 2002; Ulloa and Pineda, 2007), existing even in congenital visual deprivation (Bedny et al., 2008; Noppeney et al., 2003). pMTG is also processing visual motion related to gravity together with the posterior insula and Ri (Indovina et al., 2005; Lacquaniti et al., 2013; Miller et al., 2008). pSTS and pMTG are also multisensory regions responding to tactile, motion-related auditory and visual signals (Beauchamp, 2005; Beauchamp et al., 2004). They may even overlap with what was called the extrastriate body area or EBA, a region responding to body parts at the junction between lateral occipital cortex and posterior medial temporal cortex (Astafiev et al., 2004; Downing et al., 2001; Grossman and Blake, 2002; Urgesi et al., 2004) also recently reported to correlate with rubber hand illusion (Limanowski and Blankenburg, 2015; Limanowski et al., 2014). In the absence of cytoarchitectonic maps of pMTG, the basal part of parietal lobe according to old definitions from Von Economo and Koskinas (1925) of PH and its subdivisions, and with the ontological intersubject variability in the location of motion sensitive extrastriate multisensory regions, its stays difficult to disentangle the exact contributions of those cortices to visual, vestibular and somatosensory processing but it may be further explored with a fine resolution using dedicated multisensory tasks.

In addition, in the present study, GVS and visual stimulus were applied separately while they were applied simultaneously during previous works in fMRI but at 3T (in Frank et al., 2014 for example). In addition, we did not look for deactivations of visual cortex during vestibular stimulation or reciprocal deactivation of vestibular cortex during visual stimulation as investigated before (Brandt et al., 1998; Angela Deutschländer et al., 2002). Our data nevertheless advocate for the existence of brain regions at the single subject level which can process both vestibular and visual motion signals, extending previous studies supporting the existence of patterns of reciprocal inhibition of visual and vestibular cortices (Bense et al., 2001a; Chen et al., 2011; Deutschländer et al., 2002).

Further experiments, with imaging methods combining 7T fMRI and cytoarchitectonic maps, functional and anatomical connectivity, should take into account the temporo-spatial dynamics of visuo vestibular processing when simultaneous polysensory stimulation is applied.

Conclusion

Our data reveal the existence of visuo-vestibular convergence consisting in a large activation, starting behind the posterior insula and OP2, and encompassing the depth of inferior parietal lobule mainly in supramarginal gyrus in retroinsular cortex and partly in parietal operculum, then extending to the surface of the temporo-parietal junction still along supramarginal gyrus. A second core region of visuo-vestibular convergence was identified in pMTG with a downward and posterior extension to area hOc5 previously identified as MT+. The locus of activation suggests pMTG activations to be corresponding to the anterior part of MT-MST complex, or hMST but need to be confirmed by appropriate cytoarchitectonic-mapping methods of the middle temporal region still not available. Further studies may assess the dynamics of such convergences during complex tasks involving bimodal stimulations together or independently, as well as the respective contribution of each locus of convergence within the vestibular network. The high signal-to-noise ratio allowed by 7T fMRI in brain regions characterized by high inter-subject anatomical and functional variability allowed us to perform individual mapping of visuo-vestibular convergences in parietal and occipito-temporal cortices.

Conflict of Interest

None declared.

Acknowledgments

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References

Akbarian, S., Grusser, O.J., Guldin, W.O., 1994. Corticofugal Connections Between the Cerebral-Cortex and Brain-Stem Vestibular Nuclei in the Macaque Monkey. J. Comp. Neurol. 339, 421–437.

Akbarian, S., Grüsser, O.J., Guldin, W.O., 1993. Corticofugal projections to the vestibular nuclei in squirrel monkeys: further evidence of multiple cortical vestibular fields. J Comp Neurol 332, 89–104.

Ashburner, J., 2007. A fast diffeomorphic image registration algorithm. Neuroimage 38, 95–113. doi:10.1016/j.neuroimage.2007.07.007

Barry, C., Burgess, N., 2014. Neural mechanisms of self-location. Curr. Biol. 24, R330–9. doi:10.1016/j.cub.2014.02.049

Beauchamp, M.S., 2005. See me, hear me, touch me: multisensory integration in lateral occipital-temporal cortex. Curr. Opin. Neurobiol. 15, 145–53. doi:10.1016/j.conb.2005.03.011

Beauchamp, M.S., Lee, K.E., Argall, B.D., Martin, A., 2004. Integration of Auditory and Visual Information about Objects in Superior Temporal Sulcus. Neuron 41, 809–823. doi:10.1016/S0896-6273(04)00070-4

Bedny, M., Caramazza, A., Grossman, E., Pascual-Leone, A., Saxe, R., 2008. Concepts are more than percepts: the case of action verbs. J. Neurosci. 28, 11347–53. doi:10.1523/JNEUROSCI.3039-08.2008

Beer, A.L., Watanabe, T., Ni, R., Sasaki, Y., Andersen, G.J., 2009. 3D surface perception from motion involves a temporal-parietal network. Eur. J. Neurosci. 30, 703–13. doi:10.1111/j.1460-9568.2009.06857.x

Bense, S., Stephan, T., Yousry, T. a, Brandt, T., Dieterich, M., 2001a. Multisensory cortical signal increases and decreases during vestibular galvanic stimulation (fMRI). J. Neurophysiol. 85, 886–899.

Bense, S., Stephan, T., Yousry, T.A., Brandt, T., Dieterich, M., 2001b. Multisensory cortical signal increases and decreases during vestibular galvanic stimulation (fMRI). J Neurophysiol 85, 886–99.

Berthoz, A., Pavard, B., Young, L.R., 1975. Perception of linear horizontal self-motion induced by peripheral vision (linearvection) basic characteristics and visual-vestibular interactions. Exp Brain Res 23, 471–489.

Billington, J., Smith, A.T., 2015. Neural mechanisms for discounting head-roll-induced retinal motion. J. Neurosci. 35, 4851–6. doi:10.1523/JNEUROSCI.3640-14.2015

Blanke, O., Landis, T., Spinelli, L., Seeck, M., 2004. Out-of-body experience and autoscopy of neurological origin. Brain 127, 243–258. doi:10.1093/brain/awh040

Blanke, O., Ortigue, S., Landis, T., Seeck, M., 2002. Stimulating illusory own-body perceptions. Nature 419, 269–270. doi:10.1038/419269a

Bottini, G., Karnath, H.O., Vallar, G., Sterzi, R., Frith, C.D., Frackowiak, R.S., Paulesu, E., 2001. Cerebral representations for egocentric space: Functional-anatomical evidence from caloric vestibular stimulation and neck vibration. Brain 124, 1182–1196.

Bottini, G., Paulesu, E., Gandola, M., Loffredo, S., Scarpa, P., Sterzi, R., Santilli, I., Defanti, C.A., Scialfa, G., Fazio, F., Vallar, G., 2005. Left caloric vestibular stimulation ameliorates right hemianesthesia. Neurology 65, 1278–1283.

Brandt, T., Bartenstein, P., Janek, A., Dieterich, M., 1998. Reciprocal inhibitory visual-vestibular interaction. Visual motion stimulation deactivates the parieto-insular vestibular cortex. Brain 121 (Pt 9, 1749–1758.

Brandt, T., Dichgans, J., 1972. [Circular vection, visually induced pseudocoriolis effects, optokinetic afernystagmus. A comparative study of subjective and objective optokinetic aftereffects]. Albr. Von Graefes Arch Klin Exp Ophthalmol 184, 42–57.

Brandt, T., Dieterich, M., 1999. Does the vestibulo-ocular reflex use the same pathways for functions in roll and pitch planes? Electroencephalogr Clin Neurophysiol Suppl 50, 221–225.

Brandt, T., Wist, E., Dichgans, J., 1971. [Visually induced pseudocoriolis-effects and circularvection. A contribution to opto-vestibular interaction]. Arch Psychiatr Nervenkr 214, 365–389.

Bremmer, F., Kubischik, M., Pekel, M., Lappe, M., Hoffmann, K.P., 1999. Linear vestibular self-motion signals in monkey medial superior temporal area. Ann N Y Acad Sci 871, 272–281.

Cardin, V., Smith, A.T., 2010. Sensitivity of human visual and vestibular cortical regions to egomotion-compatible visual stimulation. Cereb. Cortex 20, 1964–1973. doi:10.1093/cercor/bhp268

Cardin, V., Smith, A.T., 2010. Sensitivity of human visual and vestibular cortical regions to egomotion-compatible visual stimulation. Cereb Cortex 20, 1964–1973. doi:bhp268 [pii] 10.1093/cercor/bhp268

Caspers, J., Zilles, K., Eickhoff, S.B., Schleicher, A., Mohlberg, H., Amunts, K., 2013. Cytoarchitectonical analysis and probabilistic mapping of two extrastriate areas of the human posterior fusiform gyrus. Brain Struct. Funct. 218, 511–526. doi:10.1007/s00429-012-0411-8

Caspers, S., 2015. Posterior Parietal Cortex: Structural and Functional Diversity, : An Encyclopedic Reference. Elsevier. doi:10.1016/B978-0-12-397025-1.00229-3

Caspers, S., Eickhoff, S.B., Geyer, S., Scheperjans, F., Mohlberg, H., Zilles, K., Amunts, K., 2008. The human inferior parietal lobule in stereotaxic space. Brain Struct. Funct. 212, 481–495. doi:10.1007/s00429-008-0195-z

Caspers, S., Geyer, S., Schleicher, A., Mohlberg, H., Amunts, K., Zilles, K., 2006. The human inferior parietal cortex: Cytoarchitectonic parcellation and interindividual variability. Neuroimage 33, 430–448. doi:10.1016/j.neuroimage.2006.06.054

Cazin, L., Precht, W., Lannou, J., 1980. Pathways mediating optokinetic responses of vestibular nucleus neurons in the rat. Pflugers Arch. 384, 19–29.

Chen, A., DeAngelis, G.C., Angelaki, D.E., 2011. Convergence of vestibular and visual self-motion signals in an area of the posterior sylvian fissure. J Neurosci 31, 11617–11627. doi:10.1523/JNEUROSCI.1266-11.2011

Chen, A., DeAngelis, G.C., Angelaki, D.E., 2010. Macaque parieto-insular vestibular cortex: responses to self-motion and optic flow. J Neurosci 30, 3022–3042. doi:30/8/3022 [pii] 10.1523/JNEUROSCI.4029-09.2010

Chen, A., Gu, Y., Takahashi, K., Angelaki, D.E., Deangelis, G.C., 2008. Clustering of self-motion selectivity and visual response properties in macaque area MSTd. J Neurophysiol 100, 2669–2683. doi:10.1152/jn.90705.2008

Cheng, K., Fujita, H., Kanno, I., Miura, S., Tanaka, K., 1995. Human cortical regions activated by wide-field visual motion: an H2(15)O PET study. J. Neurophysiol. 74, 413–427.

Claeys, K.G., Lindsey, D.T., De Schutter, E., Orban, G.A., 2003. A higher order motion region in human inferior parietal lobule: evidence from fMRI. Neuron 40, 631–42.

Cullen, K.E., Roy, J.E., Sylvestre, P.A., 2003. Signal processing in vestibular nuclei: dissociating sensory, motor, and cognitive influence, in: Harris, L.R., Jenkin, M. (Eds.), Levels of Perception. Springer Verlag, Berlin, pp. 285–309.

DeAngelis, G.C., Angelaki, D.E., 2012. Visual-Vestibular Integration for Self-Motion Perception, in: Murray, M.M., Wallace, M.T. (Eds.), The Neural Bases of Multisensory Processes. Boca Raton (FL).

Della-Justina, H.M., Gamba, H.R., Lukasova, K., Nucci-da-Silva, M.P., Winkler, A.M., Amaro, E., 2015. Interaction of brain areas of visual and vestibular simultaneous activity with fMRI. Exp. brain Res. 233, 237–52. doi:10.1007/s00221-014-4107-6

Deutschländer, A., Bense, S., Stephan, T., Schwaiger, M., Brandt, T., Dieterich, M., 2002. Sensory system interactions during simultaneous vestibular and visual stimulation in PET. Hum. Brain Mapp. 16, 92–103. doi:10.1002/hbm.10030

Deutschländer, A., Bense, S., Stephan, T., Schwaiger, M., Brandt, T., Dieterich, M., 2002. Sensory system interactions during simultaneous vestibular and visual stimulation in PET. Hum Brain Mapp 16, 92–103.

Deutschländer, A., Bense, S., Stephan, T., Schwaiger, M., Dieterich, M., Brandt, T., 2004. Rollvection Versus Linearvection: Comparison of Brain Activations in PET. Hum. Brain Mapp. 21, 143–153. doi:10.1002/hbm.10155

Dicke, P.W., Chakraborty, S., Thier, P., 2008. Neuronal correlates of perceptual stability during eye movements. Eur. J. Neurosci. 27, 991–1002. doi:10.1111/j.1460-9568.2008.06054.x

Dieterich, M., Brandt, T., 2001. Vestibular system: anatomy and functional magnetic resonance imaging. Neuroimaging Clin N Am 11, 263–73, ix.

Dula, A., Welch, E., Creasy, J., Gatenby, J., Stringer, E., Chen, L., Anderson, A., Avison, M., Gore, J., 2010. Challenges and Opportunities of Ultra-High Field MRI. The Third International Conference on the Development of Biomedical Engineering in Vietnam. IFMBE Proc. 27, 1–5.

Dumoulin, S.O., Bittar, R.G., Kabani, N.J., Baker, C.L., Le Goualher, G., Bruce Pike, G., Evans, A.C., 2000. A new anatomical landmark for reliable identification of human area V5/MT: a quantitative analysis of sulcal patterning. Cereb. Cortex 10, 454–63.

Duvernoy, H.M., 1999. The human brain. Surface, blood supply, and three-dimensional sectional anatomy. Second edition. Springer-Verlag, Wien.

Duyn, J.H., 2012. The future of ultra-high field MRI and fMRI for study of the human brain. Neuroimage. doi:10.1016/j.neuroimage.2011.10.065

Eickhoff, S.B., Amunts, K., Mohlberg, H., Zilles, K., 2006. The human parietal operculum. II. Stereotaxic maps and correlation with functional imaging results. Cereb. Cortex 16, 268–79. doi:10.1093/cercor/bhi106

Eickhoff, S.B., Paus, T., Caspers, S., Grosbras, M.H., Evans, A.C., Zilles, K., Amunts, K., 2007. Assignment of functional activations to probabilistic cytoarchitectonic areas revisited. Neuroimage 36, 511–521. doi:10.1016/j.neuroimage.2007.03.060

Eickhoff, S.B., Schleicher, A., Zilles, K., Amunts, K., 2006a. The human parietal operculum. I. Cytoarchitectonic mapping of subdivisions. Cereb Cortex 16, 254–267. doi:bhi105 [pii] 10.1093/cercor/bhi105

Eickhoff, S.B., Stephan, K.E., Mohlberg, H., Grefkes, C., Fink, G.R., Amunts, K., Zilles, K., 2005. A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. Neuroimage 25, 1325–1335. doi:10.1016/j.neuroimage.2004.12.034

Eickhoff, S.B., Weiss, P.H., Amunts, K., Fink, G.R., Zilles, K., 2006b. Identifying human parieto-insular vestibular cortex using fMRI and cytoarchitectonic mapping. Hum Brain Mapp 27, 611–621. doi:10.1002/hbm.20205

Emri, M., Kisely, M., Lengyel, Z., Balkay, L., Marian, T., Miko, L., Berenyi, E., Sziklai, I., Tron, L., Toth, A., 2003. Cortical projection of peripheral vestibular signaling. J Neurophysiol 89, 2639–2646.

Evrard, H., Craig, A., 2015. Insular Cortex, in: Toga, A.W. (Ed.), Brain Mapping: An Encyclopedic Reference. pp. 387–409.

Evrard, H.C., Logothetis, N.K., Craig, A.D.B., 2014. Modular architectonic organization of the insula in the macaque monkey. J. Comp. Neurol. 522, 64–97. doi:10.1002/cne.23436

Fetsch, C.R., Pouget, A., DeAngelis, G.C., Angelaki, D.E., 2012. Neural correlates of reliability-based cue weighting during multisensory integration. Nat Neurosci 15, 146–154. doi:10.1038/nn.2983

Flechsig, P., 1920. Anatomie des menschlichen Gehirns und Rückenmarks auf myelogenetischer Grundlage. Leipzig: Thieme.

Frank, S.M., Baumann, O., Mattingley, J.B., Greenlee, M.W., 2014. Vestibular and visual responses in human posterior insular cortex. J. Neurophysiol. 112, 2481–91. doi:10.1152/jn.00078.2014

Geyer, S., Schormann, T., Mohlberg, H., Zilles, K., 2000. Areas 3a, 3b, and 1 of human primary somatosensory cortex. Part 2. Spatial normalization to standard anatomical space. Neuroimage 11, 684–96. doi:10.1006/nimg.2000.0548

Gilaie-Dotan, S., Kanai, R., Bahrami, B., Rees, G., Saygin, A.P., 2013a. Neuroanatomical correlates of biological motion detection. Neuropsychologia 51, 457–63. doi:10.1016/j.neuropsychologia.2012.11.027

Gilaie-Dotan, S., Saygin, A.P., Lorenzi, L.J., Egan, R., Rees, G., Behrmann, M., 2013b. The role of human ventral visual cortex in motion perception. Brain 136, 2784–98. doi:10.1093/brain/awt214

Goldberg, J.M., Smith, C.E., Fernandez, C., 1984. Relation between discharge regularity and responses to externally applied galvanic currents in vestibular nerve afferents of the squirrel monkey. J Neurophysiol 51, 1236–1256.

Grosbras, M.-H., Beaton, S., Eickhoff, S.B., 2012. Brain regions involved in human movement perception: a quantitative voxel-based meta-analysis. Hum. Brain Mapp. 33, 431–54. doi:10.1002/hbm.21222

Grossman, E., Donnelly, M., Price, R., Pickens, D., Morgan, V., Neighbor, G., Blake, R., 2000. Brain areas involved in perception of biological motion. J. Cogn. Neurosci. 12, 711–20.

Grossman, E.D., Blake, R., 2002. Brain Areas Active during Visual Perception of Biological Motion. Neuron 35, 1167–75.

Grüsser, O.J., Pause, M., Schreiter, U., 1990a. Localization and responses of neurones in the parieto-insular vestibular cortex of awake monkeys (Macaca fascicularis). J Physiol 430, 537–57.

Grüsser, O.J., Pause, M., Schreiter, U., 1982. Neural responses in the parieto-insular vestibular cortex of alert Java Monkey (Macaca fascicularis), in: Roucoux, A., Crommelinck, M. (Eds.), Physiological and Pathological Aspects of Eye Movements. Jung, The Hague, Boston, London, pp. 251–270.

Grüsser, O.J., Pause, M., Schreiter, U., Grusser, O.J., Pause, M., Schreiter, U., 1990b. Vestibular neurones in the parieto-insular cortex of monkeys (Macaca fascicularis): visual and neck receptor responses. J Physiol 430, 559–83.

Gu, Y., Angelaki, D.E., Deangelis, G.C., 2008. Neural correlates of multisensory cue integration in macaque MSTd. Nat Neurosci 11, 1201–1210. doi:10.1038/nn.2191

Gu, Y., DeAngelis, G.C., Angelaki, D.E., 2007. A functional link between area MSTd and heading perception based on vestibular signals. Nat Neurosci 10, 1038–1047. doi:10.1038/nn1935

Guldin Grüsser OJ, W.O., Guldin, W.O., Grüsser, O.J., 1998. Is there a vestibular cortex? Trends Neurosci 21, 254–9.

Guldin, W.O., Akbarian, S., Grüsser, O.J., Grusser, O.J., 1992. Cortico-cortical connections and cytoarchitectonics of the primate vestibular cortex: a study in squirrel monkeys (Saimiri sciureus). J Comp Neurol 326, 375–401. doi:10.1002/cne.903260306

Guldin, W.O., Grüsser, O.J., 1998. Is there a vestibular cortex? Trends Neurosci. 21, 254–259. doi:10.1016/S0166-2236(97)01211-3

Guldin, W.O., Mirring, S., Grüsser, O.J., 1993. Connections from the neocortex to the vestibular brain stem nuclei in the common marmoset. Neuroreport 5, 113–116.

Hegemann, S., Pawlowski, M., Huonker, R., Haueisen, J., Fitzek, C., Fetter, M., 2003. Magnetoencephalography during optokinetic and vestibular activation of the posterior insula. Ann N Y Acad Sci 1004, 457–464.

Heim, S., Amunts, K., Hensel, T., Grande, M., Huber, W., Binkofski, F., Eickhoff, S.B., 2012. The Role of Human Parietal Area 7A as a Link between Sequencing in Hand Actions and in Overt Speech Production. Front. Psychol. 3, 534. doi:10.3389/fpsyg.2012.00534

Heydrich, L., Blanke, O., 2013. Distinct illusory own-body perceptions caused by damage to posterior insula and extrastriate cortex. Brain 136, 790–803. doi:10.1093/brain/aws364

Heydrich, L., Dieguez, S., Grunwald, T., Seeck, M., Blanke, O., 2010. Illusory own body perceptions: case reports and relevance for bodily self-consciousness. Conscious Cogn 19, 702–710. doi:S1053-8100(10)00130-3 [pii] 10.1016/j.concog.2010.04.010

Heydrich, L., Lopez, C., Seeck, M., Blanke, O., 2011. Partial and full own-body illusions of epileptic origin in a child with right temporoparietal epilepsy. Epilepsy Behav 20, 583–586. doi:S1525-5050(11)00011-4 [pii] 10.1016/j.yebeh.2011.01.008

Huk, A.C., Dougherty, R.F., Heeger, D.J., 2002. Retinotopy and functional subdivision of human areas MT and MST. J. Neurosci. 22, 7195–205. doi:20026661

Indovina, I., Maffei, V., Bosco, G., Zago, M., Macaluso, E., Lacquaniti, F., 2005. Representation of visual gravitational motion in the human vestibular cortex. Science (80-.). 308, 416–419.

Ionta, S., Heydrich, L., Lenggenhager, B., Mouthon, M., Fornari, E., Chapuis, D., Gassert, R., Blanke, O., 2011. Multisensory mechanisms in temporo-parietal cortex support self-location and first-person perspective. Neuron 70, 363–374. doi:S0896-6273(11)00200-5 [pii] 10.1016/j.neuron.2011.03.009

Kahane, P., Hoffmann, D., Minotti, L., Berthoz, A., 2003. Reappraisal of the human vestibular cortex by cortical electrical stimulation study. Ann Neurol 54, 615–624.

Kleinschmidt, A., Thilo, K. V, Buchel, C., Gresty, M.A., Bronstein, A.M., Frackowiak, R.S., 2002. Neural correlates of visual-motion perception as object- or self-motion. Neuroimage 16, 873–882.

Koskinas, G.V.E.C., 1925. Die cytoarchitektonik der Hirnrinde des erwachsenen Menschen,. Berlin: Springer, Wien.

Kurth, F., Eickhoff, S.B., Schleicher, A., Hoemke, L., Zilles, K., Amunts, K., 2010. Cytoarchitecture and probabilistic maps of the human posterior insular cortex. Cereb. Cortex 20, 1448–1461. doi:10.1093/cercor/bhp208

Lacquaniti, F., Bosco, G., Indovina, I., La Scaleia, B., Maffei, V., Moscatelli, A., Zago, M., 2013. Visual gravitational motion and the vestibular system in humans. Front. Integr. Neurosci. 7, 101. doi:10.3389/fnint.2013.00101

Lenggenhager, B., Lopez, C., Blanke, O., 2008. Influence of galvanic vestibular stimulation on egocentric and object-based mental transformations. Exp. Brain Res. 184, 211–21. doi:10.1007/s00221-007-1095-9

Liu, S., Angelaki, D.E., 2009. Vestibular signals in macaque extrastriate visual cortex are functionally appropriate for heading perception. J Neurosci 29, 8936–8945. doi:29/28/8936 [pii] 10.1523/JNEUROSCI.1607-09.2009

Liu, S., Dickman, J.D., Angelaki, D.E., 2011. Response Dynamics and Tilt versus Translation Discrimination in Parietoinsular Vestibular Cortex. Cereb Cortex 21, 563–573. doi:bhq123 [pii] 10.1093/cercor/bhq123

Lobel, E., Kleine, J.F., Le Bihan, D., Leroy-Willig, A., Berthoz, A., 1998. Functional MRI of galvanic vestibular stimulation. J Neurophysiol 80, 2699–709.

Lopez, C., 2015. Vestibular Cortex, Brain Mapping: An Encyclopedic Reference. Elsevier. doi:10.1016/B978-0-12-397025-1.00227-X

Lopez, C., Blanke, O., 2011. The thalamocortical vestibular system in animals and humans. Brain Res Rev 67, 119–146. doi:S0165-0173(11)00002-6 [pii] 10.1016/j.brainresrev.2010.12.002

Lopez, C., Blanke, O., Mast, F.W., 2012. The human vestibular cortex revealed by coordinate-based activation likelihood estimation meta-analysis. Neuroscience 212, 159–179. doi:10.1016/j.neuroscience.2012.03.028 S0306-4522(12)00289-8 [pii]

Lopez, C., Lenggenhager, B., Blanke, O., 2010. How vestibular stimulation interacts with illusory hand ownership. Conscious Cogn 19, 33–47. doi:S1053-8100(09)00189-5 [pii] 10.1016/j.concog.2009.12.003

Magnin, M., Putkonen, P.T., 1978. A new vestibular thalamic area: electrophysiological study of the thalamic reticular nucleus and of the ventral lateral geniculate complex of the cat. Exp Brain Res 32, 91–104.

Malikovic, A., Amunts, K., Schleicher, A., Mohlberg, H., Eickhoff, S.B., Wilms, M., Palomero-Gallagher, N., Armstrong, E., Zilles, K., 2007. Cytoarchitectonic analysis of the human extrastriate cortex in the region of V5/MT+: a probabilistic, stereotaxic map of area hOc5. Cereb. Cortex 17, 562–74. doi:10.1093/cercor/bhj181

Marques, J.P., Kober, T., Krueger, G., van der Zwaag, W., Van de Moortele, P.F., Gruetter, R., 2010. MP2RAGE, a self bias-field corrected sequence for improved segmentation and T-1-mapping at high field. Neuroimage 49, 1271–1281. doi:Doi 10.1016/J.Neuroimage.2009.10.002

Mazzola, L., Lopez, C., Faillenot, I., Chouchou, F., Mauguiere, F., Isnard, J., 2014. Vestibular responses to direct stimulation of the human insular cortex. Ann Neurol. doi:10.1002/ana.24252

Miller, W.L., Maffei, V., Bosco, G., Iosa, M., Zago, M., Macaluso, E., Lacquaniti, F., 2008. Vestibular nuclei and cerebellum put visual gravitational motion in context. J. Neurophysiol. 99, 1969–1982. doi:10.1152/jn.00889.2007

Morosan, P., Rademacher, J., Schleicher, A., Amunts, K., Schormann, T., Zilles, K., 2001. Human primary auditory cortex: cytoarchitectonic subdivisions and mapping into a spatial reference system. Neuroimage 13, 684–701. doi:10.1006/nimg.2000.0715

Noppeney, U., Friston, K.J., Price, C.J., 2003. Effects of visual deprivation on the organization of the semantic system. Brain 126, 1620–7. doi:10.1093/brain/awg152

Pavard, B., Berthoz, A., 1977. Linear acceleration modifies the perceived velocity of a moving visual scene. Perception 6, 529–540.

Paxinos, G., 2012. The Human Nervous System. Elsevier Science.

Peeters, R.R., Rizzolatti, G., Orban, G.A., 2013. Functional properties of the left parietal tool use region. Neuroimage 78, 83–93. doi:10.1016/j.neuroimage.2013.04.023

Riecke, B.E., Väljamäe, A., Schulte-Pelkum, J., 2009. Moving sounds enhance the visually-induced self-motion illusion (circular vection) in virtual reality. ACM Trans. Appl. Percept. 6, 1–27. doi:10.1145/1498700.1498701

Robinson, C.J., Burton, H., 1980a. Somatic submodality distribution within the second somatosensory (SII), 7b, retroinsular, postauditory, and granular insular cortical areas of M. fascicularis. J Comp Neurol 192, 93–108. doi:10.1002/cne.901920106

Robinson, C.J., Burton, H., 1980b. Organization of somatosensory receptive fields in cortical areas 7b, retroinsula, postauditory and granular insula of M. fascicularis. J Comp Neurol 192, 69–92. doi:10.1002/cne.901920105

Saenz, M., Lewis, L.B., Huth, A.G., Fine, I., Koch, C., 2008. Visual Motion Area MT+/V5 Responds to Auditory Motion in Human Sight-Recovery Subjects. J Neurosci 28, 5141–5148. doi:10.1523/JNEUROSCI.0803-08.2008 28/20/5141 [pii]

Saenz, M., Lewis, L.B., Huth, A.G., Fine, I., Koch, C., 2008. Visual Motion Area MT+/V5 Responds to Auditory Motion in Human Sight-Recovery Subjects. J. Neurosci. 28, 5141–8. doi:10.1523/JNEUROSCI.0803-08.2008

Salomon, R., Darulova, J., Narsude, M., van der Zwaag, W., 2014. Comparison of an 8-channel and a 32-channel coil for high-resolution FMRI at 7 T. Brain Topogr. 27, 209–12. doi:10.1007/s10548-013-0298-6

Shinder, M.E., Newlands, S.D., 2014. Sensory convergence in the parieto-insular vestibular cortex. J. Neurophysiol. 111, 2445–64. doi:10.1152/jn.00731.2013

Smith, A.T., Wall, M.B., Thilo, K. V., 2012. Vestibular inputs to human motion-sensitive visual cortex. Cereb. Cortex 22, 1068–1077. doi:10.1093/cercor/bhr179

Stephan, T., Deutschländer, A., Nolte, A., Schneider, E., Wiesmann, M., Brandt, T., Dieterich, M., 2005. Functional MRI of galvanic vestibular stimulation with alternating currents at different frequencies. Neuroimage 26, 721–732.

Takahashi, K., Gu, Y., May, P.J., Newlands, S.D., DeAngelis, G.C., Angelaki, D.E., 2007. Multimodal coding of three-dimensional rotation and translation in area MSTd: comparison of visual and vestibular selectivity. J Neurosci 27, 9742–9756. doi:10.1523/JNEUROSCI.0817-07.2007

Tootell, R.B., Tootell, R.B., Reppas, J.B., Reppas, J.B., Dale, a M., Dale, a M., Look, R.B., Look, R.B., Sereno, M.I., Sereno, M.I., Malach, R., Malach, R., Brady, T.J., Brady, T.J., Rosen, B.R., Rosen, B.R., 1995. Visual motion aftereffect in human cortical area MT revealed by functional magnetic resonance imaging. Nature. doi:10.1038/375139a0

Triarhou, L., 2013. The cytoarchitectonic map of Constantin von Economo and Georg N. Koskinas., in: Geyer, S., Turner, R. (Eds.), Microstructural Parcellation of the Humand Cerebral Cortex. Springer-Verlag Berlin Heidelberg, pp. 33–53. doi:10.1007/978-3-642-37824-9_2

Trutoiu, L.C., Mohler, B.J., Schulte-Pelkum, J., Bülthoff, H.H., 2009. Circular, linear, and curvilinear vection in a large-screen virtual environment with floor projection. Comput. Graph. 33, 47–58. doi:10.1016/j.cag.2008.11.008

Trutoiu, L.C., Streuber, S., Mohler, B.J., Schulte-Pelkum, J., Bülthoff, H.H., 2008. Tricking people into feeling like they are moving when they are not paying attention. Perception 1, 59593. doi:10.1145/1394281.1394319

Ulloa, E.R., Pineda, J.A., 2007. Recognition of point-light biological motion: mu rhythms and mirror neuron activity. Behav Brain Res 183, 188–194.

Van der Zwaag, W., Francis, S., Head, K., Peters, A., Gowland, P., Morris, P., Bowtell, R., 2009. fMRI at 1.5, 3 and 7 T: Characterising BOLD signal changes. Neuroimage 47, 1425–1434. doi:10.1016/j.neuroimage.2009.05.015

Von Economo, C. von, 2009. Cellular Structure of the Human Cerebral Cortex. Karger Medical and Scientific Publishers.

VonEconomo, C., Koskinas, G., 2008. Atlas of Cytoarchitectonics of the Adult Human Cerebral Cortex. Karger, Basel.

Waespe, W., Henn, V., n.d. Neuronal activity in the vestibular nuclei of the alert monkey during vestibular and optokinetic stimulation. Exp Brain Res 27, 523–38.

Wang, Z., Chen, M., Gong, X., Huang, W., Xu, L., Zhou, C., 2008. Why cold water delays the onset of vestibular vertigo--an functional MRI study. Eur. J. Radiol. 67, 459–65. doi:10.1016/j.ejrad.2007.08.021

Wilms, M., Eickhoff, S.B., Specht, K., Amunts, K., Shah, N.J., Malikovic, A., Fink, G.R., 2005. Human V5/MT+: Comparison of functional and cytoarchitectonic data. Anat. Embryol. (Berl). 210, 485–495. doi:10.1007/s00429-005-0064-y

Zeki, S., Shipp, S., Hajnal, J. V, Watson, J.D., Woods, R.P., Myers, R., Frackowiak, R.S., Mazziotta, J.C., 1993. Area V5 of the human brain: evidence from a combined study using positron emission tomography and magnetic resonance imaging. Cereb Cortex 3, 79–94.

Zilles, K., 2004. Architecture of the human cerebral cortex, in: Paxinos, G., Mai, J.K. (Eds.), The Human Nervous System. Academic Press, p. 1366.

Zilles, K., Palomero-Gallagher, N., Amunts, K., 2015. Cytoarchitecture and maps of the cerebral cortex, in: Toga, A. (Ed.), Brain Mapping an Encyclopedic Reference. pp. 115–135.

zu Eulenburg, P., Baumgartner, U., Treede, R.D., Dieterich, M., 2013. Interoceptive and multimodal functions of the operculo-insular cortex: tactile, nociceptive and vestibular representations. Neuroimage 83, 75–86. doi:10.1016/j.neuroimage.2013.06.057

Zu Eulenburg, P., Baumgärtner, U., Treede, R.D., Dieterich, M., 2013. Interoceptive and multimodal functions of the operculo-insular cortex: Tactile, nociceptive and vestibular representations. Neuroimage 83, 75–86. doi:10.1016/j.neuroimage.2013.06.057

zu Eulenburg, P., Caspers, S., Roski, C., Eickhoff, S.B., 2012. Meta-analytical definition and functional connectivity of the human vestibular cortex. Neuroimage 60, 162–169. doi:10.1016/j.neuroimage.2011.12.032

Zu Eulenburg, P., Caspers, S., Roski, C., Eickhoff, S.B., 2012. Meta-analytical definition and functional connectivity of the human vestibular cortex. Neuroimage 60, 162–169. doi:10.1016/j.neuroimage.2011.12.032

Chapter 3 Visuo-tactile integration during the Rubber Hand Illusion is modulated by optokinetic stimulation

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Abstract

Previous studies have shown that the body representation can be flexibly updated through a process of multisensory integration. For instance, rubber fake hands are felt as a part of the real body when stroked in visuo-tactile synchrony. However, the importance of vestibular information for the body representation is less well understood. In this study, we investigated whether vestibular stimulation, as induced by optic flow, can influence the multisensory integration of information about one's body. We used the Rubber Hand Illusion (RHI) as a classical paradigm to study multisensory processing. Importantly, we manipulated the visual context in which the illusion was presented, by superimposing the rubber hand on a coherent linear starfield inducing upward or downward vection. We found that vection selectively modulated the proprioceptive drift induced by the visuo-tactile conflict, but not the subjective ratings regarding felt ownership over the hand. When the rubber hand and the real hand were stroked in synchrony, subjects tended to locate the position of their hand as higher than their actual hand position when the rubber hand was superimposed on downward flow inducing upward vection. This finding illustrates how visuo-vestibular signals are fundamental components of the embodied self-representation.

Highlights

3-5 bullet points maximum 85 characters including spaces

- Proprioceptive drift towards the rubber hand can be modulated by vection.
- Self-location depends on the integration of visual motion and tactile cues.
- Feelings of ownership are not modulated by vection.

Keywords

Vection; Optic flow; Touch; Multisensory integration; proprioceptive drift; Bodily self-consciousness; Visuo-vestibular interactions; Bodily illusions; Rubber hand illusion

1. Introduction

Patients with asomatognosia may be characterized by a loss of awareness of specific body parts or body sites. Such conditions are usually associated with right parietal damage, right premotor or primary motor cortex stroke and typically the contralesional hemi-body is affected (Arzy, Overney et al. 2006). For instance, in a case report, a 51 years old woman was affected by a temporary loss of awareness of her left hand and forearm, while she could see through the table at the 'missing' limb location. As the example of the woman illustrates, damage to brain areas involved in the integration of multisensory information can result in changes in the body representation. In healthy humans, over the last decades many studies have shown that similar experiences of changed body awareness can be experimentally manipulated, for instance by inducing the illusory ownership of a body part or of a full body through congruent visuo-tactile stimulation (Botvinick and Cohen 1998, Lenggenhager, Tadi et al. 2007). In the rubber hand illusion (RHI), the subject gazes at a fake rubber hand while the real hand is out of view. When both the rubber hand and the real hand are stroked in synchrony, the rubber hand is experienced as one's own, which is reflected in a proprioceptive drift towards the location of the fake hand (i.e. a mislocalization of one's hand position in the direction of the fake had) and in subjective feelings of ownership (i.e. seeing the fake hand as a real part of one's body, cf. (Botvinick and Cohen 1998, Ehrsson, Holmes et al. 2005, Tsakiris and Haggard 2005, Ehrsson, Wiech et al. 2007, Moseley, Olthof et al. 2008, Kammers, de Vignemont et al. 2009, Barnsley, McAuley et al. 2011). The RHI likely results from the automatic integration of visual and tactile cues that can selectively overrule proprioceptive information regarding the position of one's real hand.

Whereas most studies have used visuo-tactile conflicts to induce illusory body ownership, recent studies underline the importance of vestibular information for the body representation. For instance, using galvanic stimulation, it has been shown that the strength of the RHI was enhanced, likely due to an enhanced visual capture of the rubber hand related to the vestibular activation (Lopez, Lenggenhager et al. 2010). Other studies also highlighted the importance of vestibular stimulation for the body representation, by showing effects of vestibular stimulation on an own body transformation task (Lenggenhager, Lopez et al. 2008, Lopez, Halje et al. 2008). In addition, caloric vestibular stimulation has been shown to modulate the experience of phantom limbs in amputees and paraplegic patients (Andre, Martinet et al. 2001, Le Chapelain, Beis et al. 2001) and, in healthy humans, vestibular stimulation can impair hand pointing tasks and reproduction of arm positions (Bresciani, Blouin et al. 2002, Mars, Archambault et al. 2003, Knox, Coppieters et al. 2006). The experienced self-location and the first person perspective could be selectively modulated by visuo-vestibular conflicts, thereby underlining the importance of vestibular processing for the global body representation (Ionta, Heydrich et al. 2011, Ferre, Bottini et al. 2013, Ferre, Day et al. 2013, Ferre, Vagnoni et al. 2013, Pfeiffer, Serino et al. 2014).

Optic flow and vestibular signals are integrated in common brain areas in humans as shown by fMRI studies, mainly in perisylvian areas . Furthermore, behavioral studies indicate that visual motion inducing vection (i.e. illusory self-motion) and vestibular signals compete to encode body motion and that these signals are weighted in a Bayesian-optimal fashion according to their respective reliability (Fetsch, Pouget et al. 2011). Moreover, the so-called vestibular cortices are known to overlap with areas generally involved in multisensory integration, mainly at the temporo-parietal junction and lesions in this area have been associated with visuo-vestibular disturbances of body scheme integrity (e.g. as during an out-of-body experience; cf. (Blanke, Ortigue et al. 2002, Blanke and Mohr 2005, Lopez and Blanke 2011, Lopez, Blanke et al. 2012).

A key characteristic of illusory motion percepts induced through full body rotation (e.g. Prsa et al., 2012; van Elk et al., 2012) or indirectly through optic flow (Brandt and Dichgans 1972, Berthoz, Pavard et al. 1975, Trutoiu LC 2009) is the direction-specific information that is conveyed through vestibular and optokinetic signals (i.e. signalling a yaw, pitch or roll rotation in a clock- or a counter-clockwise direction). The vestibular nerve discharges in response to utricle and saccule (linear motion) or semi-circular canals stimulation (circular motion), occurring during acceleration phases. But at a constant speed, the vestibular system is at rest and the optic flow delivered to the visual system is the only remaining cue allowing the subject to feel his own body in motion, as it happens in daily life in cars and public transports. Interestingly, the same visual stimuli used in fMRI experiments on visuo-vestibular convergence - coherent expanding or contracting visual motion - can be also used to induce vection, under certain circumstances. It constitutes an easy access to systematically manipulate self-location in laboratory conditions, in the absence of real body displacement. It is a perceptual phenomenon commonly experienced in daily life, gazing at the sky and the clouds moving, at water moving in the river stream, or waiting in a train while seeing the train besides starting in opposite direction. Vection has been extensively reported in visual psychophysics literature starting from Mach (Mach 1875, Berthoz, Pavard et al. 1975, Dichgans 1978, Trutoiu, Mohler et al. 2009). Bodily self-motion is felt by the subject in the direction opposite to the optic flow but on the same axis; it also leads to postural readjustments (Lestienne, Soechting et al. 1977).. Contracting or expanding optic flows have been shown to induce a subjective linear vection feeling in the opposite direction than the flow, as described before (Trutoiu, Mohler et al. 2009). Linear upward flow induces downward vection for instance, and reciprocally. The “self-other” dilemma to solve for the brain is to rely on a egocentric or an allocentric spatial referential to decide about our own self-motion: “Is the surrounding environment moving or am I moving?”.

Whereas other studies have shown a general and non-specific effect of visual and vestibular stimulation on body ownership (Lopez, Lenggenhager et al. 2010, Ionta, Heydrich et al. 2011), we exploited the fact that visuo-vestibular information induced through optic flow is *direction-specific* and may thereby modulate proprioception in a direction-specific fashion. More specifically, we investigated whether upward or downward vection would modulate the proprioceptive drift toward a fake body part, i.e. thereby enhancing the mislocalization of one’s real body parts in the direction of the fake body part. To this end we used a classical RHI paradigm and we measured the proprioceptive location of one’s arm along a vertical axis (Bekrater-Bodmann, Foell et al. 2012).

In this study, a fake right hand has been displayed to healthy subjects and stroked synchronously or asynchronously with respect to the real right hand. Importantly, the fake hand was superimposed on a 3D optic flow stimulus, inducing upward or downward vection, and the real hand was hidden below the screen.

Following the induction phase, participants were required to indicate the felt position of their real hand by pointing along a vertical axis perpendicular to the rubber hand with their left hand and answered a questionnaire about their sensations after each condition tested. In this way, it could be investigated if upward or downward vection as induced through optic flow can modulate the effects of visuo-tactile synchrony on illusory hand ownership and hand location. The classical RHI manipulates two cues (vision and touch); our study presupposes the existence of an additive effect of a third cue (vection induced by optokinetic stimuli or 'optic flows') that could further modulate the RHI. We predicted that the classical RHI effect driven by visuo-tactile integration (i.e. drift towards the rubber hand and identification with the rubber hand during synchronous stroking) would be modulated selectively by the direction of the vection (i.e. stronger drift towards the rubber hand if the flow direction implies upward vection towards the rubber hand compared to downward vection). In addition, we investigated to what extent the modulatory effect of optic flow direction on visuo-tactile synchrony further influenced subjective feelings of ownership over the fake hand.

2. Material and Methods

2.1. Participants

A total of 15 healthy volunteers took part in our experiment (6 females, 9 males), ranging in age from 21 to 36 years (mean age = 28.8 years). All had normal or corrected-to-normal vision and fully completed the entire experiment. Participants were paid for their participation, which lasted 1.5 hours. All participants gave their informed consent to take part in this study, which was approved by the local ethics committee in conformity to the Declaration of Helsinki.

2.2. General procedure

The experimental setup is presented in Figure 1 and 2. Participants were seated on a chair and a 3D screen was placed horizontally in front of the subject. During the experiment we exposed subjects to linear vection induced by a stimulus simulating white moving dots on a black background with coherent motion (an optic flow starfield). The simulated motion consisted of radial expansion or contraction inducing feelings of upward or downward.

A fake rubber hand with skin colour imitation, dimensions 23.5cm x 13 cm x 4.5 cm, was superimposed on the vection display 15 cm higher than the real hand (see Figure 1). The subject could see a right rubber hand whose medium finger basis was positioned at the centre of the optic flow. At the same time, the right hand of the subject was hidden under the screen, staying at rest on a foam platform. The experimenter was seated on the opposite side with respect to the subject's position and from this position he was able to stroke the right hand of the subject and the rubber hand synchronously or asynchronously.

Hand stroking and the onset of the vection display occurred at the same time and lasted for 60 seconds for each individual condition. In different conditions, subjects were exposed to 2 stroking modalities (synchronous with respect to the visual feedback or asynchronous) and 3 optic flow directional modalities on a cranio-caudal axis (contracting – downward flow; expanding – upward flow; random flow without coherent motion in a direction). Random flow does not induce any vection feeling; we used it as a control condition as it should not modulate the visuo-tactile conflict of the classical RHI. In sum, the full factorial design that was used in the present study consisted of the factors Flow (upwards, downwards, random) and Visuo-tactile synchrony (Synchronous, Asynchronous).

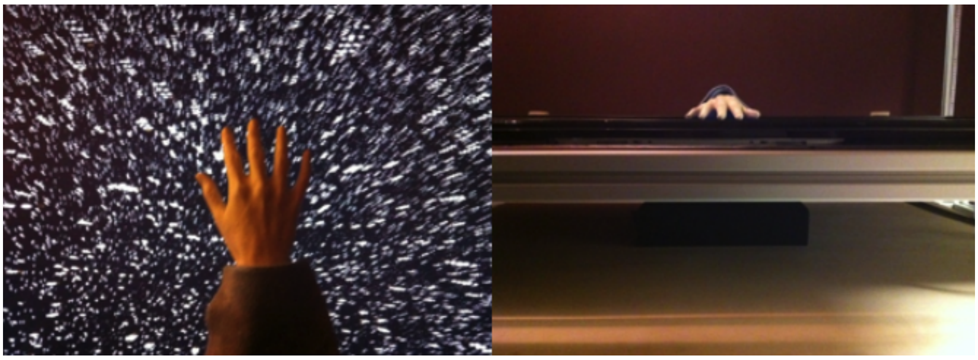

Figure 1. Visual display: optic flow and the rubber hand superimposed on the display as seen from above (left panel) and from the experimenter's point of view (right).

2.3. Visual display and optic flow stimulation

A High Definition Stereo Samsung 3-D screen was used measuring 63 x 111 cm at which stimuli could be presented with a resolution of 1920x1080, resulting in approximately 120 degrees of horizontal and 80 degrees of vertical visual angle. The optic flow was displayed with expyVR, a custom-laboratory made software package for 3-D experimental stimulus presentation. It consisted of white dots on a black background, moving with a constant velocity for upward and downward flow, and identical dots density across all conditions. It is important to note that no absolute velocity of the moving dots can be reported, as the movement is perceived within a virtual space with relative units, thereby making the perceived movement highly dependent on the scaling of the 3D parameters. The velocity parameter of the optic flow within ExpyVR was set up as a fixed value of 20 cm/sec and 60 dots/m2. Nevertheless, the movement was always identical across conditions and chosen to induce vection as verified empirically in pilot studies. Optimal parameters to induce vection are: a high velocity, high spatial frequency, and wide optic field stimulation including peripheral fields of view (Brandt, Dichgans et al. 1972, Berthoz, Pavard et al. 1975, Chu 1976, Straube and Brandt 1987, Deutschlander, Bense et al. 2004, Trutoiu LC 2009). The experiment was conducted in the dark except the luminance due to the screen to remove stable cues that may decrease the vection effect.

2.4. Behavioral measures: questionnaires and drift measures

The subjects completed both subjective ownership ratings (questionnaires) and objective (drift) measures. The following questionnaires were included: Likert questionnaires on a 7 degrees scale from -3 to 3 (illusion score, and control score) to assess the rubber hand illusion and vection scores to assess the vection feelings (see Table 1), inspired by previous studies (Botvinick and Cohen 1998, Trutoiu LC 2009).

Q1 It seemed as if I were feeling the touch at the location where I saw the rubber hand touched.

Q2 It seemed as though the touch I felt was caused by the finger touching the rubber hand.

Q3 I felt as if the rubber hand were my hand.

Q4 The rubber hand began to resemble my own (real) hand, in terms of shape, skin tone, freckles or some other visual feature.

Q5 It seemed as if the touch I was feeling came from somewhere between my own hand and the rubber hand.

Q6 It felt as if my (real) hand were turning 'rubbery'.

Q7 I felt as if I were travelling in the virtual space.

Table 1. Questionnaires: 7 questions related to the Rubber Hand Illusion score (Q1-Q3), control questions for the RHI (Q4 – Q6) and a question about the experience of vection (Q7).

The proprioceptive drift is used to measure changes in hand location during the RHI and this measure was collected both before and after each condition. To this end the participant was required to indicate with the left hand on a vertical axis the perceived height of their right hand (see Figure 2). The two measures were registered for each condition and pre and post illusion measurements were used as a factor in the analysis. The rationale for including a pre- and a post-illusion measurement of the drift was to control for the potential confound that individual differences in the ability to perceive the location of the hand may have partly confounded our effects of interest.

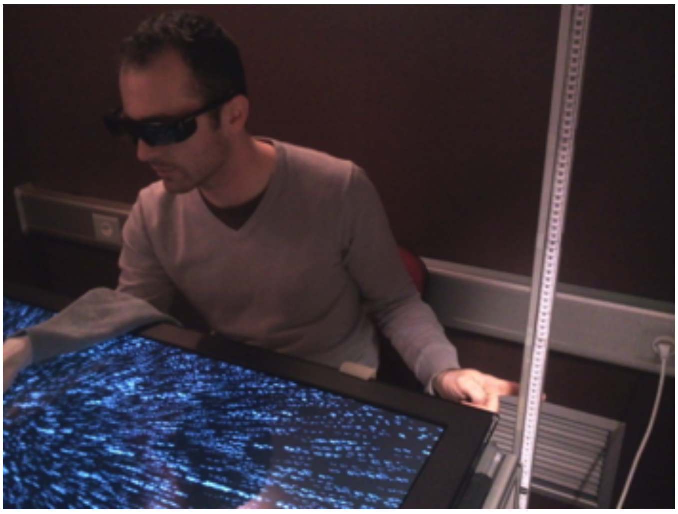

Figure 2. Proprioceptive drift measure: the participant indicates on the ruler with the left index finger the estimated height of his right hand, while keeping his eyes closed. The proprioceptive drift measure was administered both before and after 60 seconds of immersion with visuo-tactile stroking and 3D optic flow.

3. Results

3.1. Vection score

The vection scores confirmed that subjects associated the perception of downward and upward vection respectively with upward and downward flow and are represented in Figure 2. For the question, "I feel moving downward (range -3 to 0) or upward (range 0 to 3), we observed a main effect of flow $F(1,14)= 20$, $\eta^2=0.59$, $p<0.001$, confirming that subjects experienced vection in the opposite direction of optic flow direction. Random motion was not associated with consistent vection. Vection feeling was not modulated as a function of synchrony, as we did not observe interaction between flow and synchrony (*F*(1,14)=0.52, *p*=0.6*)* and no main effect of synchrony (*F*(1,14)=3.52, *p* = 0.08).

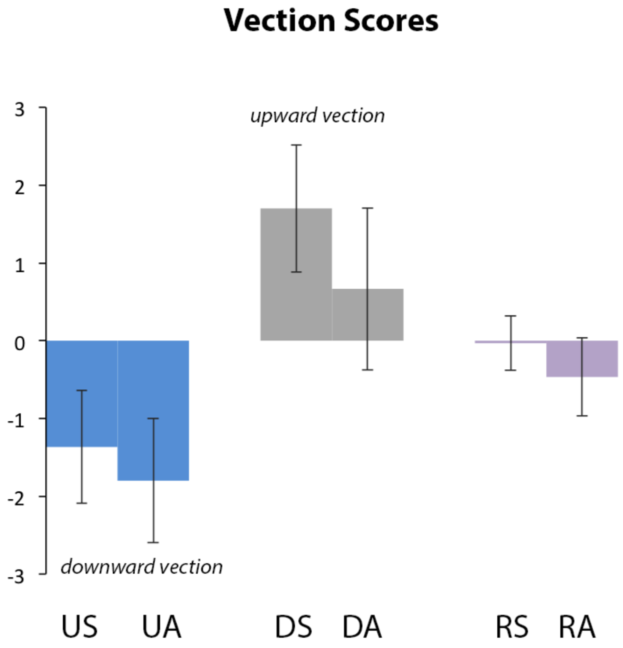

Figure 3. Vection scores. Negative scores reflect perceived downward vection and positive scores reflect upward vection. A score of zero indexes that no vection was perceived. US =upward flow synchronous visuo-tactile stimulation (VTS), UA = upward flow asynchronous VTS, DS = downward flow synchronous VTS, DA = downward flow asynchronous VTS, RS = random flow synchronous VTS, RA = random flow asynchronous VTS. Errors bars represent the standard deviation of the mean.

3.2. Proprioceptive drift

The relative difference in proprioceptive drift between the pre- and the post-session is represented in Figure 3. For the proprioceptive drift measures a main effect of Synchrony was observed $F(1,14)=8.62$, $\eta^2=0.38$, $p<0.05$, observed power = 0.78) but the main effect of flow was not significant ($F < 1$). A main effect of the hand estimation location parameter was also observed $F(1,14)=10.2$, $\eta^2=0.42$,$p<0.01$, observed power = 0.84 meaning that in general, participants estimated with a systematic bias the location of their real hand too high along the vertical axis (i.e. perceiving the position of their real hand to be higher than it actually was).

A main effect of synchrony on hand location estimation was observed, $F(1,14)=7.49$, $\eta^2=0.35$,$p<0.05$, observed power = 0.72, but the effect of optic flow on hand location estimation was not significant, $F(1,14)=2.48$, $\eta^2=0.35$,$p=0.1$, observed power = 0.46,.

A significant interaction between Synchrony and Hand Location Estimation was observed $F(1,14)=7.49$, $\eta^2=0.35$, $p<0.05$, observed power = 0.72, reflecting that participants tended to localise their hand higher (i.e. closer to the rubber hand) in the synchronous condition (*differences of means after-before*=2.99cm, *sd(before)*=1.2, *sd(after)*=1.21) than in the asynchronous condition (*differences of means after-before*=0.5cm, *sd(before)*=1.11, *sd(after)*=1.25).

Optic flow also selectively modulated the proprioceptive drift (errors in localization of position of the real hand) induced by the visuo-tactile conflict. The 15 participants located the position of their right hand higher than their real hand position on the vertical axis when they were exposed to downward flow inducing upward vection but only when the real and the rubber hands were stroked synchronously. This effect was reflected by a significant interaction between Flow, Synchrony and Hand Location Estimation, $F(1,14)=7.24$, $\eta^2=0.34$, $p<0.01$, observed power = 0.89. Post-hoc analyses showed that the drift significantly increased for synchronous stroking and downward flow visual stimulation (*mean drift*, i.e. difference between pre-experimental and post-experimental estimation = 5.4 cm, *sd*=3.83, *t*(14)=5.46, *p*<0.001), but not in the asynchronous condition and downward visual flow (*mean drift* = 0.27cm, *sd=2.98* t(14)=0.35, n.s.). In the upward flow condition, a trend for an increased drift measure after congruous visuo-tactile stimulation (i.e. synchronous) was observed (*mean drift* =1.73cm, *sd*=3.13, *t*(14)=2.15, *p*=0.05). No significant differences were observed in in the upward flow – asynchronous stroking condition (*mean drift* =1.13cm, *sd=2.8* t(14)=1.57, n.s. *p=0.14*). In the random condition, no significant differences were observed both for the synchronous condition (*mean drift* =1.83cm, *sd=4.9* t(14)=1.45, n.s.) and the asynchronous condition (*mean drift* =0.1cm, *sd=3.8* t(14)=0.1, n.s.).

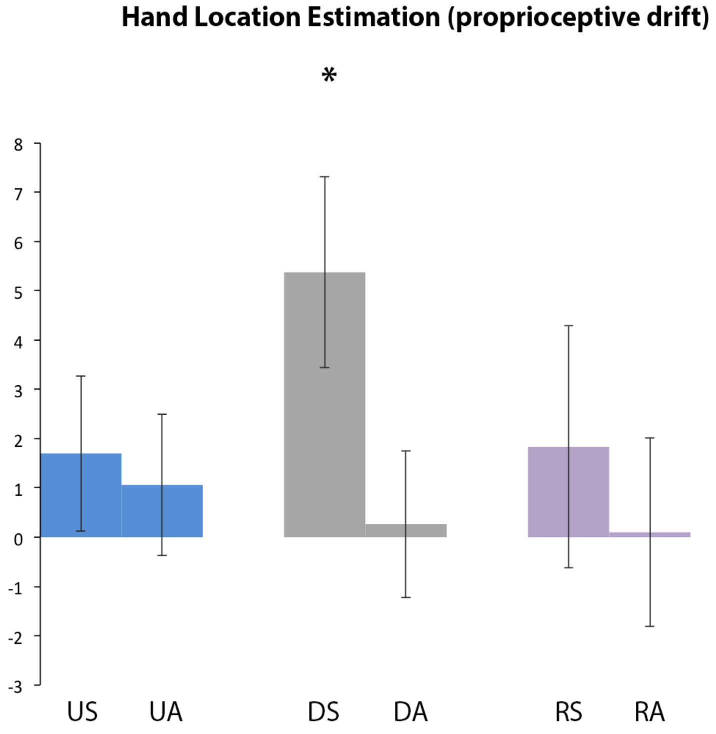

Figure 3. Relative proprioceptive drift (estimation of hand position after the induction phase – estimation of hand position before the induction phase). Positive values reflect an increased drift towards the rubber hand following the induction phase. US =upward flow synchronous visuo-tactile stimulation (VTS), UA = upward flow asynchronous VTS, DS = downward flow synchronous VTS, DA = downward flow asynchronous VTS, RS = random flow synchronous VTS, RA = random flow asynchronous VTS. Errors bars represent the standard deviation of the mean.

3.3. Illusion scores (touch and hand ownership)

Subjective feelings of body ownership were highly dependent on synchrony, as reflected in a main effect of synchrony for the illusion versus control score: $F(1,14)=100.45$, $\eta^2=0.88$, $p<0.001$, observed power=1 (see Figure 4). We also observed a main effect of illusion versus control scores $F(1,14)=38.55$, $\eta^2=0.73$, $p<0.001$, observed power=1 and a significant interaction between synchrony and scores

F(1,14)=73.23, η^2=0.84, *p*<0.001, observed power=1 but no main effect of flow *F*(1,14)=0.3, *p=0.74*. No significant interactions with Flow were observed, indicating that feelings of ownership were not modulated as a function of flow. The score and synchrony significant interaction corresponds to a strong difference between Illusion and Control scores for the synchronous conditions between *mean score illusion* =1.78, *sd=1.17* and *mean score control* =-1.3, *sd=1.48 (*t(44)=13.3, p<0.0001) but not for the asynchronous conditions *mean score illusion* =-1.43, *sd=1.47* and *mean score control* =-1.7, *sd=1.28* (t(14)=1.11, n.s.).

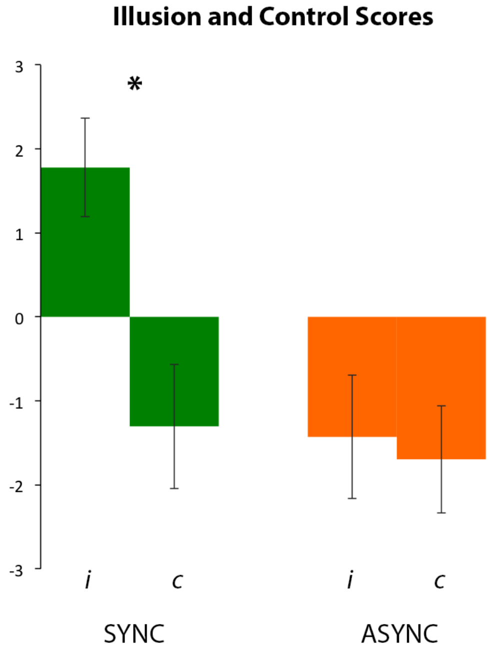

Figure 4. Illusion scores for the different experimental conditions, on a Likert scale from -3 to 3. SYNC= synchronous visuo-tactile stimulation; ASYNC= asynchronous visuo-tactile stimulation. *i* = illusion score (i.e. composite of 'ownership questions'); *c* = control score (i.e. composite measure of 'control questions'). Positive values reflect a strong illusory feeling of ownership and negative values reflect a reduced feeling of ownership for the rubber hand. Errors bars represent the standard deviation of the mean.

4. Discussion

Using a combination of two classical paradigms from modern cognitive psychology and psychophysics, we investigated the effects of optic flow on the induction of the rubber hand illusion. In our paradigm we reproduced the rubber hand illusion when drift was measured along a vertical axis. At the same time the rubber hand was superimposed on a pattern of visually induced upwards or downwards vection. It was found that optic flow and induced vection could modulate visuo-tactile integration. Inducing upwards vection (i.e. the subjective feeling of moving upwards with respect to our actual location) increased the proprioceptive drift towards the rubber hand, but only when the rubber hand was stroked in visuo-tactile synchrony with respect to the rubber hand. No significant drift was observed when the rubber hand was superimposed on downward vection or on a random motion pattern. Our study suggests that the brain readily integrates information from different sensory cues to provide an estimate of one's current body position. Vestibular signals can influence visuo-tactile integration (Lopez et al., 2009), and we suggest in our study that a multiplicity of sensory cues (i.e. tactile, visual and vestibular) biased the proprioceptive perception of one's body.

At a neural level, electrophysiological studies have previously shown in monkeys the existence of neurons responding to visual, tactile and vestibular stimulations, e.g. in the parieto-insular vestibular cortex (Grusser, Pause et al. 1990), the ventral intraparietal area (Bremmer, Klam et al. 2002) , and the somatosensory cortex (Schwarz and Fredrickson 1971, Schwarz, Fredrickson et al. 1973).

Interestingly, some authors investigating the neural correlates of the embodiment of a rubber hand showed that sensation of body ownership of the fake hand was correlated to brain activity in the posterior insula (Tsakiris, Hesse et al. 2007) and in the supramarginal gyrus, in the posterior aspect of lateral fissure, at the surface of inferior parietal lobule (Gentile, Petkova et al. 2010). Posterior insula is considered a core region of the vestibular cortex (Mazzola, Lopez et al. 2014) - and the putative human homologue of PIVC or 'parieto-insular-vestibular cortex' signals (Lopez and Blanke 2011, Lopez, Blanke et al. 2012), known to be a multimodal area integrating visual optokinetic and vestibular signals (Cardin and Smith 2010) and even somatosensory signals (zu Eulenburg, Baumgartner et al. 2013). The supramarginal cortex seems even more systematically involved in visuo-vestibular conjunctions according to recent experiments that mapped activations due to optokinetic stimulation and vestibular signals delivered through galvanic and caloric stimulation (Frank, Baumann et al. 2014). We speculate that the selective effect of vection on the RHI as observed in the present study might be also mediated by another core of motion-sensitive areas including the anterior part of hMST or hMSTd and posterior regions of medial temporal gyrus containing visuo-tactile polysensory cortices within the vestibular networks (Cardin and Smith 2010, Smith, Wall et al. 2011, Lopez, Blanke et al. 2012, Lopez, Schreyer et al. 2012, zu Eulenburg, Caspers et al. 2012). Amongst multisensory cortices known to process together vestibular, tactile, proprioceptive and optokinetic stimuli, the depth of parietal operculum (OP1-OP2) and the inferior parietal lobule (retroinsular cortex and temporo parietal junction along supramarginal gyrus) seem to be good candidates where embodiment of an external limb by visuo-tactile conflict could be reinforced by congruent optokinetic stimulus.

Interestingly, irrespective of the effects of optic flow – the subjective feelings of ownership were high in all synchronous conditions. In the present study, optic flow selectively modulated the proprioceptive drift (errors in hand localization) induced by the visuo-tactile conflict but it did not influence feelings of ownership. Thus the optokinetic stimulation seems to interact with visuo-tactile integration only at a pre-reflective level involving the proprioceptive localization of one's body parts. The dissociation between the drift measure and the feeling of ownership may indicate that exists a certain 'margin of tolerance' or 'lack of precision' with respect to bodily self-consciousness. For instance, previous studies have shown that participants automatically adjust their movements when confronted with perceptual distortions, without becoming aware of the fact they actually do (Fourneret and Jeannerod 1998, Kannape, Schwabe et al. 2010). Similarly, the optic flow could modulate the implicit perception of the location of one's hand (i.e. as measured with the proprioceptive drift) but not further enhance subjective feelings of ownership.

The effect of vection on visuo-tactile integration could also be related a size-related illusion: a hand closer to the subject is more likely to be embedded and recognize as its own hand (Moseley, Gallace et al. 2012). In fact, when one's experiences upward vection, the rubber hand may seem to be its own hand, giving the visual impression of being larger, thus enhancing the mechanisms of body ownership; in fact, it has been shown in the case of bigger rubber hands that the size of the fake hand affects the proprioceptive drift but not the subjective scores (Pavani and Zampini 2007). Further investigations would be needed to investigate whether changes in perceived body part size may solely explain the effects observed in our study (Haggard and Jundi 2009, Heed, Grundler et al. 2011) or if the dynamic aspect of the optokinetic stimulus and induced vection illusion plays a role.

The proprioceptive drift may index different neural phenomena than directly reflecting a disturbance in the estimation of self-location and this measure may in some cases be dissociated from illusion scores focusing on body ownership of a limb part. Authors who failed to replicate the proprioceptive drift as a dependent variable of visuo-tactile synchrony have proposed such an alternative view on the proprioceptive drift. In fact, proprioceptive drift has been challenged and described as an objective measure still ontologically highly variable (Holmes 2007, de Vignemont 2011). For instance, weak illusory scores have been found in association with strong drifts measures (Holmes, Snijders et al. 2006) while strong illusory scores were correlated with weak drifts only (Holmes 2007). Drift and questionnaires could be differentially affected by other factors, and similarly to our findings, drift in itself is never consciously experienced in the classical paradigm setup (Botvinick and Cohen 1998, Pavani, Spence et al. 2000, Ehrsson, Holmes et al. 2005). For instance, Haans and colleagues (Haans, Ijsselsteijn et al. 2008) also have shown that modifying the shape and texture of the rubber hand, could modulate subjective ratings but not the proprioceptive drift. Recently, another study emphasised the fact that higher-order cognitive factors affect subjective but not proprioceptive aspects of self-representation and that proprioceptive localization of the limbs obey a pure bottom-up process resistant to top-down effects (Dempsey-Jones and Kritikos 2014).

We may also notice that in all conditions (i.e. upward, downward or random optic flow information) a systematic bias towards the rubber hand was induced even with asynchronous stroking. The conscious information conveyed through vection may not alone override the strong visual signal induced by a rubber hand located closer to the eyes of the observer than the real (hidden) hand. It has been shown that visual dominance of observed body parts even in the absence of tactile stimulation can result in changes in the remapping of the body representation (van Elk, Forget et al. 2013). Similarly, another study found that subjects can experience embodiment of a rubber hand without tactile stimulation by just gazing at the rubber hand as assessed with both skin conductance and questionnaire measures (Ferri, Chiarelli et al. 2013).

In the present study we found that when the rubber hand was superimposed on random motion and when it was stroked in synchrony with the real hand no significant drift occurred as it usually occurs with a neutral visual background in the classical RHI experiment. We argue that random motion acts as a visual distractor conflicting with the effects of visuo-tactile synchrony on self-localization, but at a pre-attentional, unconscious step during the bottom-up processing of multisensory signals.

5. Conclusion

When the rubber hand and the real hand were stroked in synchrony, subjects tended to locate the position of their hand as higher than their real hand position when presented with downward flow inducing upward vection. Our results show that optokinetic signals inducing illusory-motion feelings can modulate visuo-tactile integration, thereby inducing changes in the localization of one's body parts.

It emphasises the concept that multimodal sensory signals may contribute to bodily self-consciousness in a bottom-up fashion, balanced and integrated at a pre-conscious level depending on their congruency, as shown by the dissociation of drift measures and subjective reports. Embodiment is probably not predominantly based on top-down predictions as advocated by recent works (Ferri, Chiarelli et al. 2013).

Conflict of interest

The authors have no conflict of interest to declare.

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References

Andre, J. M., Martinet, N., Paysant, J., Beis, J. M., & Le Chapelain, L. (2001). Temporary phantom limbs evoked by vestibular caloric stimulation in amputees. *Neuropsychiatry Neuropsychol Behav Neurol, 14*(3), 190-196.

Arzy, S., Overney, L. S., Landis, T., & Blanke, O. (2006). Neural mechanisms of embodiment: asomatognosia due to premotor cortex damage. *Arch Neurol, 63*(7), 1022-1025.

Barnsley, N., McAuley, J. H., Mohan, R., Dey, A., Thomas, P., & Moseley, G. L. (2011). The rubber hand illusion increases histamine reactivity in the real arm. *Curr Biol, 21*(23), R945-946. doi: S0960-9822(11)01200-0 [pii] 10.1016/j.cub.2011.10.039

Bekrater-Bodmann, R., Foell, J., Diers, M., & Flor, H. (2012). The perceptual and neuronal stability of the rubber hand illusion across contexts and over time. *Brain Res, 1452*, 130-139. doi: 10.1016/j.brainres.2012.03.001

Berthoz, A, Pavard, B, & Young, L R. (1975). Perception of linear horizontal self-motion induced by peripheral vision (linearvection) basic characteristics and visual-vestibular interactions. *Exp Brain Res, 23*(5), 471-489.

Berthoz, A., Pavard, B., & Young, L. R. (1975). Perception of linear horizontal self-motion induced by peripheral vision (linearvection) basic characteristics and visual-vestibular interactions. *Exp Brain Res, 23*(5), 471-489.

Blanke, O., & Mohr, C. (2005). Out-of-body experience, heautoscopy, and autoscopic hallucination of neurological origin Implications for neurocognitive mechanisms of corporeal awareness and self-consciousness. *Brain Res Brain Res Rev, 50*(1), 184-199.

Blanke, O., Ortigue, S., Landis, T., & Seeck, M. (2002). Stimulating illusory own-body perceptions. *Nature, 419*(6904), 269-270. doi: 10.1038/419269a

419269a [pii]

Botvinick, M, & Cohen, J. (1998). Rubber hands 'feel' touch that eyes see. *Nature, 391*(6669), 756. doi: 10.1038/35784

Botvinick, M., & Cohen, J. (1998). Rubber hands 'feel' touch that eyes see. *Nature, 391*(6669), 756-756.

Brandt, T., & Dichgans, J. (1972). [Circular vection, visually induced pseudocoriolis effects, optokinetic afernystagmus. A comparative study of subjective and objective optokinetic aftereffects]. *Albrecht Von Graefes Arch Klin Exp Ophthalmol, 184*(1), 42-57.

Brandt, T., Dichgans, J., & Koenig, E. (1972). Perception of self-rotation (circular vection) induced by optokinetic stimuli. *Pflugers Arch, 332*(Suppl), R98.

Bremmer, F., Klam, F., Duhamel, J. R., Ben Hamed, S., & Graf, W. (2002). Visual-vestibular interactive responses in the macaque ventral intraparietal area (VIP). *Eur J Neurosci, 16*(8), 1569-1586.

Bresciani, J. P., Blouin, J., Popov, K., Bourdin, C., Sarlegna, F., Vercher, J. L., & Gauthier, G. M. (2002). Galvanic vestibular stimulation in humans produces online arm movement deviations when reaching towards memorized visual targets. *Neurosci Lett, 318*(1), 34-38. doi: S0304394001024624 [pii]

Cardin, V., & Smith, A. T. (2010). Sensitivity of human visual and vestibular cortical regions to egomotion-compatible visual stimulation. *Cereb Cortex, 20*(8), 1964-1973. doi: bhp268 [pii] 10.1093/cercor/bhp268

Chu, W.H.N. (1976). *Dynamic response of human linear vection.* Cambridge MA: MIT.

de Vignemont, F. (2011). Embodiment, ownership and disownership. *Conscious Cogn, 20*(1), 82-93. doi: S1053-8100(10)00170-4 [pii] 10.1016/j.concog.2010.09.004

Dempsey-Jones, H., & Kritikos, A. (2014). Higher-order cognitive factors affect subjective but not proprioceptive aspects of self-representation in the rubber hand illusion. *Conscious Cogn, 26*, 74-89. doi: 10.1016/j.concog.2014.02.005

Deutschlander, A., Bense, S., Stephan, T., Schwaiger, M., Dieterich, M., & Brandt, T. (2004). Rollvection versus linearvection: comparison of brain activations in PET. *Hum Brain Mapp, 21*(3), 143-153. doi: 10.1002/hbm.10155

Dichgans, J, Brandt, T. (1978). Visual-vestibular interaction: Effects on self-motion perception and postural control. *Perception Handbook of Sensory Physiology, vol. VIII. Springer, New York*, 756-804.

Ehrsson, H. H., Holmes, N. P., & Passingham, R. E. (2005). Touching a rubber hand: feeling of body ownership is associated with activity in multisensory brain areas. *J Neurosci, 25*(45), 10564-10573. doi: 25/45/10564 [pii] 10.1523/JNEUROSCI.0800-05.2005

Ehrsson, H. H., Wiech, K., Weiskopf, N., Dolan, R. J., & Passingham, R. E. (2007). Threatening a rubber hand that you feel is yours elicits a cortical anxiety response. *Proc Natl Acad Sci U S A, 104*(23), 9828-9833. doi: 0610011104 [pii] 10.1073/pnas.0610011104

Ferre, E. R., Bottini, G., Iannetti, G. D., & Haggard, P. (2013). The balance of feelings: vestibular modulation of bodily sensations. *Cortex, 49*(3), 748-758. doi: 10.1016/j.cortex.2012.01.012

Ferre, E. R., Day, B. L., Bottini, G., & Haggard, P. (2013). How the vestibular system interacts with somatosensory perception: a sham-controlled study with galvanic vestibular stimulation. *Neurosci Lett, 550*, 35-40. doi: 10.1016/j.neulet.2013.06.046

Ferre, E. R., Vagnoni, E., & Haggard, P. (2013). Vestibular contributions to bodily awareness. *Neuropsychologia, 51*(8), 1445-1452. doi: 10.1016/j.neuropsychologia.2013.04.006

Ferri, F., Chiarelli, A. M., Merla, A., Gallese, V., & Costantini, M. (2013). The body beyond the body: expectation of a sensory event is enough to induce ownership over a fake hand. *Proc Biol Sci, 280*(1765), 20131140-20131140. doi: 10.1098/rspb.2013.1140

Fetsch, C. R., Pouget, A., Deangelis, G. C., & Angelaki, D. E. (2011). Neural correlates of reliability-based cue weighting during multisensory integration. *Nat Neurosci, 15*(1), 146-154. doi: 10.1038/nn.2983 [pii]

Fourneret, P., & Jeannerod, M. (1998). Limited conscious monitoring of motor performance in normal subjects. *Neuropsychologia, 36*(11), 1133-1140.

Frank, S. M., Baumann, O., Mattingley, J. B., & Greenlee, M. W. (2014). Vestibular and Visual Responses in Human Posterior Insular Cortex. *J Neurophysiol.* doi: 10.1152/jn.00078.2014

Gentile, G., Petkova, V. I., & Ehrsson, H. H. (2010). Integration of visual and tactile signals from the hand in the human brain: an FMRI study. *J Neurophysiol, 105*, 910-922. doi: jn.00840.2010 [pii] 10.1152/jn.00840.2010

Grusser, O. J., Pause, M., & Schreiter, U. (1990). Vestibular neurones in the parieto-insular cortex of monkeys (Macaca fascicularis): visual and neck receptor responses. *J Physiol, 430*, 559-583.

Haans, A., Ijsselsteijn, W. A., & de Kort, Y. A. (2008). The effect of similarities in skin texture and hand shape on perceived ownership of a fake limb. *Body Image, 5*(4), 389-394.

Haggard, P., & Jundi, S. (2009). Rubber hand illusions and size-weight illusions: self-representation modulates representation of external objects. *Perception, 38*(12), 1796-1803.

Heed, T., Grundler, M., Rinkleib, J., Rudzik, F. H., Collins, T., Cooke, E., & O'Regan, J. K. (2011). Visual information and rubber hand embodiment differentially affect reach-to-grasp actions. *Acta Psychol (Amst), 138*(1), 263-271. doi: 10.1016/j.actpsy.2011.07.003 S0001-6918(11)00136-3 [pii]

Holmes, N. P., Snijders, H. J., & Spence, C. (2006). Reaching with alien limbs: visual exposure to prosthetic hands in a mirror biases proprioception without accompanying illusions of ownership. *Percept Psychophys, 68*(4), 685-701.

Holmes, NP., Spence C. (2007). Dissociating body image and body schema with rubber hands. *Behavioral and Brain Sciences, 30*(2), 211-212.

Ionta, S., Heydrich, L., Lenggenhager, B., Mouthon, M., Fornari, E., Chapuis, D., Blanke, O. (2011). Multisensory mechanisms in temporo-parietal cortex support self-location and first-person perspective. *Neuron, 70*(2), 363-374. doi: S0896-6273(11)00200-5 [pii] 10.1016/j.neuron.2011.03.009

Kammers, M P M, de Vignemont, F, Verhagen, L, & Dijkerman, H C. (2009). The rubber hand illusion in action. *Neuropsychologia, 47*(1), 204-211. doi: 10.1016/j.neuropsychologia.2008.07.028

Kannape, O. A., Schwabe, L., Tadi, T., & Blanke, O. (2010). The limits of agency in walking humans. *Neuropsychologia, 48*(6), 1628-1636. doi: S0028-3932(10)00049-7 [pii] 10.1016/j.neuropsychologia.2010.02.005

Knox, J. J., Coppieters, M. W., & Hodges, P. W. (2006). Do you know where your arm is if you think your head has moved? *Exp Brain Res, 173*(1), 94-101. doi: 10.1007/s00221-006-0368-z

Le Chapelain, L., Beis, J. M., Paysant, J., & Andre, J. M. (2001). Vestibular caloric stimulation evokes phantom limb illusions in patients with paraplegia. *Spinal Cord, 39*(2), 85-87.

Lenggenhager, B., Lopez, C., & Blanke, O. (2008). Influence of galvanic vestibular stimulation on egocentric and object-based mental transformations. *Exp Brain Res, 184*(2), 211-221.

Lenggenhager, Bigna, Tadi, Tej, Metzinger, Thomas, & Blanke, Olaf. (2007). Video ergo sum: manipulating bodily self-consciousness. *Science, 317*(5841), 1096-1099. doi: 10.1126/science.1143439

Lestienne, F., Soechting, J., & Berthoz, A. (1977). Postural Readjustments Induced by Linear Motion of Visual Scenes. *Experimental Brain Research, 28*(3-4), 363-384.

Lopez, C., & Blanke, O. (2011). The thalamocortical vestibular system in animals and humans. *Brain Res Rev, 67*(1-2), 119-146. doi: S0165-0173(11)00002-6 [pii] 10.1016/j.brainresrev.2010.12.002

Lopez, C., Blanke, O., & Mast, F. W. (2012). The human vestibular cortex revealed by coordinate-based activation likelihood estimation meta-analysis. *Neuroscience, 212*, 159-179. doi: 10.1016/j.neuroscience.2012.03.028 S0306-4522(12)00289-8 [pii]

Lopez, C., Halje, P., & Blanke, O. (2008). Body ownership and embodiment: vestibular and multisensory mechanisms. *Neurophysiol Clin, 38*(3), 149-161. doi: S0987-7053(08)00018-X [pii] 10.1016/j.neucli.2007.12.006

Lopez, C., Lenggenhager, B., & Blanke, O. (2010). How vestibular stimulation interacts with illusory hand ownership. *Conscious Cogn, 19*(1), 33-47. doi: S1053-8100(09)00189-5 [pii] 10.1016/j.concog.2009.12.003

Lopez, C., Schreyer, H. M., Preuss, N., & Mast, F. W. (2012). Vestibular stimulation modifies the body schema. *Neuropsychologia*. doi: S0028-3932(12)00159-5 [pii] 10.1016/j.neuropsychologia.2012.04.008

Mach, E. (1875). Grundlinien der Lehre von der Bewegungsempfindung. *Engelmann, Leipzig, Germany.*

Mars, F., Archambault, P. S., & Feldman, A. G. (2003). Vestibular contribution to combined arm and trunk motion. *Exp Brain Res, 150*(4), 515-519. doi: 10.1007/s00221-003-1485-6

Mazzola, L., Lopez, C., Faillenot, I., Chouchou, F., Mauguiere, F., & Isnard, J. (2014). Vestibular responses to direct stimulation of the human insular cortex. *Ann Neurol*. doi: 10.1002/ana.24252

Moseley, G. L., Gallace, A., & Spence, C. (2012). Bodily illusions in health and disease: Physiological and clinical perspectives and the concept of a cortical 'body matrix'. *Neurosci Biobehav Rev, 36*(1), 34-46. doi: S0149-7634(11)00064-9 [pii] 10.1016/j.neubiorev.2011.03.013

Moseley, G. L., Olthof, N., Venema, A., Don, S., Wijers, M., Gallace, A., & Spence, C. (2008). Psychologically induced cooling of a specific body part caused by the illusory ownership of an artificial counterpart. *Proc Natl Acad Sci U S A, 105*(35), 13169-13173. doi: 0803768105 [pii] 10.1073/pnas.0803768105

Pavani, F., Spence, C., & Driver, J. (2000). Visual capture of touch: out-of-the-body experiences with rubber gloves. *Psychol Sci, 11*(5), 353-359.

Pavani, F., & Zampini, M. (2007). The role of hand size in the fake-hand illusion paradigm. *Perception, 36*(10), 1547-1554.

Pfeiffer, C., Serino, A., & Blanke, O. (2014). The vestibular system: a spatial reference for bodily self-consciousness. *Front Integr Neurosci, 8*, 31-31. doi: 10.3389/fnint.2014.00031

Schwarz, D. W. F., & Fredrickson, J. M. (1971). Rhesus monkey vestibular cortex: a bimodal primary projection field. *Science, 172*, 280-281.

Schwarz, D. W. F., Fredrickson, J. M., & Deecke, L. (1973). Structure and connections of the rhesus vestibular cortex. *Adv Otorhinolaryngol, 19*, 206-209.

Smith, A. T., Wall, M. B., & Thilo, K. V. (2011). Vestibular Inputs to Human Motion-Sensitive Visual Cortex. *Cereb Cortex*. doi: bhr179 [pii] 10.1093/cercor/bhr179

Straube, A., & Brandt, T. (1987). Importance of the visual and vestibular cortex for self-motion perception in man (circularvection). *Hum Neurobiol, 6*(3), 211-218.

Trutoiu, L, Mohler, B, Schulte-Pelkum, J, & Bülthoff, H. (2009). Circular, linear, and curvilinear vection in a large-screen virtual environment with floor projection. *Computers & Graphics, 33*(1), 47-58.

Trutoiu LC, Mohler BJ, Schulte-Pelkum J, Bülthoff HH. (2009). Circular, linear, and curvilinear vection in a large-screen virtual environment with floor projection. *Computers & Graphics, 33*, 47–58.

Tsakiris, M., & Haggard, P. (2005). The rubber hand illusion revisited: visuotactile integration and self-attribution. *J Exp Psychol Hum Percept Perform, 31*(1), 80-91.

Tsakiris, M., Hesse, M. D., Boy, C., Haggard, P., & Fink, G. R. (2007). Neural signatures of body ownership: a sensory network for bodily self-consciousness. *Cereb Cortex, 17*(10), 2235-2244.

van Elk, M., Forget, J., & Blanke, O. (2013). The effect of limb crossing and limb congruency on multisensory integration in peripersonal space for the upper and lower extremities. *Conscious Cogn, 22*(2), 545-555. doi: 10.1016/j.concog.2013.02.006

zu Eulenburg, P., Baumgartner, U., Treede, R. D., & Dieterich, M. (2013). Interoceptive and multimodal functions of the operculo-insular cortex: tactile, nociceptive and vestibular representations. *Neuroimage, 83*, 75-86. doi: 10.1016/j.neuroimage.2013.06.057

zu Eulenburg, P., Caspers, S., Roski, C., & Eickhoff, S. B. (2012). Meta-analytical definition and functional connectivity of the human vestibular cortex. *Neuroimage, 60*(1), 162-169. doi: 10.1016/j.neuroimage.2011.12.032

Chapter 4 The effect of limb crossing and limb congruency on multisensory integration in peripersonal space for the upper and lower extremities[1]

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Abstract

The present study investigated how multisensory integration in peripersonal space is modulated by limb posture (i.e. whether the limbs are crossed or uncrossed) and limb congruency (i.e. whether the observed body part matches the actual position of one's limb). This was done separately for the upper limbs (Experiment 1) and the lower limbs (Experiment 2). The crossmodal congruency task was used to measure peripersonal space integration for the hands and the feet. It was found that the peripersonal space representation for the hands but not for the feet is dynamically updated based on both limb posture and limb congruency. Together these findings show how dynamic cues from vision, proprioception, and touch are integrated in peripersonal limb space and highlight fundamental differences in the way in which peripersonal space is represented for the upper and lower extremity.

Keywords: Body representation; Crossmodal congruency effect; Multisensory integration; Peripersonal space; Upper and lower limbs

Introduction

Many of our everyday activities and interactions rely on an implicit representation of our body. For instance, when grasping a cup in the periphery of our visual field we rely on an implicit representation of the position of our hand and when making a pass in a football game we use an internal representation of the location of our feet to hit the ball. Usually the complex processes underlying these bodily transformations are taken for granted and are not given much further thought. Only in the case of neurological deficits the importance of these complex processes and their integration with knowledge about one's body parts becomes unmistakably clear. For instance, apractic patients and patients with autotopagnosia are characterized by an impaired ability to locate the spatial position of their body parts (e.g. Goldenberg 1995, Felician, Ceccaldi et al. 2003). An autotopagnosic patient may well be able to give an accurate verbal description of the feet, but when asked to point to the location of these body parts he may be at a complete loss (Schwoebel, Coslett et al. 2001).

Over the last decade many studies have investigated the functional and neural mechanisms underlying the representation of our body (e.g. Berlucchi and Aglioti 1997, Dijkerman and de Haan 2007, Berlucchi and Aglioti 2010, de Vignemont 2010). It has been found for instance, that neurons in the superior parietal lobe fire selectively when a fake body part is presented in an anatomically congruent position, but not when the body part is placed in an impossible position (Graziano, Cooke et al. 2000). In addition, the visual receptive field size of visuo-tactile neurons has been shown to increase to the space surrounding the end of a handheld tool (Iriki, Tanaka et al. 1996). These studies suggest that multimodal neurons in parietal areas provide an important neural mechanism supporting the flexible updating of the body representation based on current sensory input. In humans, multisensory interactions between touch and vision have been studied extensively by using the crossmodal congruency task (Spence, Pavani et al. 2000, Maravita, Spence et al. 2002, Schicke, Bauer et al. 2009). In this task participants are required to respond to tactile stimuli applied to their thumb or index finger while ignoring visual distractor stimuli. Typically, participants respond slower if the visual distractor appears at an incongruent location with respect to the tactile stimulus, which is known as the crossmodal congruency effect (CCE). It has been found that CCEs are enhanced when the visual distractors are superimposed on a rubber body part that is placed in an anatomically congruent compared to an incongruent position (Pavani, Spence et al. 2000). In addition, the CCE is larger when the visual and tactile stimuli are presented in the same side of space as compared to when presented in different sides (CCE side effect; see: Spence, Pavani et al. 2000), suggesting that the CCE provides a direct measure of the perceived proximity of visual and tactile events.

It is well known that our body representation can be flexibly updated via processes of multisensory integration, resulting in different mappings of peripersonal space (i.e. the space directly surrounding our body) based on current sensory input (Maravita and Iriki 2004). For instance, through a process of synchronous visuo-tactile stimulation participants may experience feelings of ownership for rubber body parts (Botvinick and Cohen 1998, Ehrsson, Holmes et al. 2005, Tsakiris and Haggard 2005, Costantini and Haggard 2007) and even for virtual bodies (Lenggenhager, Tadi et al. 2007, Aspell, Lenggenhager et al. 2009). With respect to tool use, it has been found that visual distractors presented at the end of a handheld tool interfere with judgments of tactile stimuli applied to the hand (Maravita, Spence et al. 2002, Maravita and Iriki 2004). Normally, the effect is stronger for visual stimuli presented at the tip of the tool on the same side as that of tactile stimulation. However, when the tools were held in a crossed posture, visual distractors presented at the end of the tool which were now in the opposite visual hemifield interfered more strongly, indicating that tool crossing resulted in a remapping of peripersonal space (Maravita, Spence et al. 2002, Maravita and Iriki 2004).

Several studies have shown that a touch to a crossed hand is initially mapped to the wrong side and then after a period of 200-400 ms remapped to the correct side (Kitazawa 2002, Azanon, Camacho et al. 2010). Other studies have shown that hand crossing across the body midline can reverse spatial compatibility effects (Riggio, Gawryszewski et al. 1986, Holmes, Sanabria et al. 2006). However, no study has directly investigated how limb crossing modulates the multisensory integration of visuo-tactile information. Furthermore, although it has been shown that *anatomical plausibility* (i.e. placing rubber limbs in an anatomically possible or impossible position) can modulate multisensory integration as measured by the CCE (Pavani, Spence et al. 2000), it remains unclear to what extent *anatomical congruency* (i.e. whether rubber limbs are in a congruent position with respect to one's actual body parts) modulates multisensory integration.

Thus, the aim of the present study was to determine the relative importance of two factors for the remapping of peripersonal space, namely *limb crossing* and *limb congruency*. To this end we used a paradigm in which participants were presented with anatomically congruent or incongruent visual body information, while their actual body parts were in a crossed or an uncrossed posture. To measure multisensory integration in peripersonal space, we used the crossmodal congruency task by applying vibro-tactile stimuli to the participant's hands and by presenting visual distractors superimposed on rubber hands (Spence, Pavani et al. 2004, Holmes, Sanabria et al. 2006, Shore, Barnes et al. 2006, Holmes, Calvert et al. 2007, Aspell, Lenggenhager et al. 2009, Salomon, van Elk et al. 2012).

We made the following predictions regarding our experimental manipulations. First, when both the real hands and the rubber hands were uncrossed we expected a stronger same side CCE (i.e. visual and tactile stimuli presented at the same side) compared to a different side CCE (i.e. visual and tactile stimuli presented at different sides). Such a finding would be indicative that the rubber hands are automatically perceived as a part of one's body proper. Second, following the notion that the crossing of body parts results in a remapping of touch (Yamamoto and Kitazawa 2001, Schicke and Roder 2006, Azanon, Camacho et al. 2010), we expected that when the real arms were crossed tactile stimuli should interfere more strongly with visual distractors presented in the opposite hemifield – similar to the remapping observed with tool use studies (Maravita, Spence et al. 2002, Holmes, Calvert et al. 2004, Maravita and Iriki 2004). Third, given the finding that crossing one's hands impairs one's ability for tactile localization (Axelrod, Thompson et al. 1968, Spence and Driver 1994, Yamamoto and Kitazawa 2001, Shore, Spry et al. 2002, Roder, Rosler et al. 2004, Wada, Yamamoto et al. 2004), we expected that hand crossing would result in an overall decline in performance.

Experiment 1

Methods

Participants

In the first experiment 18 participants (5 female participants, mean age = 21.2 years) were tested, who were all students at the École Polytechnique Fédérale de Lausanne in Switzerland.

Experimental setup

In the first experiment, participants were seated in front of a device that has been described in detail in a previous study (Lopez, Lenggenhager et al. 2010). On top of a table a wooden frame was placed with openings on the side (width: 96 cm, depth: 55 cm height: 23 cm). Participants put their real hands on the bottom plane of the wooden frame so that they were out of view. On top of the wooden frame two anatomically realistic rubber hands were placed that matched the position of the participants' real hand. The distance between the left and the right hand was 20 cm. A black blanket covered the arms of the participant and was overlaid on the wrist of the rubber hands, to give the natural impression that the rubber hands were the actual hands of the subject.

In 4 different experimental blocks the position of the participants' real hands and the rubber hands was adjusted (see Figure 1). In half of all blocks participants held their real hands in an uncrossed position and in the other half of all blocks participants placed their hands in a crossed position. Similarly, in half of all blocks the rubber hands were presented in an uncrossed position (e.g. left rubber hand placed on the left side) and in the other blocks the rubber hands were placed in a crossed position (e.g. left rubber hand placed on the right side). Block order was counterbalanced between participants.

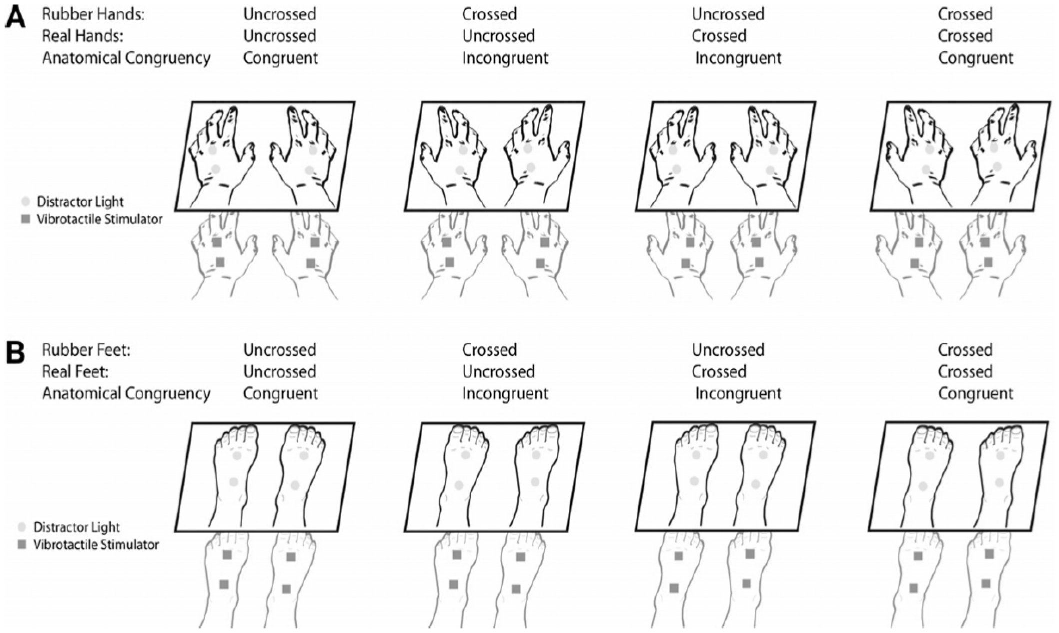


Figure 1: Experimental Setup. (A) In the first experiment participants' real hands were covered and two rubber hands were placed on the table in front of the participant. (B) In the second experiment participants' real feet were covered and two rubber feet were placed on a platform in front of the participant. Vibrotactile stimulators (dark squares) were attached to the participants' hand or feet and visual distractor stimuli (light circles) were presented on the rubber hands or feet. In different blocks, the real body parts and / or the rubber body parts were placed in an uncrossed or a crossed posture, resulting in 4 different experimental conditions (i.e. uncrossed-uncrossed, crossed-uncrossed, uncrossed-crossed, crossed-crossed).

The crossmodal congruency task was used as a measure of visuo-tactile integration in peripersonal space. Custom made vibro-tactile stimulators, consisting of a small vibrating motor (Precision MicroDrives shaftless vibration motors, model 312–101, 3V, 60mA, 9000 rpm (150 Hz), 5 g), were attached to the participants' hands. The motors had a surface area (the area touching the skin) of 113 mm^2. These were placed approximately 5 centimetres apart at the dorsal side of the hand close to the proximal phalanx of the middle finger (see Figure 1). Thus, one vibro-tactile stimulator was placed on the *anterior* side of the hand closer to the fingers and the other vibro-tactile stimulator was placed on the *posterior* side of the hand, closer to the arm. At the corresponding location as the vibro-tactile stimulators small LEDs were attached on the rubber body hand. (Please note that this setup is different from classical CCE paradigms, in which the vibro-tactile stimuli are typically applied to the index finger and thumb and the participant is required to report whether the stimulus was presented at the upper or lower side) During the experiment participants received concurrent visuo-tactile stimulations and participants were instructed to report the location of the vibro-tactile stimuli, while ignoring the visual distractor stimuli. Participants responded by releasing one of two pedals (Psychology Software Tools, Inc., Pittsburgh, PA), by lifting their toes or heels of their right foot when they perceived a vibro-tactile stimulus at respectively the anterior or posterior side of their hand.

Visual distractor stimuli were presented for 50 ms, followed by a 50 ms vibro-tactile stimulus and this sequence was repeated three times in a rapid sequence (e.g. visual-tactile-visual-tactile-visual-tactile stimulation). Previous studies have shown that this protocol results in a strong visuo-tactile crossmodal congruency effect (Salomon, van Elk et al. 2012). For each condition (i.e. crossed vs. uncrossed real hands, crossed vs. uncrossed rubber hands) 64 visuo-tactile stimuli were presented to which the participant responded. In half of all trials the visual stimuli were presented at a congruent spatial location with respect to the vibro-tactile stimuli and in the other half of all trials at an incongruent location. In addition, in half of all trials the visual distractors appeared at the same spatial side as the vibro-tactile stimuli (e.g. both the vibro-tactile stimulus and visual distractor were presented on the left side) and in the other half of all trials the visual distractor was presented at a different side (e.g. vibro-tactile stimulus at the left side, visual distractor at the right side).

It is important to note that the location of the side was defined in allocentric coordinates (i.e. whether the visual distractor was presented at the same spatial location with respect to the vibro-tactile stimulation). Accordingly, when both the real hand and the rubber hands were crossed or when they were both uncrossed, stimuli at the same side of space were presented at an anatomically congruent location (e.g. vibro-tactile stimulus at left real hand, visual distractor at rubber hand). However, when either the real hands or the rubber hands were crossed, stimuli at the same side of space were presented at an anatomically incongruent location (e.g. vibro-tactile stimulus at the real left hand, visual distractor on the right rubber hand that is close in space to the real left hand).

Participants were instructed to respond as fast and accurately as possible, indicating whether the vibro-tactile stimulus was applied to the anterior or posterior side of their hand. If the participant did not respond within 2000 ms, the next trial was initiated. Trials were separated by a variable 1000 – 2000 ms inter-trial interval. At the beginning of each block, 16 practice trials were administered, to familiarize the participant with the task. The experiment was controlled using Presentation software (Neurobehavioral Systems, Albany, CA).

Analysis

The analysis focused on reaction times and error rates for the different experimental conditions. Trials in which the subject made an error or trials that exceeded the participants' mean reaction time by more than 2 standard deviations were excluded from reaction time analysis. Reaction times were analysed using a repeated measures ANOVA with the factors Real Body part (Uncrossed vs. Crossed), Rubber Body part (Uncrossed vs. Crossed), Side (Same Spatial Side vs. Different Spatial Side) and Congruency (Congruent visuo-tactile stimulation, vs. Incongruent visuo-tactile stimulation). To control for speed-accuracy trade-offs we also analysed the error rates.

Results

Reaction times are represented in Table 1 and the crossmodal congruency effect (i.e. difference between incongruent and congruent trials) is represented in Figure 2. Analysis of the reaction times revealed a main effect of Congruency, $F(1, 17) = 160.7$, $p < .001$, $\eta^2 = .90$, which was reflected in faster reaction times to congruent (509 ms) compared to incongruent (570 ms) visuo-tactile stimulation. An interaction between Side and Congruency, $F(1, 17) = 8.9$, $p < .01$, $\eta^2 = .34$, reflected a stronger CCE when the visual distractor appeared at the same side compared to a different side. An interaction was found between Real Body part, Rubber Body part and Congruency, $F(1, 17) = 6.2$, $p < .05$, $\eta^2 = .27$, indicating that a larger CCE was found when both the real hands and the rubber hands were crossed or when both real and rubber hands were uncrossed (see Figure 2). An interaction between Real Body part, Side and Congruency, $F(1, 17) = 4.8$, $p < .05$, $\eta^2 = .21$, indicated that visuo-tactile stimuli presented at the same spatial side resulted in a stronger CCE when the real hands were uncrossed compared to when the real hands were crossed.

Finally, and most importantly, a significant 4-way interaction was found between Real Body part, Rubber Body part, Side, and Congruency, $F(1, 17) = 8.9$, $p < .01$, $\eta^2 = .34$. This interaction reflects that the CCE side effect was modulated by the position of both the real hands and the rubber hands. To explore this interaction, 4 separate ANOVAs were conducted with the factors Side (Same spatial side vs. Different spatial side) and Congruency (Congruent visuo-tactile stimulation vs. Incongruent visuo-tactile stimulation) for each of the possible real hand-rubber hand positionings. Only when both the real hands were uncrossed and the rubber hands were uncrossed, an interaction was found between Side and Congruency, $F(1, 17) = 13.6$, $p < .002$, $\eta^2 = .44$, reflecting that the CCE was larger for same side visuo-tactile stimuli compared to different side visuo-tactile stimuli (see Figure 2). For the other conditions, no interaction was observed ($F < 1$). This analysis indicates that the 4-way interaction was driven by the CCE side-effect in the condition in which both the real and the rubber hands were uncrossed.

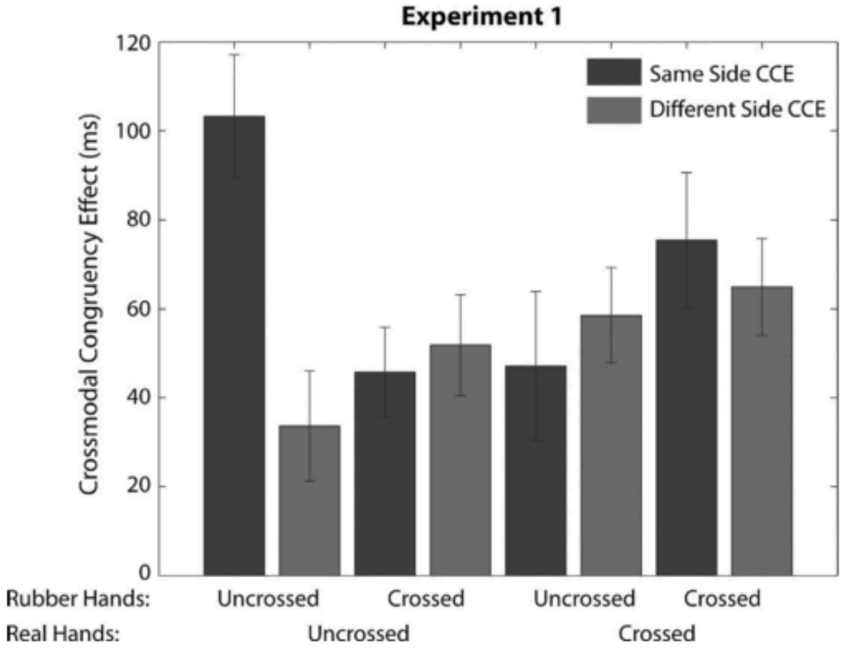
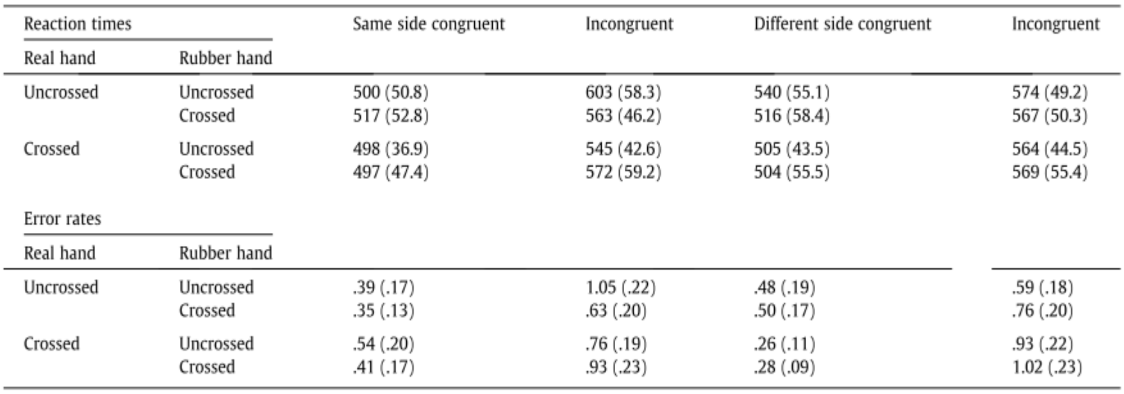


Figure 2: Behavioral Results Experiment 1. The crossmodal congruency effect (i.e. reaction time difference between incongruent and congruent visuotactile stimulation) for Experiment 1. Dark bars represent same side CCE conditions and light bars represent different side CCE conditions. The left side of each graph represents conditions in which the real body parts were uncrossed, the right side of the graph represents conditions in which the real body parts were crossed. Please note that the location of the side was defined in allocentric coordinates (i.e. whether the visual distractor was presented at the same spatial location with respect to the vibrotactile stimulation). Error bars represent standard errors.

On average, participants made errors in 9.9 % of all trials (see Table 1) and individual error rates varied between 3.1% and 20.9%. A main effect of Congruency, $F(1, 17) = 15.9$, $p < .001$, , $\eta^2 = .48$, reflected that participants made more errors to incongruent compared to congruent visuo-tactile stimulation. An interaction between Rubber Body Part and Side, $F(1, 17) = 7.1$, $p < .05$, , $\eta^2 = .29$ reflected that when the rubber hands were uncrossed participants made more errors to stimuli at the same side of space , but when the rubber hands were crossed more errors were made to different side stimuli. An interaction between Real Body Part and Congruency, $F(1, 17) = 4.8$, $p < .05$, , $\eta^2 = .22$, reflected that participants made more errors to incongruent visuo-tactile stimuli when the real hands were crossed. An interaction between Real Body Part, Side and Congruency, $F(1, 17) = 6.3$, $p < .05$, , $\eta^2 = .27$ reflects that the CCE side effect (i.e. more errors to incongruent visuo-tactile stimuli presented at the same side) differed between the hands being in an uncrossed compared to a crossed posture. Finally, a 4-way interaction between Real Body Part, Rubber Body Part, Side and Congruency, $F(1, 17) = 7.2$, $p < .05$, , $\eta^2 = .30$, was observed. This finding confirms the results from the reaction time analysis and indicates that the CCE side effect is modulated by both the position of the real hands and the rubber hands. Importantly, analysis of the error rates indicates that the reaction time results cannot be accounted for by a speed-accuracy trade-off, as participants made relatively more errors in conditions that also elicited the slowest reaction times.



Reaction times		Same side congruent	Incongruent	Different side congruent	Incongruent
Real hand	Rubber hand				
Uncrossed	Uncrossed	500 (50.8)	603 (58.3)	540 (55.1)	574 (49.2)
	Crossed	517 (52.8)	563 (46.2)	516 (58.4)	567 (50.3)
Crossed	Uncrossed	498 (36.9)	545 (42.6)	505 (43.5)	564 (44.5)
	Crossed	497 (47.4)	572 (59.2)	504 (55.5)	569 (55.4)
Error rates					
Real hand	Rubber hand				
Uncrossed	Uncrossed	.39 (.17)	1.05 (.22)	.48 (.19)	.59 (.18)
	Crossed	.35 (.13)	.63 (.20)	.50 (.17)	.76 (.20)
Crossed	Uncrossed	.54 (.20)	.76 (.19)	.26 (.11)	.93 (.22)
	Crossed	.41 (.17)	.93 (.23)	.28 (.09)	1.02 (.23)

Table 1: Reaction Times (in milliseconds; upper panel) and error rates (in percentage; lower panel) for Experiment 1 (Rubber Hand). Columns are separated according to whether the visuo-tactile stimuli were applied to the same (left part of table) or the different side (right part of the table) and according to whether the visuo-tactile stimuli were congruent (left columns) or incongruent (right columns). Rows reflect the different experimental conditions according to whether the real and the rubber body parts were uncrossed or crossed. Standard errors are represented between brackets.

Discussion

In the first experiment it was found that *limb congruency* facilitated multisensory integration, as reflected in a stronger CCE when both the real and the rubber hands were either in an uncrossed or a crossed posture. This finding replicates and extends previous findings (Pavani, Spence et al. 2000) and suggests that, in addition to *anatomical plausibility*, *anatomical congruence* between fake and real body parts facilitates multisensory integration.

In addition, a CCE side-effect (i.e. stronger same side compared to different side CCE) was observed only when both the real and the rubber hands were uncrossed. The stronger same side CCE likely reflects the perceived proximity of visual and tactile stimuli (Spence, Pavani et al. 2004, Aspell, Lenggenhager et al.

2009), suggesting that in the uncrossed-uncrossed condition visual distractor stimuli applied to the rubber hands interfered with vibrotactile judgments, as if they were applied to the real hands. This was different for the other conditions, in which no difference between same side and different side CCEs was observed. This finding suggests that both *limb incongruence* and *limb crossing* can impair multisensory integration. The absence of a CCE side-effect for the other conditions also suggests that limb crossing did not result in a complete remapping of peripersonal space, as is typically observed in tool use studies (Maravita, Spence et al. 2002, Macaluso, George et al. 2004). This was likely due to the fact that the remapping of touch according to one's arm posture takes about 300-400 ms (Kitazawa 2002, Azanon, Camacho et al. 2010), whereas in the present study tactile stimuli were applied for a shorter interval, thereby preventing a complete remapping of touch.

In sum, in the first study it was found that both *limb congruency* and *limb crossing* can modulate multisensory processing in peripersonal hand space. In a second study we aimed to investigate whether a similar mechanism applies for the representation of the feet. The rationale for testing multisensory integration for the feet was twofold. First, it has been suggested that similar mechanisms of multisensory integration apply to the hands and the feet (Roder, Kusmierek et al. 2007, Schicke, Bauer et al. 2009). However, it could well be that multisensory integration is less sensitive to limb congruence for the feet compared to the hands. In daily life we have ample experience with relating felt to observed hand representations (e.g. when typing on a keyboard, when grasping a cup), but we have less experience with relating felt to observed feet movements. As a consequence, the visual representation of our feet is probably less strongly coupled to the proprioceptive representation of our feet and accordingly multisensory integration may be less sensitive to visual-proprioceptive congruence for the feet compared to the hands. Secondly, it has been found that tactile remapping according to one's actual body posture takes longer for the feet compared to the hands (Schicke and Roder 2006). As a consequence, we expected that multisensory integration as measured with the CCE would be less sensitive to limb crossing for the feet than for the hands. That is, because the remapping of touch takes relatively long for the feet, the tactile stimuli delivered during the CCE task are initially incorrectly localised, which should be reflected in a stronger different side CCE when the feet are crossed.

Experiment 2

Participants

In the second experiment 18 participants (Experiment 2: 3 female participants, mean age = 20.6 years) were tested, who were all students at the École Polytechnique Fédérale de Lausanne in Switzerland.

Experimental setup

In the second experiment, participants were standing on their bare feet. Two wooden platforms (width: 15 cm, depth: 30 cm height: 20 cm) covered the participants' real feet. On top of these platforms two anatomically realistic rubber feet were placed that matched the position of the participants' real feet. The distance between the left and the right foot was 20 cm. A black blanket was attached to the participants' waist and covered the ankles of the rubber feet, to give the natural impression that the rubber feet were the actual feet of the participant.

As for Experiment 1, in 4 different experimental blocks the position of the participants' real feet and the rubber feet was adjusted (see Figure 1). In half of all blocks participants had their real feet in an uncrossed position and in the other half of all blocks participants had their feet in a crossed position. Similarly, in half of all blocks the rubber feet were presented in an uncrossed position (e.g. left rubber foot placed on the left side) and in the other blocks the rubber feet were placed in a crossed position (e.g. left rubber foot placed on the right side). Block order was counterbalanced across participants.

Vibro-tactile stimuli were applied at the dorsal side of the feet close to the proximal phalanx of the third toe. Tactile vibrators were applied to the anterior part of the feet (close to the toes) and the posterior part of the feet (close to the instep). In the second experiment participants responded by pressing the upper or lower button of a response box with their right hand, when they perceived a vibro-tactile stimulus at respectively the anterior or posterior side of their foot.

Results

Reaction times for the second experiment are represented in Table 2 and the crossmodal congruency effect (i.e. difference between incongruent and congruent trials) is represented in Figure 3. Analysis of the reaction times revealed a main effect of Congruency, F(1, 17) = 56.2, $p < .001$, $\eta^2 = .77$, reflecting slower reaction times to incongruent (494 ms) compared to congruent (432 ms) visuo-tactile stimulation. An interaction between Real Body part, Side and Congruency, F(1, 17) = 7.3, $p < .05$, $\eta^2 = .30$, indicated that the CCE side effect was modulated by the position of the real legs: when the legs were uncrossed a larger CCE was observed for stimuli at the same side of space , but when the legs were crossed a larger CCE was observed for different side stimuli. In contrast to the first experiment, no 4-way interaction was found between Real Body part, Rubber Body Part, Congruency and Side.

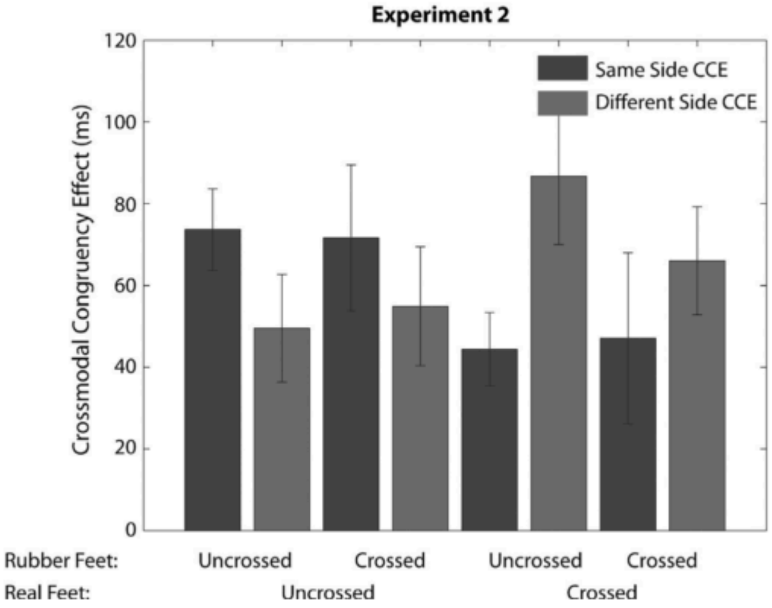
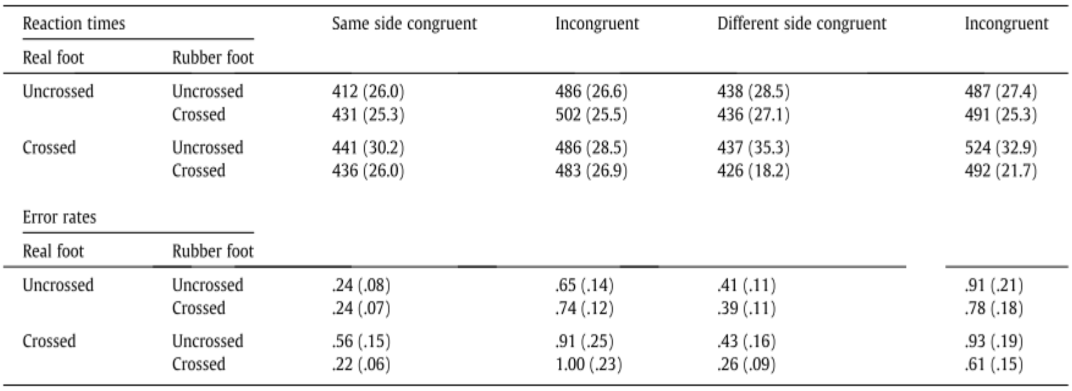


Figure 3: Behavioral Results Experiment 2. The crossmodal congruency effect (i.e. reaction time difference between incongruent and congruent visuotactile stimulation) for Experiment 2. Dark bars represent same side CCE conditions and light bars represent different side CCE conditions. The left side of each graph represents conditions in which the real body parts were uncrossed, the right side of the graph represents conditions in which the real body parts were crossed. Please note that the location of the side was defined in allocentric coordinates (i.e. whether the visual distractor was presented at the same spatial location with respect to the vibrotactile stimulation). Error bars represent standard errors.

On average, participants made errors in 9.3 % of all trials and individual error rates varies between 2.3 % and 14.8 %. Analysis of the error rates revealed a main effect of Congruency, $F(1, 17) = 16.5$, $p < .001$, , $\eta^2 = .49$, reflecting that more errors were made to incongruent compared to congruent visuo-tactile stimulation. An interaction between Real Body part and Side, $F(1, 17) = 4.7$, $p < .05$, $\eta^2 = .22$, indicated that participants made more errors to different side stimuli when the legs were uncrossed, but more errors to stimuli at the same side of space when the legs were crossed.



Reaction times		Same side congruent	Incongruent	Different side congruent	Incongruent
Real foot	Rubber foot				
Uncrossed	Uncrossed	412 (26.0)	486 (26.6)	438 (28.5)	487 (27.4)
	Crossed	431 (25.3)	502 (25.5)	436 (27.1)	491 (25.3)
Crossed	Uncrossed	441 (30.2)	486 (28.5)	437 (35.3)	524 (32.9)
	Crossed	436 (26.0)	483 (26.9)	426 (18.2)	492 (21.7)
Error rates					
Real foot	Rubber foot				
Uncrossed	Uncrossed	.24 (.08)	.65 (.14)	.41 (.11)	.91 (.21)
	Crossed	.24 (.07)	.74 (.12)	.39 (.11)	.78 (.18)
Crossed	Uncrossed	.56 (.15)	.91 (.25)	.43 (.16)	.93 (.19)
	Crossed	.22 (.06)	1.00 (.23)	.26 (.09)	.61 (.15)

Table 2: Reaction Times (in milliseconds; upper panel) and error rates (in percentage; lower panel) for Experiment 2 (Rubber Foot). Columns are separated according to whether the visuo-tactile stimuli were applied to the same (left part of table) or the different side (right part of the table) and according to whether the visuo-tactile stimuli were congruent (left columns) or incongruent (right columns). Rows reflect the different experimental conditions according to whether the real and the rubber body parts were uncrossed or crossed. Standard errors are represented between brackets.

Between-experiment comparison

A between-experiment comparison was conducted, by using a mixed ANOVA with Extremity (Upper extremities vs. Lower extremities) as an additional between-subjects factor. An interaction was found between Extremity, Real Body part, Rubber Body part and Congruency, $F(1, 34) = 4.4$, $p < .05$, $\eta^2 = .11$. This interaction reflected that for the rubber hands the CCE was higher when the rubber hands were placed in an anatomically congruent position (i.e. uncrossed-uncrossed or crossed-crossed), but for the rubber feet the CCE was not modulated according to anatomical congruency. No other interactions were found.

Discussion

In the second experiment it was found that *limb congruency* did not facilitate multisensory integration for the feet. This finding was in contrast to the first experiment, in which an enhanced CCE was found when the real and the rubber hands were placed in an anatomically congruent position. In addition, it was found that *limb crossing* did not modulate multisensory integration for the feet. In fact, visual stimuli always interfered with tactile stimuli as if the feet were uncrossed. Although previous studies have suggested that multisensory integration in peripersonal space is comparable between the hands and the feet (Schicke and Roder 2006, Roder, Kusmierek et al. 2007, Schicke, Bauer et al. 2009), the present study indicates important differences between the hands and the feet with respect to the effect of *limb congruency* and *limb crossing* on multisensory integration, which will be discussed in more detail below.

General Discussion

In the present study we investigated whether the integration of multisensory stimuli related to the hands and the feet is differentially modulated by *limb congruency* (i.e. whether the real and the rubber body parts were in a congruent or an incongruent position) and by *limb posture* (i.e. whether the real body parts were crossed or uncrossed). Multisensory integration was measured by using the crossmodal congruency task in which participants reported the elevation of tactile stimuli applied to the real hands or feet, while ignoring visual distractor stimuli superimposed on the rubber hands or feet.

When both the real and the rubber body parts were uncrossed (i.e. when the rubber body parts were placed in an anatomically congruent position) we observed a standard-size CCE for visuo-tactile stimuli applied to the hands and to the feet. For both extremities we also found that the CCEs were characterized by a side effect reflected in a stronger same-side CCE when both the real and the rubber body parts were uncrossed. These finding indicate a similar peripersonal space representation for both the hands and the feet when the limbs are in an uncrossed posture and when the rubber body parts are placed in an anatomically congruent position.

However, our findings also highlight important differences in the integration of information related to the hands and the feet in case the real and the rubber body parts were crossed. For the hands the CCE was modulated by the anatomical congruency of the rubber hands, whereas this was not the case for the feet. In addition, for the hands the CCE was modulated by the crossing of the real hands whereas for the feet the CCE was unaffected by feet crossing. As explained in more detail below, we suggest that these findings reflect that visual body information is more readily integrated with proprioceptive information for the hands compared to the feet, likely due to different functional roles and different multisensory representations of these body parts.

First, only for the hands a smaller CCE was observed when the rubber hands were placed in an anatomically incongruent position (i.e. uncrossed-crossed, crossed-uncrossed) compared to a congruent position (i.e. uncrossed-uncrossed, crossed-crossed). The effect of anatomical congruency between the real and the rubber hand observed in the present study replicates earlier findings (Pavani, Spence et al. 2000) and indicates that the CCE is sensitive to the anatomical plausibility of the position of the rubber hands based on the comparison between proprioceptive and visual signals. However, in the Pavani et al. study (2000) the anatomically incongruent condition involved rotating the rubber hands by 90°, resulting in a misalignment with the participants' real hands. In the present study we showed for the first time that the CCE is also reduced for rubber hands placed in an *anatomically incongruent* instead of an *anatomically impossible* condition. The effect of rubber hand placement on multisensory integration is also in line with studies on the rubber hand illusion (RHI), indicating that synchronous visuo-tactile stimulation can result in a feeling of ownership for the rubber hand, only if the rubber hand is placed in an anatomically congruent position (Tsakiris and Haggard 2005, Costantini and Haggard 2007). In contrast to these previous studies however, in the present study we did not actively induce a bodily illusion through visuo-tactile stroking. The finding that congruent rubber hand placement still facilitated the CCE suggests that the mere placement of rubber hands in an anatomically congruent position is already sufficient to facilitate integration in one's peripersonal space.

In contrast to the effects observed for the hands, for the feet the CCE was not modulated by the anatomical congruency between the position of the rubber feet and the participants' real feet. That is, for the feet the CCE was comparable in size irrespective of whether the real or the rubber feet were crossed or uncrossed. We suggest that this differential effect between the hands and the feet is related to differences in visual experience with observing our hands versus our feet. That is, in daily life we can readily observe our hands and visual information about our hands is strongly coupled to proprioceptive information about the position of our hands. As a consequence, visual information related to the rubber hands is more easily integrated in our hand representation if the rubber hands are in a congruent position with respect to our real hands (see also: Ehrsson, Spence et al. 2004, Tsakiris and Haggard 2005). If the rubber hands are in an anatomically incongruent position, however, this visual-proprioceptive conflict leads to a reduced CCE (cf. Pavani, Spence et al. 2000, Zopf, Savage et al. 2010).

Compared to the richness of visual signals about our hands, we have relatively less visual experience with observing our feet and therefore visual and proprioceptive information are probably less strongly coupled for the feet compared to the hands. Indeed several studies have indicated the importance of proprioceptive over visual feedback for postural control, stability and locomotion (Rossignol, Dubuc et al. 2006, Duysens, Beerepoot et al. 2008). Furthermore, Stratton already noted that - when wearing a mirror system that projected his body image as seen from above in front of him - whereas tactile information from the hands was remapped to the new visual location, this was not the case for tactile information from the legs or the feet (Stratton 1899). In the present study the CCE was not modulated by the anatomical congruency between the rubber feet and the real feet. Accordingly these data suggest that the position information of the observed feet was not automatically coupled to the position information of the real feet. These data are suggestive of fundamental differences of how visual, proprioceptive, and tactile signals are integrated.

In addition to the stronger visual-proprioceptive coupling for the hands compared to the feet, it should be noted that limb crossing was visually more salient for the hands compared to the feet (i.e. more visual features to disambiguate laterality, such as protruding thumbs). For instance, studies on motor imagery indicate that mental rotation is easier for the hands compared to the feet (Parsons 1987, Gentilucci, Daprati et al. 1998, Ionta, Fourkas et al. 2007). In addition, feet are visually more distal than the hands, thereby further reducing the relative importance of visual information for the feet compared to the hands. As a consequence, it could be that the stronger effect of *limb congruency* on multisensory integration for hands compared to feet is related to the fact that laterality could be more readily inferred for hands compared to feet.

A second major difference between the hands and the feet was observed in the CCE side effect. Typically, a stronger CCE is observed when the visual distractor stimuli are presented in the same spatial hemifield as the tactile stimuli compared to when the visual distractor appears in a different hemifield The stronger same side CCE is taken to reflect a stronger interference when the visual stimulus is perceived to be in close spatial proximity to the tactile stimulus (Spence, Pavani et al. 2004, Spence, Pavani et al. 2004). The notion that the CCE is sensitive to the perceived proximity of visual and tactile stimuli is supported by tool use studies, indicating that crossing tools results in a reversal of the CCE side effect, such that visual stimuli presented at the end of a handheld tool interfere with a tactile stimulus applied to the hand that is actually in the opposite hemifield (Maravita, Spence et al. 2002, Maravita and Iriki 2004, Holmes, Sanabria et al. 2007). In the present study for the hands the CCE side effect was modulated by the position of both the real hands and the rubber hands. More specifically, a stronger CCE was observed when visuo-tactile stimuli appeared at the same location compared to a different location when both the real hands and the rubber hands were uncrossed. When both the real and the rubber hands were crossed, a reduction in the CCE side effect was observed. Interestingly though, we did not observe a complete reversal of the CCE side effect, as is typically observed in studies on active tool use (Maravita, Spence et al. 2002, Maravita and Iriki 2004, Sengul, van Elk et al. 2012). This suggests that although limb crossing did modulate multisensory integration, it did not result in a complete remapping of peripersonal space. The absence of a complete remapping is likely related to the relatively short duration of the tactile stimulations that were used in the present study. Previous studies have indicated that the remapping of touch according to one's body posture takes about 300-400 ms (Schicke and Roder 2006, Azanon and Soto-Faraco 2008, Azanon, Camacho et al. 2010), and the tactile stimuli used in the present CCE-task were likely too short to result in a complete remapping.

This interpretation is further supported by the finding that the CCE was not modulated by the crossing of the feet. That is, when the real feet were in an uncrossed posture, same side visual distractors interfered more strongly as it happened for the hand. However, when the real feet were in a crossed posture, different side visual distractors interfered more strongly. In other words: even though the real feet were crossed, visual distractors interfered with tactile judgments as if the feet were uncrossed. This finding indicates that no remapping of tactile information occurred according to the position of the real or the rubber feet. It could well be that due to the crossing of the feet, tactile stimuli were incorrectly localised thereby interfering more strongly with visual distractors presented at a different side. This suggestion is in line with the finding that the remapping of tactile stimuli on the hand according to proprioceptive signal is quicker than for tactile stimuli on the feet (Schicke and Roder 2006). As visual distractor stimuli were presented in close temporal proximity to the tactile stimuli, the tactile stimuli may have been incorrectly localised, resulting in an interference effect with different side visual distractors when the feet were crossed.

In the present study, participants were statically holding their hands or feet in either an uncrossed or a crossed posture. With this design we observed a partial updating of the peripersonal space representation based on body posture only for the hands, but not for the feet. An interesting question is whether dynamic instead of static crossing of the feet would result in a stronger updating of the body representation, similar to the effects observed for actively crossing and uncrossing tools (Maravita, Spence et al. 2002, Maravita and Iriki 2004). Dynamic crossing may yield the actual position of one's body parts more salient or relevant, thus resulting in a stronger updating of one's body representation. In addition, an interesting question would be to what extent the remapping of peripersonal hand and foot space differs between individuals who have profound experience with using either the hands or the feet (e.g. aplasic subjects). Given the notion that action experience has a strong effect on the visuo-motor and visuo-proprioceptive representation of our body (Calvo-

Merino, Grezes et al. 2006, Gazzola, van der Worp et al. 2007), one would expect that peripersonal space would be more readily remapped for body parts with which we have profound experience.

In sum, the finding that the CCE was differentially modulated for hands and feet according to limb congruency and limb crossing suggests important differences in the processes underlying the representation of peripersonal space around these body parts. Multisensory integration was modulated by both limb crossing and limb congruency only for the hands but not for the feet. This finding indicates that the coupling between visual and proprioceptive information may be stronger for our hands than for our feet, which might be related to differences in the visual experience related to actions performed with our hands and feet.

Acknowledgments

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References

Andre, J. M., N. Martinet, J. Paysant, J. M. Beis and L. Le Chapelain (2001). "Temporary phantom limbs evoked by vestibular caloric stimulation in amputees." Neuropsychiatry Neuropsychol Behav Neurol 14(3): 190-196.

Arzy, S., L. S. Overney, T. Landis and O. Blanke (2006). "Neural mechanisms of embodiment: asomatognosia due to premotor cortex damage." Arch Neurol 63(7): 1022-1025.

Arzy, S., M. Seeck, S. Ortigue, L. Spinelli and O. Blanke (2006). "Induction of an illusory shadow person." Nature 443(7109): 287.

Aspell, J. E., B. Lenggenhager and O. Blanke (2009). "Keeping in touch with one's self: multisensory mechanisms of self-consciousness." PLoS One 4(8): e6488.

Axelrod, S., L. W. Thompson and L. D. Cohen (1968). "Effects of senescence on the temporal resolution of somesthetic stimuli presented to one hand or both." J Gerontol 23: 191-195.

Azanon, E., K. Camacho and S. Soto-Faraco (2010). "Tactile remapping beyond space." Eur J Neurosci 31(10): 1858-1867.

Azanon, E. and S. Soto-Faraco (2008). "Changing reference frames during the encoding of tactile events." Curr Biol 18(14): 1044-1049.

Barnsley, N., J. H. McAuley, R. Mohan, A. Dey, P. Thomas and G. L. Moseley (2011). "The rubber hand illusion increases histamine reactivity in the real arm." Curr Biol 21(23): R945-946.

Bekrater-Bodmann, R., J. Foell, M. Diers and H. Flor (2012). "The perceptual and neuronal stability of the rubber hand illusion across contexts and over time." Brain Res 1452: 130-139.

Berlucchi, G. and S. Aglioti (1997). "The body in the brain: neural bases of corporeal awareness." Trends Neurosci 20(12): 560-564.

Berlucchi, G. and S. M. Aglioti (2010). "The body in the brain revisited." Exp Brain Res 200(1): 25-35.

Berthoz, A., B. Pavard and L. R. Young (1975). "Perception of linear horizontal self-motion induced by peripheral vision (linearvection) basic characteristics and visual-vestibular interactions." Exp Brain Res 23(5): 471-489.

Berthoz, A., B. Pavard and L. R. Young (1975). "Perception of linear horizontal self-motion induced by peripheral vision (linearvection) basic characteristics and visual-vestibular interactions." Exp Brain Res 23(5): 471-489.

Blanke, O. and C. Mohr (2005). "Out-of-body experience, heautoscopy, and autoscopic hallucination of neurological origin Implications for neurocognitive mechanisms of corporeal awareness and self-consciousness." Brain Res Brain Res Rev 50(1): 184-199.

Blanke, O., S. Ortigue, T. Landis and M. Seeck (2002). "Stimulating illusory own-body perceptions." Nature 419(6904): 269-270.

Botvinick, M. and J. Cohen (1998). "Rubber hands 'feel' touch that eyes see." Nature 391(6669): 756-756.

Botvinick, M. and J. Cohen (1998). "Rubber hands 'feel' touch that eyes see." Nature 391(6669): 756.

Brandt, T. and J. Dichgans (1972). "[Circular vection, visually induced pseudocoriolis effects, optokinetic afernystagmus. A comparative study of subjective and objective optokinetic aftereffects]." Albrecht Von Graefes Arch Klin Exp Ophthalmol 184(1): 42-57.

Brandt, T., J. Dichgans and E. Koenig (1972). "Perception of self-rotation (circular vection) induced by optokinetic stimuli." Pflugers Arch 332(Suppl): R98.

Bremmer, F., F. Klam, J. R. Duhamel, S. Ben Hamed and W. Graf (2002). "Visual-vestibular interactive responses in the macaque ventral intraparietal area (VIP)." Eur J Neurosci 16(8): 1569-1586.

Bresciani, J. P., J. Blouin, K. Popov, C. Bourdin, F. Sarlegna, J. L. Vercher and G. M. Gauthier (2002). "Galvanic vestibular stimulation in humans produces online arm movement deviations when reaching towards memorized visual targets." Neurosci Lett 318(1): 34-38.

Calvo-Merino, B., J. Grezes, D. E. Glaser, R. E. Passingham and P. Haggard (2006). "Seeing or doing? Influence of visual and motor familiarity in action observation." Curr Biol 16(19): 1905-1910.

Cardin, V. and A. T. Smith (2010). "Sensitivity of human visual and vestibular cortical regions to egomotion-compatible visual stimulation." Cereb Cortex 20(8): 1964-1973.

Chu, W. H. N. (1976). Dynamic response of human linear vection.

Costantini, M. and P. Haggard (2007). "The rubber hand illusion: sensitivity and reference frame for body ownership." Conscious Cogn 16(2): 229-240.

de Vignemont, F. (2010). "Body schema and body image--pros and cons." Neuropsychologia 48(3): 669-680.

de Vignemont, F. (2011). "Embodiment, ownership and disownership." Conscious Cogn 20(1): 82-93.

Dempsey-Jones, H. and A. Kritikos (2014). "Higher-order cognitive factors affect subjective but not proprioceptive aspects of self-representation in the rubber hand illusion." Conscious Cogn 26: 74-89.

Destrieux, C., B. Fischl, A. Dale and E. Halgren (2010). "Automatic parcellation of human cortical gyri and sulci using standard anatomical nomenclature." Neuroimage 53(1): 1-15.

Deutschlander, A., S. Bense, T. Stephan, M. Schwaiger, M. Dieterich and T. Brandt (2004). "Rollvection versus linearvection: comparison of brain activations in PET." Hum Brain Mapp 21(3): 143-153.

Dichgans, J., Brandt, T (1978). "Visual-vestibular interaction: Effects on self-motion perception and postural control." Perception Handbook of Sensory Physiology, vol. VIII. Springer, New York: 756-804.

Dijkerman, H. C. and E. H. de Haan (2007). "Somatosensory processes subserving perception and action." Behav Brain Sci 30(2): 189-201; discussion 201-139.

Duvernoy, H. C., EA.; Duvernoy, HM.; Cabanis, EA.; (1991). "The Human brain: surface, three-dimensional sectional anatomy and MRI." Springer-Verlag Wien: 11.

Duysens, J., V. P. Beerepoot, P. H. Veltink, V. Weerdesteyn and B. C. Smits-Engelsman (2008). "Proprioceptive perturbations of stability during gait." Neurophysiol Clin 38(6): 399-410.

Ehrsson, H. H., N. P. Holmes and R. E. Passingham (2005). "Touching a rubber hand: feeling of body ownership is associated with activity in multisensory brain areas." J Neurosci 25(45): 10564-10573.

Ehrsson, H. H., C. Spence and R. E. Passingham (2004). "That's my hand! Activity in premotor cortex reflects feeling of ownership of a limb." Science 305(5685): 875-877.

Ehrsson, H. H., K. Wiech, N. Weiskopf, R. J. Dolan and R. E. Passingham (2007). "Threatening a rubber hand that you feel is yours elicits a cortical anxiety response." Proc Natl Acad Sci U S A 104(23): 9828-9833.

Felician, O., M. Ceccaldi, M. Didic, C. Thinus-Blanc and M. Poncet (2003). "Pointing to body parts: a double dissociation study." Neuropsychologia 41(10): 1307-1316.

Ferre, E. R., G. Bottini, G. D. Iannetti and P. Haggard (2013). "The balance of feelings: vestibular modulation of bodily sensations." Cortex 49(3): 748-758.

Ferre, E. R., B. L. Day, G. Bottini and P. Haggard (2013). "How the vestibular system interacts with somatosensory perception: a sham-controlled study with galvanic vestibular stimulation." Neurosci Lett 550: 35-40.

Ferre, E. R., E. Vagnoni and P. Haggard (2013). "Vestibular contributions to bodily awareness." Neuropsychologia 51(8): 1445-1452.

Ferri, F., A. M. Chiarelli, A. Merla, V. Gallese and M. Costantini (2013). "The body beyond the body: expectation of a sensory event is enough to induce ownership over a fake hand." Proc Biol Sci 280(1765): 20131140-20131140.

Fetsch, C. R., A. Pouget, G. C. Deangelis and D. E. Angelaki (2011). "Neural correlates of reliability-based cue weighting during multisensory integration." Nat Neurosci 15(1): 146-154.

Fourneret, P. and M. Jeannerod (1998). "Limited conscious monitoring of motor performance in normal subjects." Neuropsychologia 36(11): 1133-1140.

Frank, S. M., O. Baumann, J. B. Mattingley and M. W. Greenlee (2014). "Vestibular and Visual Responses in Human Posterior Insular Cortex." J Neurophysiol.

Gazzola, V., H. van der Worp, T. Mulder, B. Wicker, G. Rizzolatti and C. Keysers (2007). "Aplasics born without hands mirror the goal of hand actions with their feet." Current Biology 17(14): 1235-1240.

Gentile, G., V. I. Petkova and H. H. Ehrsson (2010). "Integration of visual and tactile signals from the hand in the human brain: an FMRI study." J Neurophysiol 105: 910-922.

Gentilucci, M., E. Daprati and M. Gangitano (1998). "Right-handers and left-handers have different representations of their own hand." Brain Res Cogn Brain Res 6(3): 185-192.

Goldenberg, G. (1995). "Imitating gestures and manipulating a mannikin--the representation of the human body in ideomotor apraxia." Neuropsychologia 33(1): 63-72.

Graziano, M. S., D. F. Cooke and C. S. Taylor (2000). "Coding the location of the arm by sight." Science 290(5497): 1782-1786.

Grusser, O. J., M. Pause and U. Schreiter (1990). "Vestibular neurones in the parieto-insular cortex of monkeys (Macaca fascicularis): visual and neck receptor responses." J Physiol 430: 559-583.

Haans, A., W. A. Ijsselsteijn and Y. A. de Kort (2008). "The effect of similarities in skin texture and hand shape on perceived ownership of a fake limb." Body Image 5(4): 389-394.

Haggard, P. and S. Jundi (2009). "Rubber hand illusions and size-weight illusions: self-representation modulates representation of external objects." Perception 38(12): 1796-1803.

Heed, T., M. Grundler, J. Rinkleib, F. H. Rudzik, T. Collins, E. Cooke and J. K. O'Regan (2011). "Visual information and rubber hand embodiment differentially affect reach-to-grasp actions." Acta Psychol (Amst) 138(1): 263-271.

Holmes, N., Spence C. (2007). "Dissociating body image and body schema with rubber hands." Behavioral and Brain Sciences 30(2): 211-212.

Holmes, N. P., G. A. Calvert and C. Spence (2004). "Extending or projecting peripersonal space with tools? Multisensory interactions highlight only the distal and proximal ends of tools." Neurosci Lett 372(1-2): 62-67.

Holmes, N. P., G. A. Calvert and C. Spence (2007). "Tool use changes multisensory interactions in seconds: evidence from the crossmodal congruency task." Exp Brain Res 183(4): 465-476.

Holmes, N. P., D. Sanabria, G. A. Calvert and C. Spence (2006). "Multisensory interactions follow the hands across the midline: evidence from a non-spatial visual-tactile congruency task." Brain Res 1077(1): 108-115.

Holmes, N. P., D. Sanabria, G. A. Calvert and C. Spence (2007). "Tool-use: capturing multisensory spatial attention or extending multisensory peripersonal space?" Cortex 43(3): 469-489.

Holmes, N. P., H. J. Snijders and C. Spence (2006). "Reaching with alien limbs: visual exposure to prosthetic hands in a mirror biases proprioception without accompanying illusions of ownership." Percept Psychophys 68(4): 685-701.

Ionta, S., A. D. Fourkas, M. Fiorio and S. M. Aglioti (2007). "The influence of hands posture on mental rotation of hands and feet." Exp Brain Res 183(1): 1-7.

Ionta, S., L. Heydrich, B. Lenggenhager, M. Mouthon, E. Fornari, D. Chapuis, R. Gassert and O. Blanke (2011). "Multisensory mechanisms in temporo-parietal cortex support self-location and first-person perspective." Neuron 70(2): 363-374.

Iriki, A., M. Tanaka and Y. Iwamura (1996). "Coding of modified body schema during tool use by macaque postcentral neurones." Neuroreport 7(14): 2325-2330.

Kammers, M. P. M., F. de Vignemont, L. Verhagen and H. C. Dijkerman (2009). "The rubber hand illusion in action." Neuropsychologia 47(1): 204-211.

Kannape, O. A., L. Schwabe, T. Tadi and O. Blanke (2010). "The limits of agency in walking humans." Neuropsychologia 48(6): 1628-1636.

Kitazawa, S. (2002). "Where conscious sensation takes place." Consciousness and Cognition 11(3): 475-477.

Knox, J. J., M. W. Coppieters and P. W. Hodges (2006). "Do you know where your arm is if you think your head has moved?" Exp Brain Res 173(1): 94-101.

Le Chapelain, L., J. M. Beis, J. Paysant and J. M. Andre (2001). "Vestibular caloric stimulation evokes phantom limb illusions in patients with paraplegia." Spinal Cord 39(2): 85-87.

Lenggenhager, B., C. Lopez and O. Blanke (2008). "Influence of galvanic vestibular stimulation on egocentric and object-based mental transformations." Exp Brain Res 184(2): 211-221.

Lenggenhager, B., T. Tadi, T. Metzinger and O. Blanke (2007). "Video ergo sum: manipulating bodily self-consciousness." Science 317(5841): 1096-1099.

Lestienne, F., J. Soechting and A. Berthoz (1977). "Postural Readjustments Induced by Linear Motion of Visual Scenes." Experimental Brain Research 28(3-4): 363-384.

Lopez, C. and O. Blanke (2011). "The thalamocortical vestibular system in animals and humans." Brain Res Rev 67(1-2): 119-146.

Lopez, C., O. Blanke and F. W. Mast (2012). "The human vestibular cortex revealed by coordinate-based activation likelihood estimation meta-analysis." Neuroscience 212: 159-179.

Lopez, C., P. Halje and O. Blanke (2008). "Body ownership and embodiment: vestibular and multisensory mechanisms." Neurophysiol Clin 38(3): 149-161.

Lopez, C., B. Lenggenhager and O. Blanke (2010). "How vestibular stimulation interacts with illusory hand ownership." Conscious Cogn 19(1): 33-47.

Lopez, C., H. M. Schreyer, N. Preuss and F. W. Mast (2012). "Vestibular stimulation modifies the body schema." Neuropsychologia.

Macaluso, E., N. George, R. Dolan, C. Spence and J. Driver (2004). "Spatial and temporal factors during processing of audiovisual speech: a PET study." Neuroimage 21(2): 725-732.

Mach, E. (1875). " Grundlinien der Lehre von der Bewegungsempfindung." Engelmann, Leipzig, Germany.

Maravita, A. and A. Iriki (2004). "Tools for the body (schema)." Trends Cogn Sci 8(2): 79-86.

Maravita, A., C. Spence, S. Kennett and J. Driver (2002). "Tool-use changes multimodal spatial interactions between vision and touch in normal humans." Cognition 83(2): B25-34.

Mars, F., P. S. Archambault and A. G. Feldman (2003). "Vestibular contribution to combined arm and trunk motion." Exp Brain Res 150(4): 515-519.

Mazzola, L., C. Lopez, I. Faillenot, F. Chouchou, F. Mauguiere and J. Isnard (2014). "Vestibular responses to direct stimulation of the human insular cortex." Ann Neurol.

Moseley, G. L., A. Gallace and C. Spence (2012). "Bodily illusions in health and disease: Physiological and clinical perspectives and the concept of a cortical 'body matrix'." Neurosci Biobehav Rev 36(1): 34-46.

Moseley, G. L., N. Olthof, A. Venema, S. Don, M. Wijers, A. Gallace and C. Spence (2008). "Psychologically induced cooling of a specific body part caused by the illusory ownership of an artificial counterpart." Proc Natl Acad Sci U S A 105(35): 13169-13173.

Parsons, L. M. (1987). "Imaged spatial transformations of one's hands and feet." Cogn Psychol 19: 178-241.

Pavani, F., C. Spence and J. Driver (2000). "Visual capture of touch: out-of-the-body experiences with rubber gloves." Psychol Sci 11(5): 353-359.

Pavani, F. and M. Zampini (2007). "The role of hand size in the fake-hand illusion paradigm." Perception 36(10): 1547-1554.

Pfeiffer, C., A. Serino and O. Blanke (2014). "The vestibular system: a spatial reference for bodily self-consciousness." Front Integr Neurosci 8: 31-31.

Riggio, L., L. Gawryszewski and C. Umiltà (1986). "What is crossed in crossed-hand effects?" Acta Psychol (Amst) 62: 89-100.

Roder, B., A. Kusmierek, C. Spence and T. Schicke (2007). "Developmental vision determines the reference frame for the multisensory control of action." Proc Natl Acad Sci U S A 104(11): 4753-4758.

Roder, B., F. Rosler and C. Spence (2004). "Early vision impairs tactile perception in the blind." Curr Biol 14(2): 121-124.

Rossignol, S., R. Dubuc and J. P. Gossard (2006). "Dynamic sensorimotor interactions in locomotion." Physiol Rev 86(1): 89-154.

Salomon, R., M. van Elk, J. E. Aspell and O. Blanke (2012). "I feel who I see: Visual body identity affects visual-tactile integration in peripersonal space." Conscious Cogn 21(3): 1355-1364.

Schicke, T., F. Bauer and B. Roder (2009). "Interactions of different body parts in peripersonal space: how vision of the foot influences tactile perception at the hand." Exp Brain Res 192(4): 703-715.

Schicke, T. and B. Roder (2006). "Spatial remapping of touch: confusion of perceived stimulus order across hand and foot." Proc Natl Acad Sci U S A 103(31): 11808-11813.

Schwarz, D. W. F. and J. M. Fredrickson (1971). "Rhesus monkey vestibular cortex: a bimodal primary projection field." Science 172: 280-281.

Schwarz, D. W. F., J. M. Fredrickson and L. Deecke (1973). "Structure and connections of the rhesus vestibular cortex." Adv Otorhinolaryngol 19: 206-209.

Schwoebel, J., H. B. Coslett and L. J. Buxbaum (2001). "Compensatory coding of body part location in autotopagnosia: Evidence for extrinsic egocentric coding." Cogn Neuropsychol 18(4): 363-381.

Sengul, A., M. van Elk, G. Rognini, J. E. Aspell, H. Bleuler and O. Blanke (2012). "Extending the body to virtual tools using a robotic surgical interface: evidence from the crossmodal congruency task." PLoS One 7(12): e49473.

Shore, D. I., M. E. Barnes and C. Spence (2006). "Temporal aspects of the visuotactile congruency effect." Neurosci Lett 392(1-2): 96-100.

Shore, D. I., E. Spry and C. Spence (2002). "Confusing the mind by crossing the hands." Brain Res Cogn Brain Res 14(1): 153-163.

Smith, A. T., M. B. Wall and K. V. Thilo (2011). "Vestibular Inputs to Human Motion-Sensitive Visual Cortex." Cereb Cortex.

Spence, C. and J. Driver (1994). "Covert spatial orienting in audition: exogenous and endogenous mechanisms facilitate sound localization." J Exp Psychol Hum Percept Perform 20: 555-574.

Spence, C., F. Pavani and J. Driver (2000). "Crossmodal links between vision and touch in covert endogenous spatial attention." J Exp Psychol Hum Percept Perform 26(4): 1298-1319.

Spence, C., F. Pavani and J. Driver (2004). "Spatial constraints on visual-tactile cross-modal distractor congruency effects." Cogn Affect Behav Neurosci 4(2): 148-169.

Spence, C., F. Pavani, A. Maravita and N. Holmes (2004). "Multisensory contributions to the 3-D representation of visuotactile peripersonal space in humans: evidence from the crossmodal congruency task." J Physiol Paris 98(1-3): 171-189.

Stratton, G. M. (1899). "The spatial harmony of touch and sight." Mind 8(32): 492-505.

Straube, A. and T. Brandt (1987). "Importance of the visual and vestibular cortex for self-motion perception in man (circularvection)." Hum Neurobiol 6(3): 211-218.

Trutoiu, L., B. Mohler, J. Schulte-Pelkum and H. Bülthoff (2009). "Circular, linear, and curvilinear vection in a large-screen virtual environment with floor projection." Computers & Graphics 33(1): 47-58.

Trutoiu LC, M. B., Schulte-Pelkum J, Bu̇lthoff HH (2009). "Circular, linear, and curvilinear vection in a large-screen virtual environment with floor projection." Computers &
Graphics 33: 47–58.

Tsakiris, M. and P. Haggard (2005). "The rubber hand illusion revisited: visuotactile integration and self-attribution." J Exp Psychol Hum Percept Perform 31(1): 80-91.

Tsakiris, M., M. D. Hesse, C. Boy, P. Haggard and G. R. Fink (2007). "Neural signatures of body ownership: a sensory network for bodily self-consciousness." Cereb Cortex 17(10): 2235-2244.

van Elk, M., J. Forget and O. Blanke (2013). "The effect of limb crossing and limb congruency on multisensory integration in peripersonal space for the upper and lower extremities." Conscious Cogn 22(2): 545-555.

Wada, M., S. Yamamoto and S. Kitazawa (2004). "Effects of handedness on tactile temporal order judgment." Neuropsychologia 42(14): 1887-1895.

Yamamoto, S. and S. Kitazawa (2001). "Reversal of subjective temporal order due to arm crossing." Nat Neurosci 4(7): 759-765.

Zopf, R., G. Savage and M. A. Williams (2010). "Crossmodal congruency measures of lateral distance effects on the rubber hand illusion." Neuropsychologia 48(3): 713-725.

zu Eulenburg, P., U. Baumgartner, R. D. Treede and M. Dieterich (2013). "Interoceptive and multimodal functions of the operculo-insular cortex: tactile, nociceptive and vestibular representations." Neuroimage 83: 75-86.

zu Eulenburg, P., S. Caspers, C. Roski and S. B. Eickhoff (2012). "Meta-analytical definition and functional connectivity of the human vestibular cortex." Neuroimage 60(1): 162-169.

Chapter 5 Mixed out-of-body and heautoscopic experiences of epileptic origin associated with a developmental venous anomaly and a focal cortical micro-dysplasia of the left angular gyrus

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Bullet points

Heautoscopy is a rare syndrome where bodily self-consciousness is affected.

In heautoscopy, self-location is shared between a real and an illusory body.

Heautoscopy is reported to be associated with focal cortical microdysplasia.

Heautoscopy may be linked to left angular gyrus lesions.

Focal cortical microdysplasia can be associated to a developmental venous anomaly.

Abstract

We explored the case of EM, a young female 15 years old patient, treated for partial seizures, happening several times a day at the onset of the disease. Each seizure episode lasted between 1 and 2 minutes and associated typical symptoms of mesial epilepsy (absences seizures, epigastric sensations) with a rare disorder of somatognosia called heautoscopy (HAS). Interestingly, symptoms were fully cured by the introduction of a medical antiepileptic treatment, removed progressively after 2 years. Brain imaging showed the presence of a Developmental Venous Anomaly (DVA) in the left angular gyrus, a multisensory region important in bodily self-consciousness. Lesions of angular gyrus have been linked to disorders of somatognosia. A cortical micro-dysplasia was observed in the vicinity of the DVA. The epileptogenicity of DVAs is still debated but previous studies report cases of DVAs associated with complex partial seizures and histological brain changes even in the absence of bleeding event.

1. Introduction

Disorders of somatognosia characterized by visual body reduplication can happen transiently in healthy humans or patients with neurological conditions and affect the two main components of bodily self-consciousness: self-location and self-identification. Three categories of alterations of bodily self-consciousness have been identified and described (Brugger, 2002; Mohr and Blanke, 2005) according to their respective phenomenology, their associations to specific clinical context and brain regions that are affected: out-of-body experience (OBE), autoscopic hallucination

(AH) and heautoscopy (HAS). HAS represents an intermediate form between OBE and AH. A patient experiencing HAS sees himself or his double in the extrapersonal space with a difficulty to disentangle if the self is located within his body or hallucinated from the virtual body location. It has been also frequently reported in HAS an alternation from those two different visuo-spatial perspectives: from the physical body or from the duplicated body (Blanke et al., 2004). In OBE, the disembodiment predominates as the self is located in the virtual body's location where the subject sees his physical body from an elevated perspective while in AH the self localization stays within the physical body; in AH the visual component is the major component of the percept and the subject sees himself or a double in the extrapersonal space. HAS is predominantly characterized by the ambiguous localization of the self (Blanke and Mohr, 2005; Brugger et al., 2006, 1994). In AH self-processing (agency, visuo-spatial perspective and self-other distinction) is preserved. AH has been commonly associated to extra striate body area (Astafiev et al., 2004; Downing et al., 2001). But OBEs have been repeatedly associated with brain lesions or transient disturbances in the inferior parietal lobule, commonly described as temporo-parietal junction (TPJ), mainly the angular gyrus (AG), the supramarginal gyrus (SMG) and the posterior part of the superior temporal gyrus (STG) (Blanke, 2004; Blanke et al., 2004, 2002b, 2000; Brugger, 1997; Brugger et al., 2006, 1994; De Ridder et al., 2007; Heydrich and Blanke, 2013; Heydrich et al., 2010, 2011; Ionta et al., 2011). As the 3d person perspective or alter-ego perspective dominates in OBE, they have been associated with right TPJ while HAS is more commonly associated with pathological activity related to left TPJ.

Different medical neurological conditions, general (encephalitis, intoxications, general anaesthesia) or more focal (mainly epilepsy and more rarely brain trauma, migraine, tumour) have been described as aetiologies of autoscopic phenomena (Blanke et al., 2004; Bünning and Blanke, 2005). Focal epilepsy on the right parietal lobe has been reported to be associated to heautoscopy (Anzellotti et al., 2011), or also autoscopy at the postictal phase has been observed (Tadokoro et al., 2006) but parietal lobe epilepsy manifested with autoscopic phenomena stay a more rare phenomenon according to previous reviews (Brandt et al., 2005; Salanova et al., 1995; Sveinbjornsdottir and Duncan, 1993).

Development Venous Anomaly (DVA) clinical expression is still a controversial topic as some authors found them to be epileptogenic only in cases of secondary complications, mostly haemorrhagic, or with a concomitant presence of cavernoma or cortical dysplasia. It is also a common incidental finding in healthy people, up to 2.6% in a series of 4’069 brain autopsies (Sarwar and McCormick, 1978). Nevertheless, DVA without complications seem sometimes the only candidate of a pathological condition whether a causal link is difficult to establish, and questions the limit about spatial resolution of the radiological diagnosis. Moreover, in some cases, DVA can also be associated with cortical dysplasia, common source of epilepsy (Madan and Grant, 2009).

2. Case presentation

We present the case of EM, is a 15-year-old female, right handed and French native speaker patient that we first examined in the Neurology Department of

Geneva. She suffered her first partial complex seizures for a year. The habitual seizure frequency (in the absence of any antiepileptic medical treatment) during the first 7 months course of the disease was of 3-4 crisis per day, following a stereotypical semiology that was reported as follows by the patient: her typical seizures start like classical mesial seizures, with an epigastric sensation (described as a "boule dans le ventre", a "ball inside the belly"). She describes this feeling as starting from the level of the stomach then ascending to reach the upper thorax behind the sternal line (she added that the sensation reminded her as if she were taking a roller coaster and there is a sudden bump downwards). Some chills and a feeling of heat accompany it, and it was also associated with an impossibility of talking with her mates if some are present. She reports being still able to perceive voices as if she would be in a crowd but somehow less understandable, and loosing ability to interact at this time with language production.

This is immediately followed by a sudden vision of her own body "from outside". It occurs almost with each seizure, several times a day, before the introduction of the treatment. She defined her self-location as "in front of herself", as if she would be outside of her own physical body and facing it; she sees her body in the position she was in before the seizure (either standing or sitting (one seizure happened when she was lying on the bed but she does not remember if she was feeling like floating in the air). She also describes to see her immediate environment (she quotes the bench where she was eventually sitting, the trees, or the room), while she does not explain it to be duplicated. If human beings surrounded her before the seizure, there are not seen anymore from the autoscopic body location. Nevertheless, astonishingly, while she explains the new self-location seems to be inside the autoscopic body location, her description contradicts herself, as she still hears voices around her (again, she actually reports a self-location within the real body by explaining those details), but cannot respond verbally or interact. The body she sees is always immobile and always with eyes opened ("Je me vois comme bloquée", "I see myself as blocked"). She cannot interact with the body she sees. The impression is a view of her whole body image at 2 meters distance, not lateralized, and not partial. She describes the body seen with details corresponding to her real physical body characteristics before the seizure (colour, necklace, clothes, all identical to what she is actually wearing) but without details on limbs shapes. She describes this feeling as not really scary: the first times she just felt "bizarre", "not normal" but without describing any strong positive or negative emotional component. There is never any feeling of progressive disembodiment or vertiginous gravitational or rotatory sensations associated. It never occurred while she was walking. It only happened once when she was lying but only with the visceral heating feeling without autoscopic phenomena further.

3. Methods

3.1 Neuropsychology and paraclinical investigations

Clinical routine neuropsychological batteries of tests, testing number sense, word reading, writing, and executive control were performed. A drawing of her experiences was asked to the patient while she was still having daily crisis episodes. Electroencephalographic (EEG) clinical evaluation awake and by night monitoring were also done during a short hospital stay.

3.2 Neuroimaging

Magnetic Resonance Imaging acquisition was performed on a 3 Tesla MR scanner (Trio, Siemens, Erlangen, Germany) using a 32-multichannel receiver head coil. The imaging protocol included a pre-gadolinium MP2RAGE acquisition (TR/TE = 5000/2.84 ms, inversion times TI1 = 700 ms and TI2 = 2500 ms, FA1 = 4°, FA2 = 5°). The MP2RAGE is a 3-dimensional (3D) magnetization-prepared rapid gradient echo derivative providing homogeneous T1 weighting and simultaneous T1 mapping MP2RAGE and to obtain improved grey to white matter contrast in respect to conventional T1-w protocols (Marques et al., 2010). It was completed by clinical routine sequences including 3D fluid-attenuated inversion recovery or FLAIR, Diffusor Tensor Imaging or DTI, T2 1mm in coronal and axial plane passing by the parietal lesion and the hippocampus, Willis Polygon time of flight MRI arteriography and post-gadolinium arterial 3D volumetric, high-resolution T1-weighted Magnetization Prepared Rapid Gradient Echo or MPRAGE before and after intravenous injection of Gadolinium (TR/TE = 2300/2.84 ms, inversion time TI = 900 ms, voxel size = 1×1×1.2 mm^3, matrix size = 256×240×160). DTI was acquired in the axial plane with diffusion sensitization gradients applied in six non – collinear directions with b-value of $1000s/mm^2$.

4. Results

4.1 Neuropsychology

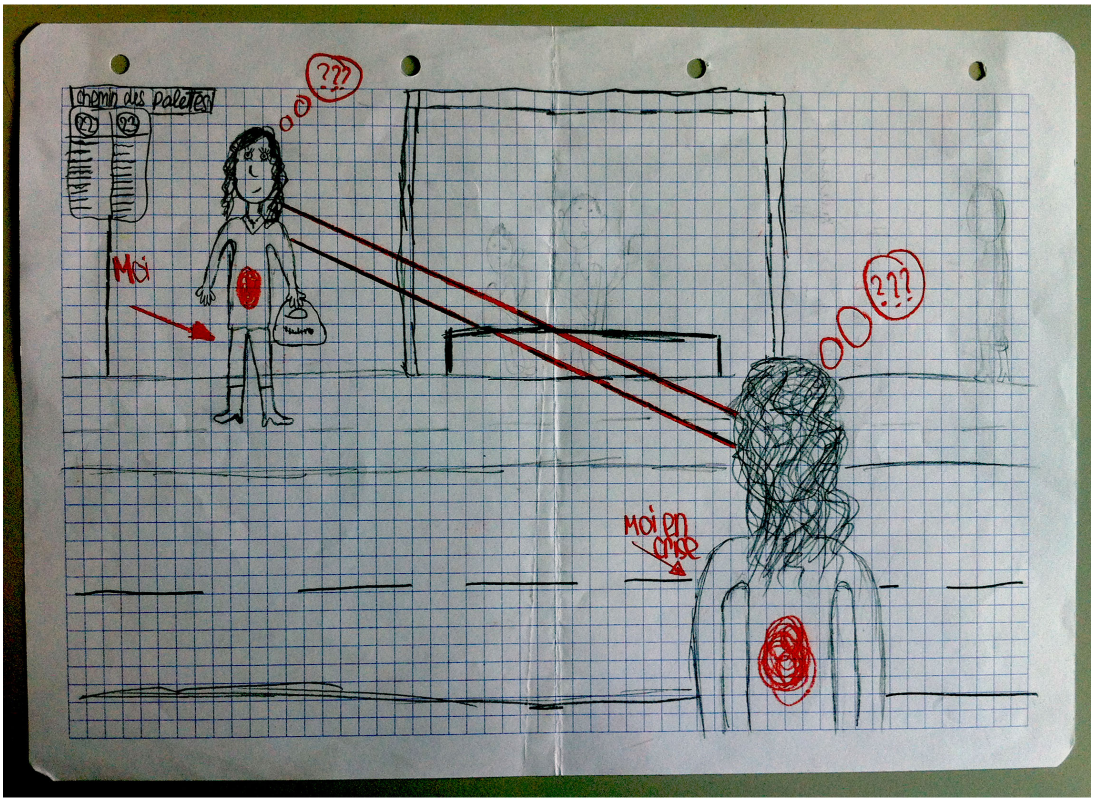

Figure 1: Graphical representation of her symptoms by the patient showing disembodied location with ambiguous shared self-location in the physical and in the illusory body, and also hesitating self-identification to one of the two bodies.

Neuropsychological tests did not show any deficit in any cognitive functions. The drawing made by EM (figure 1) is evoking the same ambiguity as in her description about her self-location: sometimes in the autoscopic body, sometimes in her real body. It emphasises the strong ambiguity about the actual self-location and self-identification during the seizure that we noticed during the interviews. She writes "moi" ("me") to designate both physical and autoscopic body and both seem to look at each other and being surprised of their mutual presence (represented by interrogation points). She indicates "moi en crise" ("me in crisis") on the autoscopic body, located on the other side of the street than her real body, and it is drawn as less dark than the real body, as if it looks less real than her real body. The real body is represented as surrounded by her environment before the crisis (bus stop, bench, people also rendered as blurred and half real - half inexistent, similar to her oral description).

4.2 Neuroimaging

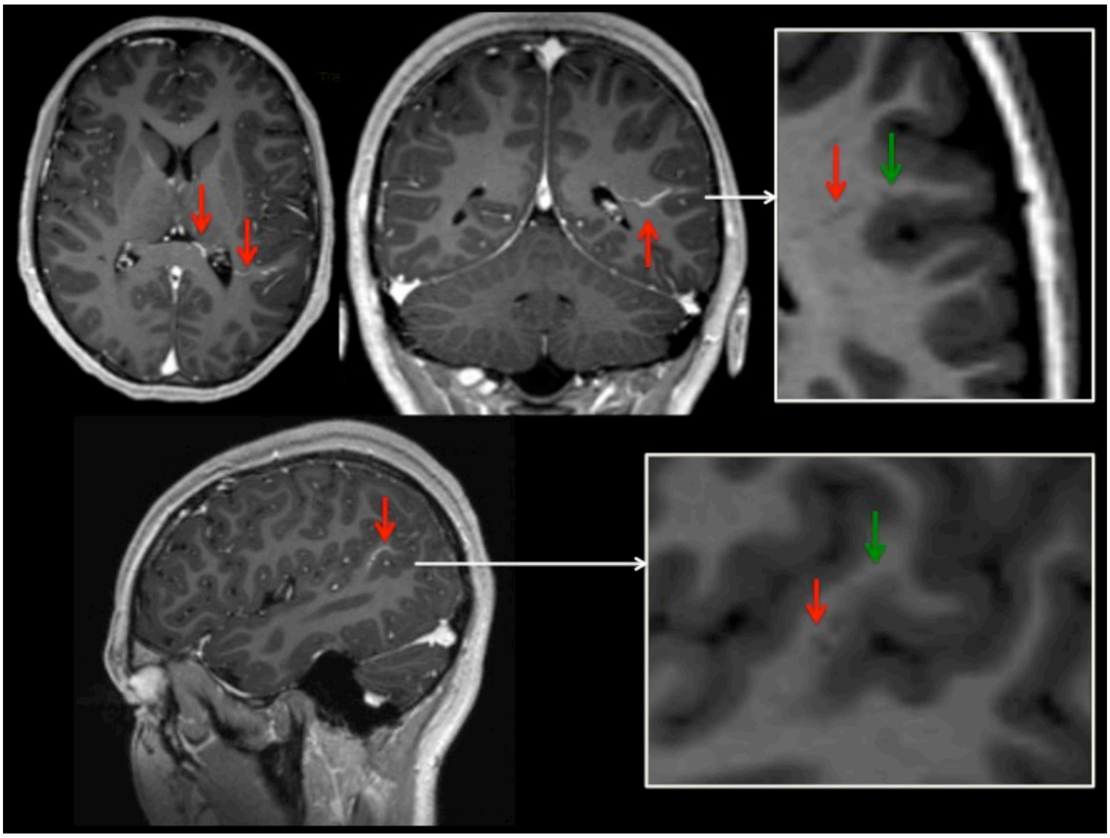

Figure 2: Left angular DVA, visible in MPRAGE Coronal, axial and sagittal slices (left side) after Gadolinium enhancement showing the DVA in hypersignal T1 and before Gadolinium enhancement showing the DVA in hyposignal T1 and the cortical microdysplasia as irregular cortical ribbon ill defined with the subcortical white matter (zoomed images, on the right side). The DVA is running from left angular gyrus, then anteriorly between supramarginal and STG then going with an orthogonal pathway to the deep white matter, and finally drained in the left cerebral internal vein.

The MRI scanner showed a locus of focal cortical microdysplasia (Figure 2). It was located on the inferior part of the left angular gyrus, between the superior and the superior margin of posterior part of the horizontal part of STG and the ascending branch of lateral fissure leading to SMG, with those veins draining white matter immediately under the cortical layer at this location, also described as *sulcus intermedius primus* (of Jensen), and which separates the inferior parietal lobule into supramarginal (anterior and upper) and angular (posterior) gyri (Duvernoy 1991, Destrieux, Fischl et al. 2010). Interestingly, we observed in direct contact with this cortical anomaly the presence of a Developmental Venous Anomaly (DVA) with a '*caput medusae*' typical shape located. In this study, we found no proof of white matter lesions unspecific lesions surrounding the focal microdysplastic cortical ribbon as FLAIR and T2 sequences did not shown any hyperintensity signal in the surrounding white matter. The locus of cortical microdysplasia appeared under the appearance of blurred grey-white matter delineation, with grey matter irregularities of the deepest cortical layer in angular gyrus. It consisted in gyral irregularity in continuity to the cortical ribbon immediately under the DVA vessels and appearing as an increased T1 and decreased T2 subcortical signal. On the most medial part of the cortical sulcus affected, we noticed the infiltration of the cortex and subcortical white matter by the venous anomaly, appearing under the form of a hyperintense line in unified maps on MP2RAGE and T1-w images. The venous collector was then going to the deep white matter, and drained in the left cerebral internal vein, before the junction with the great vein of Galen, making this DVA in the category of deep DVA compared to those draining in pial veins. No stenosis or obstruction of the collecting vein was observed, and no calcification, no cavernous angioma or acute or chronic haemorrhage could be identified in gradient echo sequences with T2*-weighting. We did not identify any expansive intra or extra-axial mass, no hydrocephaly, no pathological enhancement, no hippocampal atrophy or morphologic abnormality, no acute or chronic ischemic lesion and no brain haemorrhage. No cortical, subcortical or subependymal ectopic grey matter was identified. No other cortical sulcation or gyration disorder was observed.

4.3 Other paraclinical investigations

Electroencephalographic (EEG) clinical evaluation awake and by night monitoring was performed and did not show any focal seizure at the time where the investigation was performed 6 months after the onset of the symptoms. All clinical examination including cardiac, oncologic and neurological care came back negative. Only the hyperventilation test during 60 seconds evoked to the patient the feeling of prodromal symptoms with epigastric and thoracic heating feeling but without triggering of autoscopic hallucination.

4.4 Treatment and follow-up

The patient started to be treated by her neurologist after clinical and paraclinical investigations 7 months after initial appointment. Since beginning of her symptoms, the patient faced more and more troubles described as attentional deficits and social conflicts at school. After first MRI and EEG exams failed to find a constitutive brain epileptic source, she benefited of a test treatment for epilepsy with complex partial seizures without secondary generalization. A significant drop of these autoscopic episodes started after she began medical treatment with Keppra (Levetiracetam). Due to important side effects, the medication was rapidly switched to Lamictal (Lamotrigine) with following pattern: Lamotrigine, 100mg-0-100mg, then switched to 100mg-0-125mg after 6 months, to reach 100mg-0-150mg one week later, until a prolonged 150mg-0-150mg pattern during one year. After 2 years and a progressive reduced treatment pattern and with successful dramatic drop of seizures incidence, the treatment was totally stopped and the patient is still free of seizure 2 years after the treatment stopped.

5. **Discussion**

Our patient was affected by typical mesial focal seizures signs with epigastric heat feelings, then followed by the apparition of an autoscopic body, with a 'partial' disembodiment: self-location and self-identification, 2 key ingredients of bodily-self consciousness, seemed to be shared between the autoscopic body and real body. In fact, our patient feelings' compete between self-identification and self-location with the double and with the real body. Sometimes she felt her surrounding environment as before the onset of the crisis (that would explain that her self-location did not change and that the new body she sees is a autoscopic double in front of her physical body), and at the same time, she told us that she sees herself from outside her real body, from the autoscopic body perspective.

Our case corresponds to one of the very rare cases linking heautoscopy and epilepsy, with a particular semiology. The causality of an epileptic context has been established by the disappearance of the symptoms with the introduction of the antiepileptic treatment and by the discovery of a focal cortical microdysplasia in the left angular gyrus. Following semiological descriptions as in Blanke and Mohr (Blanke and Mohr 2005), visual hallucinations were dominant and tactile and auditory percepts were reduced compared to her normal state. Body scheme disturbances were present, with associated neurological signs mainly interoceptive visceral sensations ("bawl in the stomach") similar to motion sickness and intra-thoracic pressure. Vestibular hallucinations were not present but interoceptive visceral feelings are closed to early feelings during vestibular experiences. The autoscopic body was always standing like in most cases of HAS and AH, and the physical body was always sitting or standing when the symptoms occurred, while only 30% of OBE occur when patients were sitting or standing. The bilocation was reported orally and by the drawing, which is the most common characteristic of HAS. Typically, no positive emotions have been reported but more negative emotions in first episodes, with adaptation leading to neutral emotions as the seizures became frequent and the patient anticipated what would happen. It was experienced as highly realistic as common in OBE and HAS. As most of other cases of the 3 forms of autoscopic phenomena, epileptic seizure was the diagnosis associated. Lesion side was on the left, common for more than 50% of HAS but not in AH or OBE. Temporo parietal lesion location was common for both HAS and OBE, while occipital lesions are more associated with AH (60%). This case shows a mixed symptomatology of OBE and HAS:

a. Typically for HAS:

- the disembodiment was not felt with strong vestibular feelings as it occurs in OBE,

- the self-location seems to be shared between the two bodies which is typical for HAS,
- the axis of disembodiment is more typical for heautoscopic phenomenon than for OBE as it happens in upright position.

b. Not typical for HAS:

- the autoscopic body was always seen in front-view (face to face), which is systematic in AH and almost always in OBE but rarely in HAS,

- no actions of the heautoscopic body have been reported, which is normally happening in 80% of HAS cases, but stays uncommon in AH and absent in OBE. Sharing of thoughts, words and actions seemed limited to questioning about the actual self-location and the strangeness of the situation.

In general, idiopathic epilepsy in teenagers show a good response to the medical treatment and this one can be suspended after long-interval remission of the disease, as in this case (Camfield and Camfield, 2002; Scheidegger et al., 2013). But in majority of cases, focal cortical dysplasia is difficult to manage with medical treatment and surgery is required (Kabat and Król, 2012), which was not the case for our patient.

This case challenged both our conventional views on DVAs and focal cortical microdysplasia. In most of cases, DVAs are chance findings on MRI routine exams, without symptomatology (except rare cases of haemorrhagic events or associated cavernous angiomas). They may be associated to a cortical dysplasia. Pattern of cortical dysplasia cannot be considered as a unified entity, while it extends from very mild lesions called microdysgenesis or microdysplasia under usual radiological detectability thresholds, to huge cortical rearrangement (Colombo et al., 2003). Abnormal dysplastic cortical ribbon may be epileptogenic but under diagnosed in daily practice with resolution obtained by conventional radiological investigations at 1.5 and 3T for such cases of microdysgenesis or when the EEG results do not help orientate the research of cortical abnormalities (Madan and Grant, 2009). In our patient, the very small cortical irregularity in the vicinity of DVA *caput medusae* could be easily missed with standard routine examination and in the absence of orienting symptoms towards left TPJ. Here, we did manage to identify cortical dysplasia at a location coherent with temporo-parietal junction lesions associated with autoscopic phenomena and OBEs in previous literature. More precisely, the left hemisphere, where we found the cortical lesion and the DVA, has been the main identified candidate for heautoscopic phenomena in previous casuistic (Heydrich et al., 2010; Ionta et al., 2011). HAS has been associated with visceroceptive phenomena, usually absent in OBE, and with lesion on the left hemisphere (in posterior insula in Heydrich et al. 2013) while right hemisphere lesions, but more posterior in inferior parietal lobule, at the angular gyrus location, have been associated to OBE. Interestingly, the semiology of the patient is shared between OBE features and HAS features that could be explained by the location of the cortical lesion, on the left hemisphere (more typical for heautoscopic phenomena see Heydrich et al. 2013) but on the angular gyrus (more typical for OBE phenomena, see Blanke et al 2002).

The potentiality of DVA to lead to seizures is still debated. In general, some authors refuse the idea of a link between DVAs and epilepsy, based on the absence of epilepsy in most of people with brain DVAs (Morioka et al., 1999; Striano et al., 2000). Of course, DVAs may be associated with surrounding gliosis or hemosiderin following a microscopic bleeding event that contributes to the onset of epileptic disease (Rammos et al., 2009). But even in the apparent absence of macroscopic grey matter abnormalities diagnosed as focal cortical microdysplasia, recent works also claim for an association between DVA and epilepsy cases (Andrea et al., 2015; Scheidegger et al., 2013). Rare post-mortem pathological descriptions of DVA reveal the existence of abnormalities in adjacent brain tissue underestimated by radiological conventional techniques. An historical pathological reports from Noran et al. (Noran, 1945) speaks about "demyelination, degenerative alterations of nerve cells, gliosis and leukomalacia (…)" around DVAs, as quoted by San Millan Ruiz and Gailloud (San Millán Ruíz and Gailloud, 2010), which is in the same line with documented reports of white matter abnormalities on CT and MRI studies around DVAs (San Millan Ruiz et al., 2007). Such microscopic neural changes unseen with routine MRI and CT exams could be the source of seizures even in the absence of obvious macroscopic focal cortical dysplasia.

6. Consent

Written consent was obtained from the patient for publication of this case report and accompanying images.

7. Conflict of interest statement

None of the authors has any conflict of interest to disclose.

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References

Aglioti, S., Smania, N., Manfredi, M., Berlucchi, G., 1996. Disownership of left hand and objects related to it in a patient with right brain damage. Neuroreport 8, 293–296.

André, J.M., Martinet, N., Paysant, J., Beis, J.M., Le Chapelain, L., Andre, J.M., Martinet, N., Paysant, J., Beis, J.M., Le Chapelain, L., 2001. Temporary phantom limbs evoked by vestibular caloric stimulation in amputees. Neuropsychiatry Neuropsychol Behav Neurol 14, 190–196.

Andrea, Š.K., Jakov, M., Nikola, G., 2015. Epilepsy in a boy with a developmental venous anomaly-case-based update. Childs. Nerv. Syst. doi:10.1007/s00381-015-2663-0

Angelaki, D.E., Gu, Y., Deangelis, G.C., 2011. Visual and vestibular cue integration for heading perception in extrastriate visual cortex. J Physiol 589, 825–833. doi:10.1113/jphysiol.2010.194720

Anzellotti, F., Onofrj, V., Maruotti, V., Ricciardi, L., Franciotti, R., Bonanni, L., Thomas, A., Onofrj, M., 2011. Autoscopic phenomena: case report and review of literature. Behav Brain Funct 7, 2. doi:10.1186/1744-9081-7-2

Arzy, S., Seeck, M., Ortigue, S., Spinelli, L., Blanke, O., 2006. Induction of an illusory shadow person. Nature 443, 287. doi:10.1038/443287a

Aspell, J.E., Lenggenhager, B., Blanke, O., 2009. Keeping in touch with one's self: multisensory mechanisms of self-consciousness. PLoS One 4, e6488.

Astafiev, S. V, Stanley, C.M., Shulman, G.L., Corbetta, M., 2004. Extrastriate body area in human occipital cortex responds to the performance of motor actions. Nat Neurosci 7, 542–548. doi:10.1038/nn1241

Beer, J., Blakemore, C., Previc, F.H., Liotti, M., 2002. Areas of the human brain activated by ambient visual motion, indicating three kinds of self-movement. Exp Brain Res 143, 78–88. doi:10.1007/s00221-001-0947-y

Berthoz, A., Pavard, B., Young, L.R., 1975. Perception of linear horizontal self-motion induced by peripheral vision (linearvection) basic characteristics and visual-vestibular interactions. Exp Brain Res 23, 471–489.

Bisiach, E., Rusconi, M.L., Vallar, G., 1991. Remission of somatoparaphrenic delusion through vestibular stimulation. Neuropsychologia 29, 1029–1031. doi:0028-3932(91)90066-H [pii]

Blanke, O., 2004. Out of body experiences and their neural basis. Bmj 329, 1414–1415.

Blanke, O., Landis, T., Seeck, M., 2000. Electrical cortical stimulation of the human prefrontal cortex evokes complex visual hallucinations. Epilepsy Behav. 1, 356–361. doi:10.1006/ebeh.2000.0109

Blanke, O., Landis, T., Spinelli, L., Seeck, M., 2004. Out-of-body experience and autoscopy of neurological origin. Brain 127, 243–258. doi:10.1093/brain/awh040

Blanke, O., Metzinger, T., 2009. Full-body illusions and minimal phenomenal selfhood. Trends Cogn. Sci. 13, 7–13. doi:10.1016/j.tics.2008.10.003

Blanke, O., Mohr, C., 2005. Out-of-body experience, heautoscopy, and autoscopic hallucination of neurological origin Implications for neurocognitive mechanisms of corporeal awareness and self-consciousness. Brain Res. Brain Res. Rev. 50, 184–99. doi:10.1016/j.brainresrev.2005.05.008

Blanke, O., Ortigue, S., Landis, T., Seeck, M., 2002a. Stimulating illusory own-body perceptions. Nature 419, 269–270. doi:10.1038/419269a

Blanke, O., Ortigue, S., Landis, T., Seeck, M., 2002b. Stimulating illusory own-body perceptions. Nature 419, 269–70. doi:10.1038/419269a

Bottini, G., Bisiach, E., Sterzi, R., Vallar, G., 2002. Feeling touches in someone else's hand. Neuroreport 13, 249–252.

Botvinick, M., Cohen, J., 1998. Rubber hands "feel" touch that eyes see. Nature 391, 756.

Brandt, C., Brechtelsbauer, D., Bien, C.G., Reiners, K., 2005. [Out-of-body experience as possible seizure symptom in a patient with a right parietal lesion]. Nervenarzt 76, 1259,1261–1262. doi:10.1007/s00115-005-1904-y

Brandt, T., Bartenstein, P., Janek, A., Dieterich, M., 1998. Reciprocal inhibitory visual-vestibular interaction. Visual motion stimulation deactivates the parieto-insular vestibular cortex. Brain 121 (Pt 9, 1749–1758.

Bresciani, J.P., Blouin, J., Popov, K., Bourdin, C., Sarlegna, F., Vercher, J.L., Gauthier, G.M., 2002. Galvanic vestibular stimulation in humans produces online arm movement deviations when reaching towards memorized visual targets. Neurosci Lett 318, 34–38. doi:S0304394001024624 [pii]

Brugger, P., 2002. Reflective mirrors: perspective-taking in autoscopic phenomena. Cogn. Neuropsychiatry 7, 179–194.

Brugger, P., 1997. Illusory reduplication of one's own body: phenomenology and classification of autoscopic phenomena. Cogn. Neuropsychiatry 2, 19–38.

Brugger, P., Agosti, R., Regard, M., Wieser, H.G., Landis, T., 1994. Heautoscopy, epilepsy, and suicide. J Neurol Neurosurg Psychiatry 57, 838–839.

Brugger, P., Blanke, O., Regard, M., Bradford, D.T., Landis, T., 2006. Polyopic heautoscopy: Case report and review of the literature. Cortex 42, 666–674.

Bünning, S., Blanke, O., 2005. The out-of-body experience: precipitating factors and neural correlates. Prog Brain Res 150, 333–353.

Camfield, P., Camfield, C., 2002. Epileptic Syndromes in Childhood: Clinical Features, Outcomes, and Treatment. Epilepsia 43, 27–32. doi:10.1046/j.1528-1157.43.s.3.3.x

Cavanna, A.E., Trimble, M.R., 2006. The precuneus: a review of its functional anatomy and behavioural correlates. Brain 129, 564–583. doi:awl004 [pii] 10.1093/brain/awl004

Colombo, N., Tassi, L., Galli, C., Citterio, A., Lo Russo, G., Scialfa, G., Spreafico, R., 2003. Focal Cortical Dysplasias: MR Imaging, Histopathologic, and Clinical Correlations in Surgically Treated Patients with Epilepsy. AJNR Am. J. Neuroradiol. 24, 724–733.

Crick, F., 1994. The astonishing hypothesis : the scientific search for the soul. Scribner ; Maxwell Macmillan International, New York.

De Ridder, D., Van Laere, K., Dupont, P., Menovsky, T., Van de Heyning, P., 2007. Visualizing out-of-body experience in the brain. N. Engl. J. Med. 357, 1829–1833. doi:10.1056/NEJMoa070010

DeAngelis, G.C., Angelaki, D.E., 2012. Visual-Vestibular Integration for Self-Motion Perception, in: Murray, M.M., Wallace, M.T. (Eds.), The Neural Bases of Multisensory Processes. Boca Raton (FL).

Dehaene, S., Naccache, L., 2001. Towards a cognitive neuroscience of consciousness: basic evidence and a workspace framework. Cognition 79, 1–37. doi:S0010-0277(00)00123-2 [pii]

Dennett, D.C., 2015. Why and How Does Consciousness Seem the Way it Seems ? 10. doi:10.15502/9783958570245

Dennett, D.C., 1991. Consciousness explained, 1st ed. Little, Brown and Co., Boston.

Deutschländer, A., Bense, S., Stephan, T., Schwaiger, M., Dieterich, M., Brandt, T., Deutschlander, A., Bense, S., Stephan, T., Schwaiger, M., Dieterich, M., Brandt, T., 2004. Rollvection versus linearvection: comparison of brain activations in PET. Hum Brain Mapp 21, 143–153. doi:10.1002/hbm.10155

Dichgans, J., Brandt, T., 1978. Visual-vestibular interaction: effects on self-motion perception and postural control, in: Held, R., Leibowitz, H.W., Teuber, H.-L. (Eds.), Handbook of Sensory Physiology. Springer-Verlag, pp. 755–804.

Downing, P.E., Jiang, Y., Shuman, M., Kanwisher, N., 2001. A cortical area selective for visual processing of the human body. Science (80-.). 293, 2470–2473. doi:10.1126/science.1063414

Ehrsson, H.H., 2007. The experimental induction of out-of-body experiences. Science 317, 1048. doi:10.1126/science.1142175

Eickhoff, S.B., Schleicher, A., Zilles, K., Amunts, K., 2006. The human parietal operculum. I. Cytoarchitectonic mapping of subdivisions. Cereb Cortex 16, 254–267. doi:bhi105 [pii] 10.1093/cercor/bhi105

Ferrè, E.R., Bottini, G., Iannetti, G.D., Haggard, P., 2013. The balance of feelings: Vestibular modulation of bodily sensations. Cortex 49, 748–758. doi:10.1016/j.cortex.2012.01.012

Ferre, E.R., Lopez, C., Haggard, P., 2014. Anchoring the Self to the Body: Vestibular Contribution to the Sense of Self. Psychol Sci. doi:10.1177/0956797614547917

Ferre, E.R., Sedda, A., Gandola, M., Bottini, G., 2010. How the vestibular system modulates tactile perception in normal subjects: a behavioural and physiological study. Exp Brain Res. doi:10.1007/s00221-010-2450-9

Ferre, E.R., Vagnoni, E., Haggard, P., 2013. Vestibular contributions to bodily awareness. Neuropsychologia 51, 1445–1452. doi:10.1016/j.neuropsychologia.2013.04.006

Fetsch, C.R., Pouget, A., DeAngelis, G.C., Angelaki, D.E., 2012. Neural correlates of reliability-based cue weighting during multisensory integration. Nat Neurosci 15, 146–154. doi:10.1038/nn.2983

Fetsch, C.R., Pouget, A., DeAngelis, G.C., Angelaki, D.E., 2011. Neural correlates of reliability-based cue weighting during multisensory integration. Nat. Neurosci. doi:10.1038/nn.2983

Glasser, M.F., Van Essen, D.C., 2011. Mapping human cortical areas in vivo based on myelin content as revealed by T1- and T2-weighted MRI. J Neurosci 31, 11597–11616. doi:31/32/11597 [pii] 10.1523/JNEUROSCI.2180-11.2011

Goldberg JM and Cullen KE, W.V.J., 2012. The Vestibular System: A Sixth Sense. Oxford Univ. Press.

Halligan, P.W., Marshall, J.C., Wade, D.T., 1995. Unilateral somatoparaphrenia after right hemisphere stroke: a case description. Cortex 31, 173–182.

Heydrich, L., Blanke, O., 2013. Distinct illusory own-body perceptions caused by damage to posterior insula and extrastriate cortex. Brain 136, 790–803. doi:10.1093/brain/aws364

Heydrich, L., Dieguez, S., Grunwald, T., Seeck, M., Blanke, O., 2010. Illusory own body perceptions: case reports and relevance for bodily self-consciousness. Conscious Cogn 19, 702–710. doi:S1053-8100(10)00130-3 [pii] 10.1016/j.concog.2010.04.010

Heydrich, L., Lopez, C., Seeck, M., Blanke, O., 2011. Partial and full own-body illusions of epileptic origin in a child with right temporoparietal epilepsy. Epilepsy Behav 20, 583–586. doi:S1525-5050(11)00011-4 [pii] 10.1016/j.yebeh.2011.01.008

Ionta, S., Heydrich, L., Lenggenhager, B., Mouthon, M., Fornari, E., Chapuis, D., Gassert, R., Blanke, O., 2011. Multisensory mechanisms in temporo-parietal cortex support self-location and first-person perspective. Neuron 70, 363–374. doi:S0896-6273(11)00200-5 [pii] 10.1016/j.neuron.2011.03.009

Kabat, J., Król, P., 2012. Focal cortical dysplasia - review. Pol. J. Radiol. 77, 35–43.

Kleinschmidt, A., Thilo, K. V, Buchel, C., Gresty, M.A., Bronstein, A.M., Frackowiak, R.S., 2002. Neural correlates of visual-motion perception as object- or self-motion. Neuroimage 16, 873–882.

Knox, J.J., Coppieters, M.W., Hodges, P.W., 2006. Do you know where your arm is if you think your head has moved? Exp Brain Res 173, 94–101. doi:10.1007/s00221-006-0368-z

Kovács, G., Raabe, M., Greenlee, M.W., 2008. Neural correlates of visually induced self-motion illusion in depth. Cereb. Cortex 18, 1779–1787. doi:10.1093/cercor/bhm203

Le Chapelain, L., Beis, J.M., Paysant, J., Andre, J.M., 2001. Vestibular caloric stimulation evokes phantom limb illusions in patients with paraplegia. Spinal Cord 39, 85–87.

Lenggenhager, B., Lopez, C., 2015. Vestibular Contributions to the Sense of Body , Self , and Others. doi:10.15502/9783958570023

Lenggenhager, B., Lopez, C., Blanke, O., 2008. Influence of galvanic vestibular stimulation on egocentric and object-based mental transformations. Exp. Brain Res. 184, 211–221. doi:10.1007/s00221-007-1095-9

Lenggenhager, B., Tadi, T., Metzinger, T., Blanke, O., 2007. Video ergo sum: manipulating bodily self-consciousness. Science 317, 1096–1099. doi:10.1126/science.1143439

Lestienne, F., Soechting, J., Berthoz, A., 1977. Postural readjustments induced by linear motion of visual scenes. Exp Brain Res 28, 363–384.

Lopez, C., 2015. Vestibular Cortex, Brain Mapping: An Encyclopedic Reference. Elsevier. doi:10.1016/B978-0-12-397025-1.00227-X

Lopez, C., 2013. A neuroscientific account of how vestibular disorders impair bodily self-consciousness. Front. Integr. Neurosci. 7, 91. doi:10.3389/fnint.2013.00091

Lopez, C., Blanke, O., 2011. The thalamocortical vestibular system in animals and humans. Brain Res Rev 67, 119–146. doi:S0165-0173(11)00002-6 [pii] 10.1016/j.brainresrev.2010.12.002

Lopez, C., Blanke, O., Mast, F.W., 2012. The human vestibular cortex revealed by coordinate-based activation likelihood estimation meta-analysis. Neuroscience 212, 159–179. doi:10.1016/j.neuroscience.2012.03.028 S0306-4522(12)00289-8 [pii]

Lopez, C., Halje, P., Blanke, O., 2008. Body ownership and embodiment: vestibular and multisensory mechanisms. Neurophysiol Clin 38, 149–161. doi:S0987-7053(08)00018-X [pii] 10.1016/j.neucli.2007.12.006

Lopez, C., Lenggenhager, B., Blanke, O., 2010. How vestibular stimulation interacts with illusory hand ownership. Conscious Cogn 19, 33–47. doi:S1053-8100(09)00189-5 [pii] 10.1016/j.concog.2009.12.003

Mach, E., 1875. Grundlinien der Lehre von den Bewegungsempfindungen. Engelmann, Leipzig.

Madan, N., Grant, P.E., 2009. New directions in clinical imaging of cortical dysplasias. Epilepsia 50 Suppl 9, 9–18. doi:10.1111/j.1528-1167.2009.02292.x

Marques, J.P., Kober, T., Krueger, G., van der Zwaag, W., Van de Moortele, P.F., Gruetter, R., 2010. MP2RAGE, a self bias-field corrected sequence for improved segmentation and T-1-mapping at high field. Neuroimage 49, 1271–1281. doi:Doi 10.1016/J.Neuroimage.2009.10.002

Mars, F., Archambault, P.S., Feldman, A.G., 2003. Vestibular contribution to combined arm and trunk motion. Exp Brain Res 150, 515–519. doi:10.1007/s00221-003-1485-6

Mazzola, L., Lopez, C., Faillenot, I., Chouchou, F., Mauguiere, F., Isnard, J., 2014. Vestibular responses to direct stimulation of the human insular cortex. Ann Neurol. doi:10.1002/ana.24252

Mohr, C., Blanke, O., 2005. The demystification of autoscopic phenomena: experimental propositions. Curr Psychiatry Rep 7, 189–195.

Morioka, T., Nishio, S., Ishibashi, H., Muraishi, M., Hisada, K., Shigeto, H., Yamamoto, T., Fukui, M., 1999. Intrinsic epileptogenicity of focal cortical dysplasia as revealed by magnetoencephalography and electrocorticography. Epilepsy Res 33, 177–187.

Noran, H.H., 1945. Intracranial vascular tumors and malformations. Arch Path 39, 393–416.

Ohshiro, T., Angelaki, D.E., DeAngelis, G.C., 2011. A normalization model of multisensory integration. Nat. Neurosci. 14, 775–782. doi:10.1038/nn.2815

Penfield, W., 1957. Vestibular sensation and the cerebral cortex. Ann Otol Rhinol Laryngol 66, 691–698.

Pfeiffer, C., Lopez, C., Schmutz, V., Duenas, J.A., Martuzzi, R., Blanke, O., 2013. Multisensory origin of the subjective first-person perspective: visual, tactile, and vestibular mechanisms. PLoS One 8, e61751. doi:10.1371/journal.pone.0061751

Pfeiffer, C., Serino, A., Blanke, O., 2014. The vestibular system: a spatial reference for bodily self-consciousness. Front Integr Neurosci 8, 31. doi:10.3389/fnint.2014.00031

Previc, F.H., Liotti, M., Blakemore, C., Beer, J., Fox, P., 2000. Functional imaging of brain areas involved in the processing of coherent and incoherent wide field-of-view visual motion. Exp Brain Res 131, 393–405.

Rammos, S.K., Maina, R., Lanzino, G., 2009. Developmental venous anomalies: current concepts and implications for management. Neurosurgery 65, 20–9; discussion 29–30. doi:10.1227/01.NEU.0000347091.06694.3E

Salanova, V., Andermann, F., Rasmussen, T., Olivier, A., Quesney, L.F., 1995. Parietal lobe epilepsy. Clinical manifestations and outcome in 82 patients treated surgically between 1929 and 1988. Brain 118 (Pt 3, 607–627.

San Millan Ruiz, D., Delavelle, J., Yilmaz, H., Gailloud, P., Piovan, E., Bertramello, A., Pizzini, F., Rufenacht, D.A., 2007. Parenchymal abnormalities associated with developmental venous anomalies. Neuroradiology 49, 987–995. doi:10.1007/s00234-007-0279-0

San Millán Ruíz, D., Gailloud, P., 2010. Cerebral developmental venous anomalies. Child's Nerv. Syst. 26, 1395–1406. doi:10.1007/s00381-010-1253-4

Sarwar, M., McCormick, W.F., 1978. Intracerebral venous angioma. Case report and review. Arch Neurol 35, 323–325.

Scheidegger, O., Wiest, R., Jann, K., König, T., Meyer, K., Hauf, M., 2013. Epileptogenic developmental venous anomaly: insights from simultaneous EEG/fMRI. Clin. EEG Neurosci. 44, 157–60. doi:10.1177/1550059412464463

Slobounov, S., Wu, T., Hallett, M., Shibasaki, H., Slobounov, E., Newell, K., 2006. Neural underpinning of postural responses to visual field motion. Biol Psychol 72, 188–197. doi:S0301-0511(05)00164-X [pii] 10.1016/j.biopsycho.2005.10.005

Smith, A.T., Wall, M.B., Thilo, K. V., 2012. Vestibular inputs to human motion-sensitive visual cortex. Cereb. Cortex 22, 1068–1077. doi:10.1093/cercor/bhr179

Striano, S., Nocerino, C., Striano, P., Boccella, P., Meo, R., Bilo, L., Cirillo, S., 2000. Venous angiomas and epilepsy. Neurol Sci 21, 151–155.

Sveinbjornsdottir, S., Duncan, J.S., 1993. Parietal and occipital lobe epilepsy: a review. Epilepsia 34, 493–521.

Tadokoro, Y., Oshima, T., Kanemoto, K., 2006. Postictal autoscopy in a patient with partial epilepsy. Epilepsy Behav 9, 535–540. doi:10.1016/j.yebeh.2006.07.003

Trutoiu, L.C., Mohler, B.J., Schulte-Pelkum, J., Bülthoff, H.H., 2009. Circular, linear, and curvilinear vection in a large-screen virtual environment with floor projection. Comput. Graph. 33, 47–58. doi:10.1016/j.cag.2008.11.008

Wiest, G., Zimprich, F., Prayer, D., Czech, T., Serles, W., Baumgartner, C., 2004. Vestibular processing in human paramedian precuneus as shown by electrical cortical stimulation. Neurology 62, 473–475.

Zu Eulenburg, P., Caspers, S., Roski, C., Eickhoff, S.B., 2012. Meta-analytical definition and functional connectivity of the human vestibular cortex. Neuroimage 60, 162–169. doi:10.1016/j.neuroimage.2011.12.032

Chapter 6 General Discussion

6.1. Summary of main results

Chapter 2: Using GVS and optokinetic stimuli, we found evidence for ubiquitous brain regions processing both vestibular and visual signals, especially in areas of inferior parietal lobule, at the temporo-parietal junction and in posterior middle temporal gyrus. All those regions are part of a vestibular network (see figure 4) made of highly multisensory cortices processing visual, vestibular and somatosensory inputs (Cardin and Smith, 2010; Frank et al., 2014; Ionta et al., 2011; Smith et al., 2012; Ventre-Dominey, 2014; Zu Eulenburg et al., 2013). When regions of inferior parietal cortex have been shown to be impaired (Blanke and Mohr, 2005; Heydrich and Blanke, 2013; Heydrich et al., 2011, 2010; Ionta et al., 2011) or are stimulated by electrical currents (Blanke et al., 2002b; Tong, 2003), some disturbances of bodily self-consciousness, altering body schema and/or body image can occur (de Vignemont, 2010).

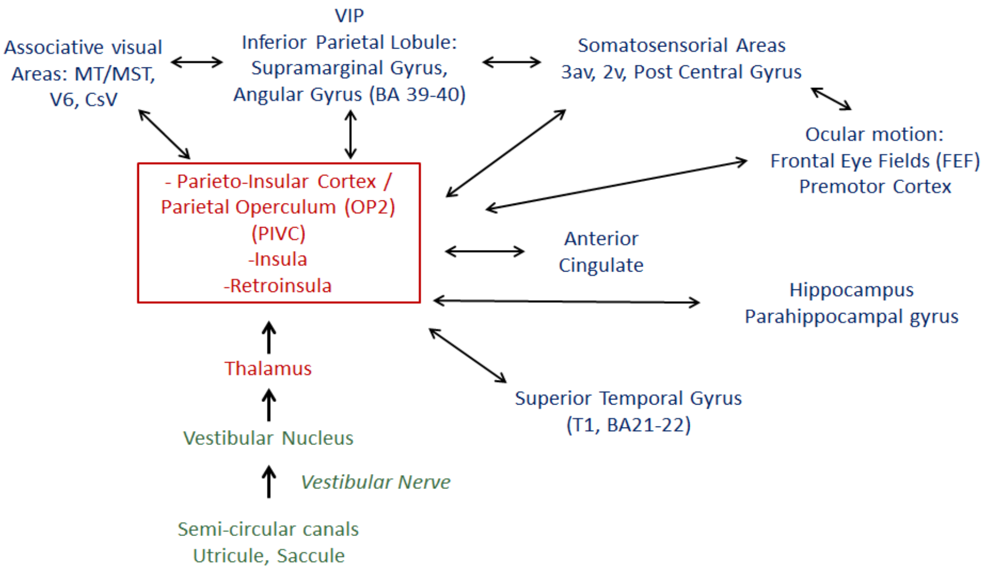

Figure 4. Schema of important relays of the vestibular neuronal network Copyright Forget Joachim, 2015

Chapter 3: We also showed that visuo-tactile integration for the embodiment of an external limb could be modulated by visuo-vestibular stimulation made of optokinetic stimuli inducing vection. When vection evoked a whole body displacement towards the rubber hand, an unconscious component of rubber hand illusion, the proprioceptive drift towards the rubber hand, is increased while the conscious experience of the illusion, the self-identification to the rubber hand is reproducible while vection is felt, but is not increased or diminished significantly by vection.

Chapter 4: Peripersonal space can be easily remapped through visuo-proprioceptive conflicts when crossing limbs over the midline, but only for superior limbs and not for inferior limbs. It emphasises again a visual dominance phenomenon over proprioceptive and somatosensory signals. It also suggests the ontological plastic nature of the body schema in peripersonal space and its ecological need for optimal processing of complex body movements for preservation of body integrity.

Chapter 5: Regions from the depth to the surface of the inferior parietal lobule are known to contribute to bodily self-consciousness, partly through multisensory processes, including visuo-vestibular mechanisms (Blanke, 2012). When a lesion occurs in those cortices, somatognosia can be affected, as in our epileptic patient showing an original and rare semiology mixed between out-of-body experiences and heautoscopy.

6.2 Overlap of neural networks for visuo-vestibular processing and bodily self-consciousness

The multisensory character of visuo-vestibulo-somatosensory pathways has been assessed at multiple levels of the nervous system in animals and in humans. Relays are identified in the vestibular nuclei, in the thalamus and in the cortex (Lopez, 2015; see figure 5).

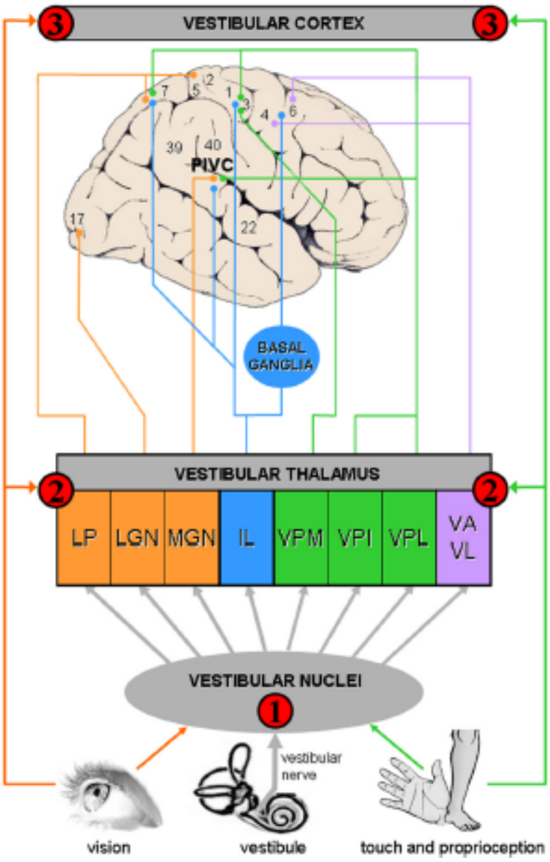

Figure 5. Convergence of vestibular, visual, and somatosensory signals in vestibulo-thalamo-cortical structures, from Lopez (2015). The schema summarizes animal and human data, showing multisensory convergence in three vestibular relays. Vestibular signals are first processed in the vestibular nuclei in the brainstem, a region that is highly multisensory. A second level of vestibular processing takes place in the thalamus. Multiple thalamic nuclei contain neurons that respond to vestibular stimulation such as the ventro posterior complex (VPM, ventral posterior medial nucleus; VPI, ventral posterior inferior nucleus; VPL, ventral posterior lateral nucleus), ventro anterior (VA) and ventro lateral (VL) nuclear complex, intralaminar nuclei (IL), thalamic posterior nuclear group (MGN, medial geniculate nucleus; LGN, lateral geniculate nucleus) and lateral posterior nucleus (LP). Most of these thalamic nuclei contain multisensory neurons. A third level of vestibular processing occurs in the cerebral cortex. Neuroimaging studies used caloric (CVS) and galvanic (GVS) vestibular stimulation and revealed activations centred on the insula, parietal operculum, and temporo-parietal junction (Lopez et al., 2012a; zu Eulenburg et al., 2012). This area may be similar to a region known as the parieto-insular vestibular cortex (PIVC) in monkeys (Grüsser et al., 1990a,b; Guldin and Grüsser 1998; Chen et al., 2010). The PIVC is considered the core region of the vestibular cortex because it is strongly connected or interconnected with most of the other vestibular cortical areas. At least 10 other cortical areas process vestibular signals including somatosensory (areas 2 and 3), superior parietal, cingulate, and premotor cortex.

Through our 7T fMRI study on visuo-vestibular convergence, we have shown the existence of multiple regions processing both visual and vestibular inputs in perisylvian areas. As seen in chapter 2, those visuo-vestibular regions seem to be distributed over a large and ubiquitous network, from extrastriate and medial temporal cortex to retroinsular cortex and parietal operculum, including also the surface of TPJ along supramarginal gyrus and angular gyrus. Other authors focused also on extrastriate visual cortex (Bense et al., 2001; Frank et al., 2014; Smith et al., 2012; Stephan et al., 2005; Wang et al., 2008) and posterior cingulate areas where they also found visuo-vestibular convergences (Cardin and Smith, 2010; Smith et al., 2012). Other multisensory mechanisms implying vestibular tactile and nociceptive signals are also associated with parietal operculum and posterior insula, and S2 and OP1 for tactile stimuli and OP3 and frontal operculum for nociceptive stimuli (Zu Eulenburg et al., 2013). Vestibular neurons are found also in hippocampus, in the insula and in frontal operculum (Lopez and Blanke, 2011; Lopez, 2015; Lopez et al., 2012b; Zu Eulenburg et al., 2012).

It is very attempting to compare this large multimodal vestibular network with the networks of bodily self-consciousness, as many brain regions associated with illusory hand ownership, self-location and self-identification are actually overlapping with vestibular regions and mainly visuo-vestibular regions. Blanke (2012) reviewed multisensory brain mechanisms of bodily self-consciousness and showed that a large fronto-parieto-temporal network (see also Ionta et al., 2014) is associated with self-identification, self-location and body ownership (see above figures 6, 7 and 8 reproduced and adapted from Blanke 2012), including the intraparietal sulcus (IPS), the dorsal premotor cortex (PMC), the medial prefrontal cortex, the primary somatosensory cortex (S1), the TPJ, the posterior superior temporal gyrus (pSTG), and the extrastriate body area (EBA). Importantly, illusory hand ownership has been also associated with S2 and SMG exactly in regions of visuo-vestibular convergence we found (Gentile et al., 2011). A close look at data from Gentile et al (2011) actually suggests that the locus of brain activations goes beyond the SMG and S2, and also extends posteriorly in Ri and parietal operculum.

In addition, pMTG and pSTS loci of visuo-vestibular convergence in our fMRI study seem in the vicinity or may overlap with many multisensory regions (Beauchamp, 2005; Berger and Ehrsson, 2014) including EBA, a region responding to body parts at the junction between lateral occipital cortex and posterior medial temporal cortex (Astafiev et al., 2004; Downing et al., 2001; Grossman and Blake, 2002; Urgesi et al., 2004). EBA was also recently reported as a neural correlate of rubber hand illusion (Limanowski and Blankenburg, 2015; Limanowski et al., 2014).

Finally, Guterstam et al. (2015) suggested that retrosplenial posterior cingulate areas could also have a key role in the integration of neural representation of self-location and body ownership (Guterstam et al., 2015). Interestingly, medial parietal cortices in precuneus are involved in vection and human navigation (Antal et al., 2008; Ghaem et al., 1997; Wiest et al., 2004) and posterior cingulate has been shown to be activated by visual and vestibular stimulation (Cardin and Smith, 2010; Fischer et al., 2012; Smith et al., 2012) and by pure vestibular stimulation in BA23 (Bense et al., 2001; Bottini et al., 1994; Della-Justina et al., 2015; Dieterich et al., 2003; Fasold et al., 2002; Miyamoto et al., 2007). Vestibular influences on rubber hand ownership seem to occur only when a visual feedback is available (Lopez et al., 2012a). In animals, no recording of vestibular neurons in this region has been done up to now, but tracer studies showed interconnection of a vestibular cingulate region with the PIVC and somatosensory area 3a described in monkeys (Guldin and Grüsser, 1998).

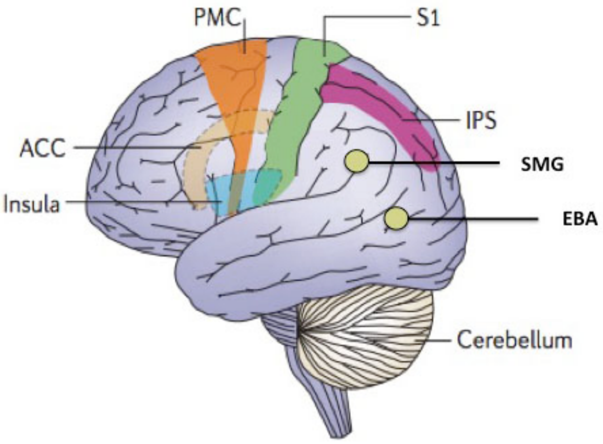

Figure 6. Illusory Hand ownership, modified after Blanke 2012. The main brain regions that are associated with illusory hand ownership and changes in perceived hand position. Regions include the ventral and dorsal premotor cortex (PMC), primary somatosensory cortex (S1), intraparietal sulcus (IPS), insula, anterior cingulate cortex (ACC) and the cerebellum. Data from recent literature also include EBA and SMG to brain regions associated to illusory hand ownership, in yellow and bold characters in the figure.

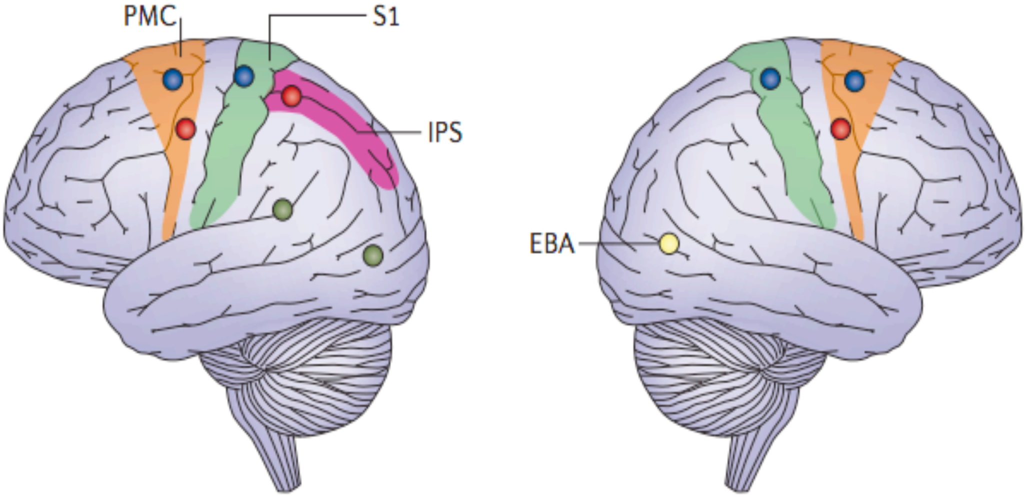

Figure 7. Brain mechanisms of illusory self-identification, from Blanke (2012). The drawing shows the different brain regions that have been implicated in illusory self-identification. Regions include the ventral premotor cortex (vPMC), primary somatosensory cortex (S1), intraparietal sulcus (IPS), extrastriate body area (EBA) and the putamen (not shown). Data by (Petkova et al., 2011) are shown in red, by Lenggenhager et al.(Lenggenhager et al., 2011) in blue and by Ionta et al. (Ionta et al., 2011) in yellow. The location of brain damage leading to heautoscopy is also shown (Blanke and Mohr 2005) in green.

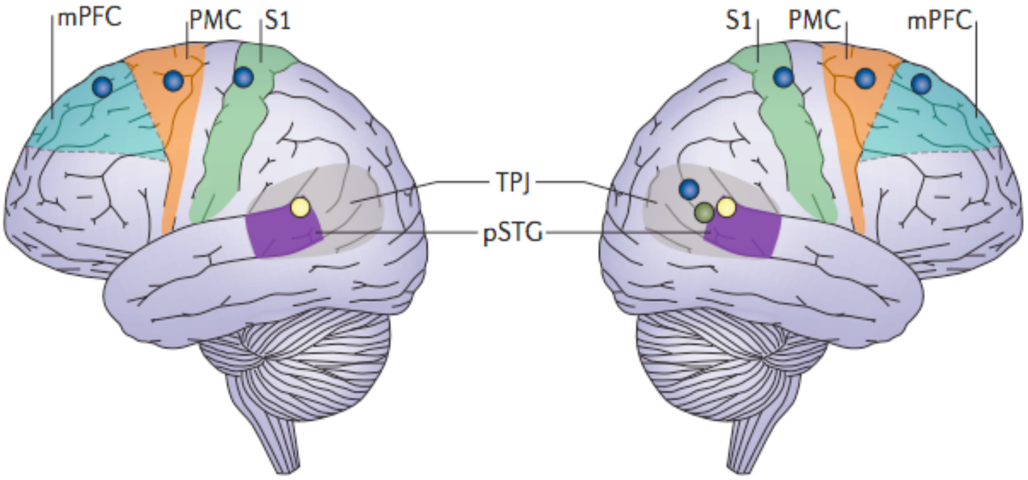

Figure 8. Brain mechanisms of illusory self-location and first-person perspective from Blanke (2012). The drawing shows the different brain regions that were activated during illusory self-location and changes in the first-person perspective in different studies. Regions include the right and left posterior superior temporal gyrus (pSTG), right temporoparietal junction (TPJ), primary somatosensory cortex (S1) and medial premotor cortex (mPMC) and adjacent medial prefrontal cortex (mPFC). Data by Lenggenhager et al. (2009) are shown in blue, data by Ionta et al. (2012) are shown in yellow and the location of brain damage at the right angular gyrus that leads to out-of-body experiences is shown in green.

6.3 Visuo-vestibular interactions and cognitive functions

6.3.1 Visuo-vestibular and cognition: generalities

Visuo-vestibular mechanisms contribute to cognition in very different ways. For a very long time, the vestibular system was known to contribute to postural and oculomotor control (Goldberg and Cullen, 2012) while vection is also affecting posture, as it leads to postural readjustments to compensate illusory-motion perceived by the observer (Baumberger et al., 2004; Clément et al., 1985; Lestienne et al., 1977). The links between vestibular system and cognition are now better assessed with spatial navigation, memory functions, perception of gravity, and metacognitive functions of the human brain such as visual awareness and bodily self-consciousness (Barra et al., 2010; Blanke, 2012; Brandt et al., 2005; Ferre et al., 2013; Indovina et al., 2005; Lacquaniti et al., 2013; Lopez et al., 2008a; Mast et al., 2014; Smith, 1997). Loss of vestibular or visual functions can lead to dramatic conditions for body motion and integrity, as it can be observed in aging (Deshpande and Patla, 2007; Herdman et al., 2000; Kobayashi et al., 2002; Schubert et al., 2002) where an increased temporal window of multisensory integration is also reported (Cyran et al., 2015; Mozolic et al., 2012), or after brain lesion or vestibular deficits (Lacour et al., 2009; Philbeck et al., 2006, 2004; Redfern et al., 2004). Moreover, if visuo-vestibular mechanisms are so important for human cognition, other polysensory interactions linked with the vestibular system seem fundamental, such as auditory and visuo-vestibular integration. Sounds can interact with visually induced vection for example (Blum et al., 1979; Riecke et al., 2009; Väljamäe and Soto-Faraco, 2008). Also, visceroceptive feelings as those observed in mesial seizures (such as in our patient in chapter 4), disgust sensations, stomach feelings (closed to those observed in motion sickness) and semantics expressing vestibular and visuo-vestibular feelings should be studied further. Link between emotions and vestibular feelings seem also obvious (such as when people vertigos and visual symptoms during happy or stressful conditions) but were not extensively studied. Psychiatric consequences of vestibular lesions are known to exist and should be also more investigated (Best et al., 2009, 2006; C. Best et al., 2007; Chua et al., 2003; Hanes and McCollum, 2006). Increased self-focus is enhanced in major depression where patients are less sensitive to external stimuli, while self-related brain networks as the default mode network are normally deactivated when an external object becomes conscious (Crone et al., 2013). The visual and vestibular contributions to mood disorders are a very challenging and promising topic of research.

6.3.2 Visuo-vestibular contributions to altered states of bodily self-consciousness and further research needed

In the general framework of body awareness, vestibular feelings observed during GVS could be somehow considered as transient out-of-body experiences or ‘partial disembodiment’ such as suggested by Lopez (2008), where a mismatch occurs, as an illusory body motion is experienced in the absence of actual body motion. Some of those troubles of somatognosia nevertheless rely more on visual components such as autoscopic phenomena or heautoscopy. In OBEs and in the case of lesions of the parieto-insular cortex, the disembodiment is often associated to vertiginous sensations. Blanke and Mohr (2005) posit that some failure of integration occurs between visual, tactile and vestibular signals, leading to pathological self-identification and self-location. Failure of integration can also trigger some disturbances of body schema such as neck and head enlargement feelings occurring in patients or in healthy volunteers during CVS or GVS. Interestingly, the parieto-insular cortex is not only a visuo-vestibular region of convergence but also a region where convergence has been assessed between somatosensory signals and vestibular signals triggered by CVS (Bottini et al., 2005, 2001, 1995; Ferre et al., 2012). Hippocampus, a region reported to be part of the vestibular cortex, is also linked with amnesia occurring while eliciting OBEs by visuo-tactile conflict in a recent fMRI study (Bergouignan et al., 2014). Future research should gather in a systematic way the spared casuistic of diseases related to disturbed embodiment and their respective associated brain lesions and their overlap with multisensory vestibular regions. The understanding of such pathologies would be itself boosted by a better knowledge of multimodal brain networks by further studies and rely on a higher resolution for the anatomical description of inferior parietal cortex but with a clear 'connexionist' approach, as the vestibular system seems ontologically multisensory, acting at all neural relays in bottom-up and top-down directions. Anatomical research should also target structural quantitative MRI studies and qualitative analysis of the microstructure with 7T MRI of multisensory vestibular cortices, and link studies of the associated connectome. A good lesion model would be the use of bilateral vestibular loss patients to study brain plasticity of vestibular networks resulting from deafferentation; but those patients are very rare and an important percentage of them benefits from a cochlear implant to overcome the auditory deficit, which prevents any study within the constraining magnetic free MR environment for those who were implanted before the existence of MRI compatible material. Unilateral lesions of the vestibular system can also be used as a model for vestibular deafferentation as these patients never recover a normal balance even after intensive vestibular rehabilitation. Vestibular lesions are due to pharmaceutical toxicity (e.g. post-antibiotics therapy with gentamycin), a traumatic origin, or post-surgery lesions like labyrinthectomy. The loss of unilateral vestibular function can be assessed clinically but the main challenge of such a study with classical quantitative methods (voxel-based morphometry for example) would be the inherent inter-subject variability of the results in vestibular neuroimaging.

6.4 Models of visual awareness and bodily self-consciousness

6.4.1 Attempting to compare models

Our data showing distributed brain networks with long-range axonal links raise the question of a parallel between bodily self-consciousness and visual awareness, widely described in the theoretical framework of global workspace (Barttfeld et al., 2015; Dehaene and Changeux, 2004, 2003; Dehaene and Naccache, 2001; Dehaene et al., 2006; Schurger et al., 2015). Dehaene et al. (2014) suggests that: "Reportability is defined as one of the main criterion for whether a piece of information is or not conscious." Amongst the "great variety of representations that can be accessed", the authors suggest that "Self-consciousness is a particular instance of conscious access where the conscious 'spotlight' is oriented toward internal states" (Dehaene et al., 2014). Such networks of visual awareness were widely explored through paradigms like visual masking (Naccache et al., 2002), temporal integration (Forget et al., 2010) or attentional blink (Sergent and Dehaene, 2004). Dehaene and Naccache (2001) advocate for the existence of a brain network with long distance axons, interconnecting different individual specialized modules through recurrent loops making the information available within a global workspace. Successive metastable states of this network constitute series of conscious states.

In fact, bodily self-consciousness networks, including visuo-vestibular integration cortical regions, seem to be distributed within all cortical lobes, bilaterally, with an important reciprocal connections between different 'modules' of human cognition; it seems to impact body posture and cognition from very basic reflexes (vestibulo-ocular reflex, vestibulo-cervical reflex) in the first neural relays (brainstem, thalamus, cerebellum), or later at the cortical level. Some mechanisms that do not require a complex cortical processing seem to occur very fast as bottom-up processes. In opposite, conscious reports of vestibular feelings take time, like visual awareness but even slower. In vision, a minimal time window of 300 ms to become conscious is considered by previous works (Dehaene and Naccache, 2001; Sergent and Dehaene, 2004). Percepts faster than 10 Hz cannot be correctly distinguished (Coltheart, 1983, 1980; Forget et al., 2010). In fact, reaction times to GVS stimulation are also very slow (Barnett-Cowan and Harris, 2009; Barnett-Cowan et al., 2012). In Barnett-Cowan's series of experiments, head movement were reported only 438 +/- 49 ms after the onset of the stimulation and reaction times to touches (245 +/- 14 ms), to lights (220 +/- 13 ms) or sounds (197 +/- 13 ms) were much faster. In Barnett-Cowan and Harris (2009) temporal order and simultaneity judgments also show that if GVS occur until 160 ms before other stimuli, both stimuli could be integrated as one percept, which is significantly less than what could be predicted by reaction times difference. It suggests that integration processes are occurring before becoming aware of the vestibular stimulation. This window is interestingly much larger than the window of integration of brief visual events for simple lights, the critical fusion frequency (Andrews et al., 1996). It is even larger than the window of integration where independent visual letters can be detected as words even if presented with temporal delays (Forget et al 2013). In general, vestibular perception seems to be a slow phenomenon, as an immediate physiological neural response without awareness is preferred in priority, and where awareness of the stimulation is delayed because of multiple multisensory integration processes occurring at all levels (Barnett-Cowan, 2013). We could hypothesise the existence of a huge time tolerance to integrate vestibular percepts in a large time window with other sensory stimuli. Thus, an external event would be keener to be detected as only one event responsible of head motion, while merging different sensory evidences towards the source of stimulation. Knowing where the head is located could be more relevant for a human being than knowing the exact head velocities during motion, but it requests the time of multisensory integration; the exact velocity knowledge (vestibular system is actual transducing acceleration to a velocity signal, see Fernandez and Goldberg, 1971) might be a less relevant signal, physiologically (empirically we are not good to detect high velocities without visual control actually; its allows us to feel comfortable in very fast planes for instance). Similarly, vection experience seems also to be a slow phenomenon (Keshavarz and Berti, 2014) requiring 2 to 3 seconds to be induced (Mohler and Thompson, 2005; Trutoiu et al., 2009). It would be very interesting to distinguish visuo-vestibular phenomena that need to occur with and without conscious control and apply mental chronometry paradigms and neurophysiology measures by ERPs to appreciate how optokinetic stimuli injected to the visual system propagate in the global workspace. It stays an open question if visuo-vestibular inputs are processed differentially than visual, motor, somatosensory or auditory signals. Many visuo-vestibular processes also occur in daily life under the conscious threshold, such as mechanisms involved in some basic functions (walking, heading, limbs movement correction, head and body coordination). On the other hand, we postulate that the conscious experience of vertigos and visuo-vestibular feelings such as vection could take some time to occur after the onset of a new situation, following the same rules as any other conscious object from another sensory modality. The temporal resolution of vestibular and visuo-vestibular perception could be also explored to better characterize those processes. The ubiquity of visual and vestibular neurons across the brain suggests the importance to maintain intact visuo-vestibular functions in case of brain lesion. Visual and vestibular sensors detect signals that are permanently integrated and balanced through optimal cue integration (Fetsch et al., 2012, 2010; Prsa et al., 2012) to allow the survival of an individual in a moving environment. Awareness does not seem to be a prerequisite for bodily self-consciousness which stays 'under the threshold' in most of situations such as for walking trajectories towards a target (Kannape et al., 2010). Body percepts may nevertheless occur and the conscious content can be even modulated by attention (Juravle et al., 2011; Spence et al., 2004; Van Hulle et al., 2013a, 2013b). Interoceptive sensations such as heartbeat are most of the time unconscious as our homeostasis escapes to our conscious scope but can be enhanced though interoceptive learning via the insular cortex (Canales-Johnson et al., 2015) and perceived more strongly when needed (effort, threat for instance), and differentially from one individual to another (Craig, 2002, 2004). Similarly, a relevant event for one's own life would access consciousness depending on the context (a bump on the road does not have similar statistical significance for his brain neither the same perceptual saliency for a driver on a highway compared to a motorbike driver in a chaotic field).

Otoliths signals cancellation is also gated when proprioceptive feedback matches the motor-based expectation in active self-motion, while neurons respond more robustly during passive head translations (Carriot et al., 2013). Unconscious, efficient and rapid mechanisms occur in early vestibular mechanisms within the vestibular nuclei and brainstem (Cullen et al., 2003; Roy and Cullen, 2004) but more complex situations may require bodily self-awareness to adapt the behaviour (Brooks and Cullen, 2014).

6.4.2 Midline cortex and bodily self-consciousness

Recent studies on vigilance and disorders of consciousness may let us speculate on a close link between the neural correlates of self-referential processing and the resting-state activity in cortical midline areas (Araujo et al., 2014; Crone et al., 2013; Huang et al., 2014; Kelley et al., 2002; Lamm et al., 2011; Mitchell et al., 2005; Northoff and Bermpohl, 2004; Platek et al., 2008; Uddin et al., 2007; Yaoi et al., 2009; Zhu et al., 2007). It includes anterior cingulate and posterior cingulate regions, within the default-mode network and also the inferior parietal lobule (Salomon et al., 2014). Visual detection can be predicted by spontaneous fluctuations of neural responses to heartbeats in posterior right inferior parietal lobule and ventral anterior cingulate in a recent MEG study (Park et al., 2014). Guterstam et al (2015) supported the relevance of retrosplenial posterior cingulate cortex as a 'hub' between self-identification and limb ownership. Also, optokinetic stimulations inducing vection and vestibular stimulations lead to activations of precuneus (Wiest et al., 2004), anterior and posterior cingulate (Antal et al., 2008; Dieterich et al., 2003;

Fischer et al., 2012; Kovács et al., 2008; Lopez et al., 2012b). Even visual and vestibular convergence seems to occur in the posterior cingulate sulcus (Cardin and Smith, 2010; Fischer et al., 2012; Wall and Smith, 2008) but such activations could be general activations related to the self as well. As visual and vestibular contributions to bodily self-consciousness seem to be mandatorily weighted and present (Prsa et al., 2012), a lack of sensitivity to those components should be expected in several disturbances of the self related to the activation of the default-mode network, such as depression, and particularly in midline cortical structures (Grimm et al., 2009; Lemogne et al., 2012; Nejad et al., 2013). In vestibular dysfunctions, depressive syndromes are reported. It would be interesting to know better how visual and vestibular function contribute to the self through the activation and deactivation of default mode network (Best et al., 2006; C Best et al., 2007; Gomez-Alvarez and Jauregui-Renaud, 2011; Smith et al., 2005).

Self-related versus other stimuli activate the anterior regions such as anterior cingulate (Qin and Northoff, 2011). Deactivated patterns of anterior cingulate are seen when a conscious effort toward the external world or high cognitive demand occurs (Greicius and Menon, 2004; Shulman et al., 1997b). Previous authors hypothesised that it may correspond to the redirection of cognitive resources from internal ongoing processes towards the new task requiring consciousness (Gusnard et al., 2001; Raichle and Snyder, 2007). Self-related stimuli do not interrupt the anterior cingulate activity (Qin and Northoff, 2011) while other stimuli do interrupt it (Shulman et al., 1997a). Qin and Northoff (2011) support the idea of a preserved self-oriented processes while awareness of other external stimuli occurs but we hypothesise a distinction should be done between self-related processes needing consciousness and self-related processes which do not need conscious control. Further research should disentangle which components of the self-processing stay under conscious threshold and when they need to become conscious and what is the ecological function of vection occurring sometimes during optokinetic stimulation, in respect to vestibular perception (Palmisano et al., 2015).

6.5 Visuo-vestibular representations in human culture

Visuo-vestibular representations are quite present in human culture, and the selection of individuals having the most "optimal integration" of visual and vestibular cues is a feature of human societies, such as in sport activities requiring fine motion control (piloting car, planes or motorbikes, dance, ice skating). Human beings are highly addicted to visuo-vestibular strong experiences as an amusement, as much as they can be addicted to music, the auditory system being the anatomical twin of vestibular sense. Functionally, auditory and vestibular systems are also closely linked. Noises can induce vestibular sensations even used as an experimental condition to trigger vestibular sensations (Freeman et al., 1999; Lopez et al., 2012b; Murofushi et al., 2005; Yokota, 2000; zu Eulenburg et al., 2012) and loud music can evoke vestibular responses that could be responsible of pleasurable sensations of self-motion (Phillips-Silver and Trainor, 2008; Todd and Cody, 2000). People look for such sensations for those who crave for loud music in dance clubs and rock concerts, even enhanced by their own body motion while dancing. Congruent tactile and auditory cues ease the discrimination between march-like rhythms and waltz-like rhythms (Huang et al., 2012) while vestibular inputs can interfere with notes important to recognize music metrics, and make a sequence perceived as binary or ternary (Phillips-Silver and Trainor, 2008, 2007, 2005; Trainor et al., 2009). Head motion is empirically a component of music experience while being in the audience and a performer, while musicians also claim "to feel" the music "inside" of them, evoking tactile and interoceptive components as well. The huge value of vestibular and auditory sensations in human societies within a multisensory framework invites for fascinating research in consciousness studies, beyond the exploration of several sensory modalities as vestibular and vision, to explain "how" and "why" those sensations were selected in human culture and also how it impacts human social bonds.

Finally, visuo-vestibular mechanisms are also associated to the ritual lives of human beings in religions, mysticism and "transcendental" experiences. Dervishes in the contemplative Muslim sufi traditions inspired by Rumi (Ambrosio et al., 2006) and originated from Konya in Turkey and in Western Balkans, are used to trigger bodily self-illusions making dissociation of the body and environment experienced duality, based on dances like in Mevlevi groups, and on rhythmic body linear motion back and forth in Bektashi and Halevi groups with breathing methods inducing hypercapnia. The dancer in Mevlevi tradition turns during 10-15 minutes in counter clockwise rotations, with the head on the right side, and actually triggering pitch rotations, right hand in the sky symbolizing the link with the sky and left hand with palm toward the ground to make the link with earth. Based on daily practices, the dancer starts using tricks like fixation the thumb of left hand to prevent motion sickness but then either close or open eyes and try to lose physiological visual referential leading to alleviate the feeling of embodiment and experience the "fusion with universe". With habits, they are used to not feel anymore the vestibular aftereffects when they stop turning. Those traditions may actually induce such trances phenomena through visuo-vestibular conflicts disturbing bodily self-consciousness and are liked to be observed by observers, such as in touristic demonstrations in Konya and in Tanura, an Egyptian version of the rotating dances of sufi communities (Forget et al., work in preparation).

Experimental psychology could manipulate bodily self-consciousness as we have seen with visuo-tactile conflicts. It can also use a variety of less famous strategies such as the levitation illusions (see figure 9) when a familiar scene viewed by supine observers through a mirror oriented at 45 degrees appears vertical when, optically, it is horizontal and above the head (Howard and Hu, 2001; Howard et al., 2005). Room tilt illusions can be induced with tilt rooms in healthy subjects (de Graaf et al., 1992; Groen et al., 2002; Howard and Childerson, 1994). They can also occur in neurological conditions (Arjona and Fernandez-Romero, 2002; Malis and Guyot, 2003; Tiliket et al., 1996). Gravity and observer's body orientation influence the visual perception of human body postures (Lopez et al., 2009) while spatial orientation loss in weightless environments in astronauts can also induce body tilt illusions (Lackner and Levine, 1979; Lackner, 1992a, 1992b).

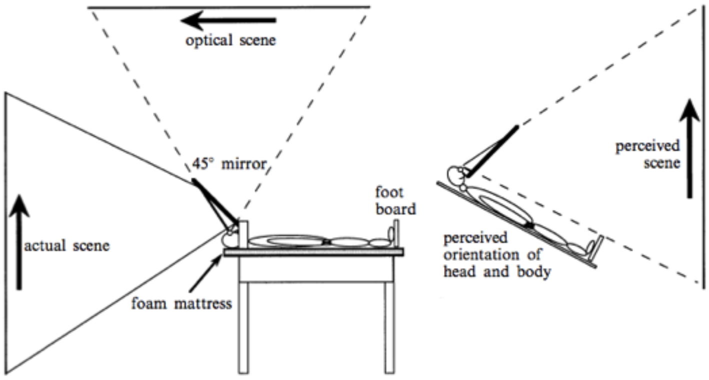

Figure 9. The levitation illusion (Howard et al., 2005). The mirror bed showing the actual and reflected scene can bee seen on the left. The perceived positions and orientation of the scene for an observer experiencing a reorientation illusion can be seen on the right. Typically, the torso feels pitched up by about 20° and the head feels pitched up to a greater degree. The observer cannot see his or her own body.

In contemporary plastic arts, visuo-vestibular mechanisms and relativity of bodily self-location in respect to the environment, such as rivalry for verticality, have been exploring such phenomena like in the work of the famous French artist Philippe Ramette (see catalogue in Ramette and Onfray, 2010 and figures 10 and 11). Those tricks of visual and bodily cues are exploited to develop abstract metacognitive thinking in the observer. Beyond the evident sense of humour in such unedited pictures (the artist really posed in those situations), the artist leaves cues to disentangle the rivalry for verticality in such scenes (face tension to indicate it is not a natural stance, visibility of the prostheses used to maintain the body in such stances). It is striking that even the presence of such cues is not enough to kill the rivalry for verticality experienced while looking at those pictures, enhancing the idea that a body inside a frame, for individuals' visual systems biased to detect human shapes as vertical lines, even a strong suggestion that the environment gives the real verticality orientation is not enough.

Figure 10. Contemplation irrationnelle, 2003

Credits: colour photographs, original format 150 x 120 cm, photograph. © Marc Domage and Philippe Ramette, ADAGP, Courtesy galerie Xippas and Philippe Ramette.

Figure 11. Balcon 2 (Hong-Kong), 2001

Credits: colour photographs, original format 150 x 120 cm, photograph. © Marc Domage and Philippe Ramette, ADAGP, Courtesy galerie Xippas and Philippe Ramette.

Chapter 7 Conclusions

Visuo-vestibular mechanisms are key components of bodily self-consciousness. Ubiquitous brain regions integrate visual and vestibular signals and those brain regions are very important to encode bodily signals in general and create phenomenologically the experience of "I", the global and unitary feeling of the self, distinct from an environment. The statistically optimal weighting of optokinetic information and head motion makes an individual better in its interaction with this environment. Proprioceptive, auditory and somatosensory signals also provide important information for bodily-self consciousness.

The body schema and its peripersonal space can be easily reshaped as some components of bodily self-consciousness such as limb ownership, self-location, self-identification and body motion, are highly plastic representations, sensitive to multisensory mismatch, triggered in laboratory conditions but also occurring in daily routine, such as it is the case of vection. Limb ownership and plasticity of peripersonal space can be transitorily remapped to allow tool learning and to recover after brain lesions, while self-location and self-identification plasticity are probably important for social cognition and for metacognitive skills where one's need to project in space and time.

Visual and vestibular signals are mandatorily present and balanced, and a better knowledge of their neural correlates will enhance our understanding of neural correlated of consciousness and also refine our understanding of brain lesions semiology in multisensory cortices such as found in parietal operculum and inferior parietal lobule. Visual and vestibular mechanisms and their ‘rivalry’ as dominant cues for bodily self-consciousness amongst other sensory modalities is an important component of human culture, where individuals performing an optimal visuo-vestibular integration may be preferentially selected.

Appendix

Chapter 2. Supplementary data

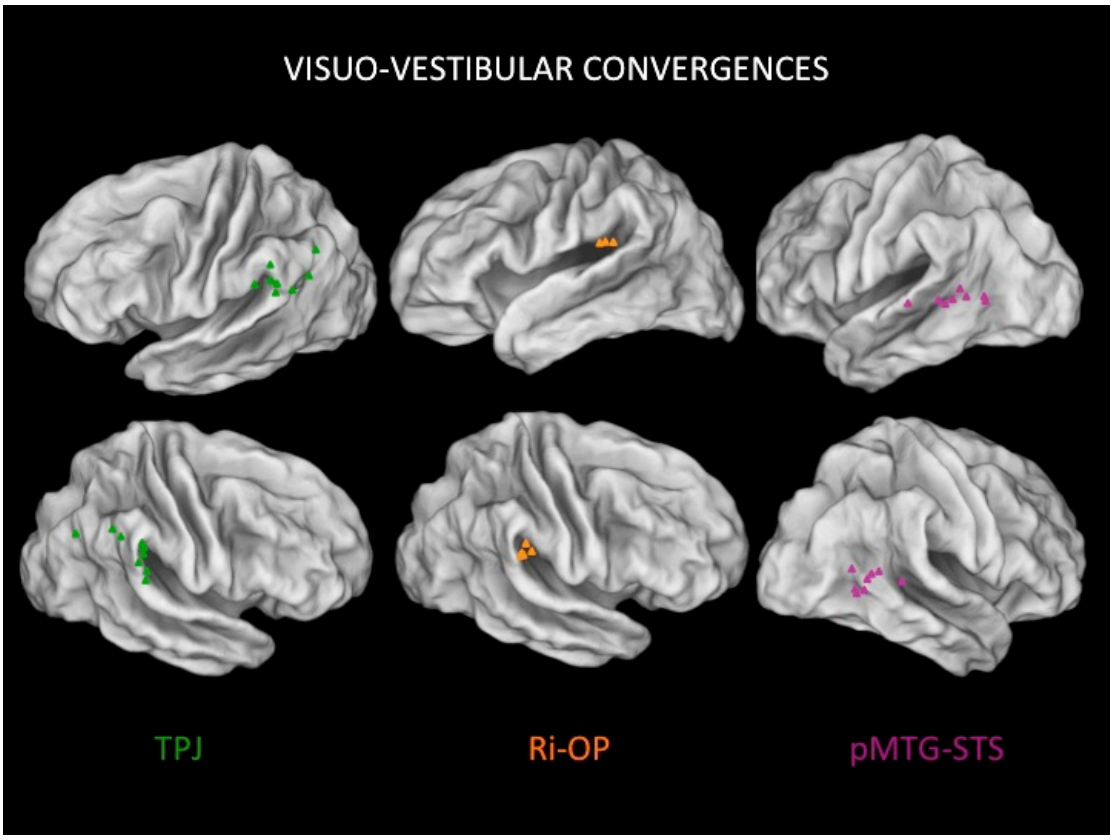

Figure A. Summary of convergences: same data than figure 4 but displayed on semi-inflated generic brains (centres of convergence of visuo-vestibular for each subject showing a convergence in this location)

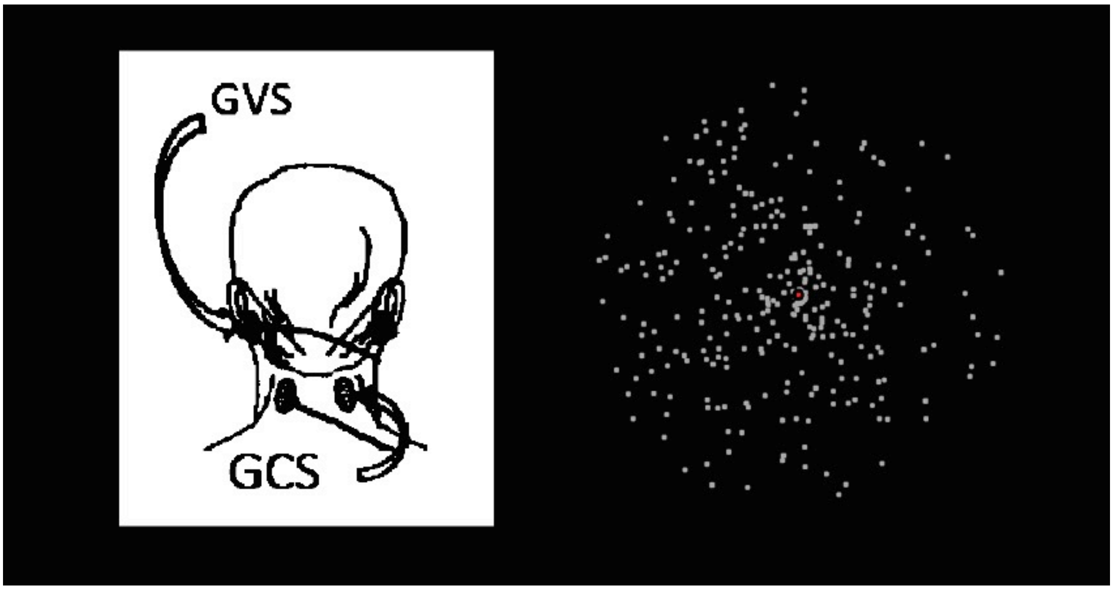

Figure B. Schema of the GVS and GCS stimulation (left) and static representations of the visual stimulation (right)

General References

Aglioti, S., Smania, N., Manfredi, M., Berlucchi, G., 1996. Disownership of left hand and objects related to it in a patient with right brain damage. Neuroreport 8, 293–296.

Alais, D., Burr, D., 2004. The ventriloquist effect results from near-optimal bimodal integration. Curr. Biol. 14, 257–62. doi:10.1016/j.cub.2004.01.029

Ambrosio, A., Feuillebois, E., Zarcone, T., 2006. Les derviches tourneurs, collection. ed. Editions du cerf.

André, J.M., Martinet, N., Paysant, J., Beis, J.M., Le Chapelain, L., Andre, J.M., Martinet, N., Paysant, J., Beis, J.M., Le Chapelain, L., 2001. Temporary phantom limbs evoked by vestibular caloric stimulation in amputees. Neuropsychiatry Neuropsychol Behav Neurol 14, 190–196.

Andrews, T.J., White, L.E., Binder, D., Purves, D., 1996. Temporal events in cyclopean vision. Proc. Natl. Acad. Sci. U. S. A. 93, 3689–92.

Angelaki, D.E., Gu, Y., Deangelis, G.C., 2011. Visual and vestibular cue integration for heading perception in extrastriate visual cortex. J Physiol 589, 825–833. doi:10.1113/jphysiol.2010.194720

Antal, a, Baudewig, J., Paulus, W., Dechent, P., 2008. The posterior cingulate cortex and planum temporale/parietal operculum are activated by coherent visual motion. Vis. Neurosci. 25, 17–26. doi:10.1017/S0952523808080024

Araujo, H.F., Kaplan, J., Damasio, H., Damasio, A., 2014. Involvement of cortical midline structures in the processing of autobiographical information. PeerJ 2, e481. doi:10.7717/peerj.481

Arjona, A., Fernandez-Romero, E., 2002. [Room tilt illusion: Report of two cases and terminological review]. Neurologia 17, 338–341.

Arslan, O., 2001. Neuroanatomical Basis of Clinical Neurology. Macmillan Heinemann.

Arzy, S., Seeck, M., Ortigue, S., Spinelli, L., Blanke, O., 2006. Induction of an illusory shadow person. Nature 443, 287. doi:10.1038/443287a

Aspell, J.E., Lenggenhager, B., Blanke, O., 2009. Keeping in touch with one's self: multisensory mechanisms of self-consciousness. PLoS One 4, e6488.

Astafiev, S. V, Stanley, C.M., Shulman, G.L., Corbetta, M., 2004. Extrastriate body area in human occipital cortex responds to the performance of motor actions. Nat Neurosci 7, 542–548. doi:10.1038/nn1241

Barnett-Cowan, M., 2013. Vestibular perception is slow: a review. Multisens. Res. 26, 387–403.

Barnett-Cowan, M., Harris, L.R., 2009. Perceived timing of vestibular stimulation relative to touch, light and sound. Exp. brain Res. 198, 221–31. doi:10.1007/s00221-009-1779-4

Barnett-Cowan, M., Raeder, S.M., Bülthoff, H.H., 2012. Persistent perceptual delay for head movement onset relative to auditory stimuli of different durations and rise times. Exp. brain Res. 220, 41–50. doi:10.1007/s00221-012-3112-x

Barra, J., Marquer, A., Joassin, R., Reymond, C., Metge, L., Chauvineau, V., Perennou, D., 2010. Humans use internal models to construct and update a sense of verticality. Brain 133, 3552–3563. doi:awq311 [pii] 10.1093/brain/awq311

Barttfeld, P., Uhrig, L., Sitt, J.D., Sigman, M., Jarraya, B., Dehaene, S., 2015. Signature of consciousness in the dynamics of resting-state brain activity. Proc. Natl. Acad. Sci. 112, 201418031. doi:10.1073/pnas.1418031112

Baumberger, B., Isableu, B., Flückiger, M., 2004. The visual control of stability in children and adults: Postural readjustments in a ground optical flow. Exp. Brain Res. 159, 33–46. doi:10.1007/s00221-004-1930-1

Beauchamp, M.S., 2005. See me, hear me, touch me: multisensory integration in lateral occipital-temporal cortex. Curr. Opin. Neurobiol. 15, 145–53. doi:10.1016/j.conb.2005.03.011

Beer, J., Blakemore, C., Previc, F.H., Liotti, M., 2002. Areas of the human brain activated by ambient visual motion, indicating three kinds of self-movement. Exp Brain Res 143, 78–88. doi:10.1007/s00221-001-0947-y

Beierholm, U.R., Quartz, S.R., Shams, L., 2009. Bayesian priors are encoded independently from likelihoods in human multisensory perception. J Vis 9, 23 1–9. doi:10.1167/9.5.23 /9/5/23/ [pii]

Bense, S., Stephan, T., Yousry, T. a, Brandt, T., Dieterich, M., 2001. Multisensory cortical signal increases and decreases during vestibular galvanic stimulation (fMRI). J. Neurophysiol. 85, 886–899.

Berger, C.C., Ehrsson, H.H., 2014. The fusion of mental imagery and sensation in the temporal association cortex. J. Neurosci. 34, 13684–92. doi:10.1523/JNEUROSCI.0943-14.2014

Bergouignan, L., Nyberg, L., Ehrsson, H.H., 2014. Out-of-body-induced hippocampal amnesia. Proc. Natl. Acad. Sci. U. S. A. 111, 4421–6. doi:10.1073/pnas.1318801111

Berthoz, A., Pavard, B., Young, L.R., 1975. Perception of linear horizontal self-motion induced by peripheral vision (linearvection) basic characteristics and visual-vestibular interactions. Exp Brain Res 23, 471–489.

Best, C., Bense, S., Dieterich, M., 2007. Vestibular dysfunction in major depression. Neuroscience 147, 865–866. doi:10.1016/j.neuroscience.2007.05.005

Best, C., Bense, S., Dieterich, M., 2007. Vestibular dysfunction in major depression. Neuroscience 147, 865–866.

Best, C., Eckhardt-Henn, A., Diener, G., Bense, S., Breuer, P., Dieterich, M., 2006. Interaction of somatoform and vestibular disorders. J Neurol Neurosurg Psychiatry 77, 658–664.

Best, C., Eckhardt-Henn, A., Tschan, R., Dieterich, M., 2009. Psychiatric morbidity and comorbidity in different vestibular vertigo syndromes. Results of a prospective longitudinal study over one year. J Neurol 256, 58–65. doi:10.1007/s00415-009-0038-8

Bisiach, E., Rusconi, M.L., Vallar, G., 1991. Remission of somatoparaphrenic delusion through vestibular stimulation. Neuropsychologia 29, 1029–1031. doi:0028-3932(91)90066-H [pii]

Blanke, O., 2012. Multisensory brain mechanisms of bodily self-consciousness. Nat. Rev. Neurosci. 13, 556–71. doi:10.1038/nrn3292

Blanke, O., Landis, T., Spinelli, L., Seeck, M., 2004. Out-of-body experience and autoscopy of neurological origin. Brain 127, 243–258. doi:10.1093/brain/awh040

Blanke, O., Metzinger, T., 2009. Full-body illusions and minimal phenomenal selfhood. Trends Cogn. Sci. 13, 7–13. doi:10.1016/j.tics.2008.10.003

Blanke, O., Mohr, C., 2005. Out-of-body experience, heautoscopy, and autoscopic hallucination of neurological origin Implications for neurocognitive mechanisms of corporeal awareness and self-consciousness. Brain Res. Brain Res. Rev. 50, 184–99. doi:10.1016/j.brainresrev.2005.05.008

Blanke, O., Ortigue, S., Landis, T., Seeck, M., 2002. Stimulating illusory own-body perceptions. Nature 419, 269–70. doi:10.1038/419269a

Blum, P.S., Abraham, L.D., Gilman, S., 1979. Vestibular, auditory, and somatic input to the posterior thalamus of the cat. Exp Brain Res 34, 1–9.

Bottini, G., Bisiach, E., Sterzi, R., Vallar, G., 2002. Feeling touches in someone else's hand. Neuroreport 13, 249–252.

Bottini, G., Karnath, H.O., Vallar, G., Sterzi, R., Frith, C.D., Frackowiak, R.S., Paulesu, E., 2001. Cerebral representations for egocentric space: Functional-anatomical evidence from caloric vestibular stimulation and neck vibration. Brain 124, 1182–1196.

Bottini, G., Paulesu, E., Gandola, M., Loffredo, S., Scarpa, P., Sterzi, R., Santilli, I., Defanti, C.A., Scialfa, G., Fazio, F., Vallar, G., 2005. Left caloric vestibular stimulation ameliorates right hemianesthesia. Neurology 65, 1278–1283.

Bottini, G., Paulesu, E., Sterzi, R., Warburton, E., Wise, R.J., Vallar, G., Frackowiak, R.S., Frith, C.D., 1995. Modulation of conscious experience by peripheral sensory stimuli. Nature 376, 778–81.

Bottini, G., Sterzi, R., Paulesu, E., Vallar, G., Cappa, S.F., Erminio, F., Passingham, R.E., Frith, C.D., Frackowiak, R.S., 1994. Identification of the central vestibular projections in man: a positron emission tomography activation study. Exp Brain Res 99, 164–169.

Botvinick, M., Cohen, J., 1998. Rubber hands "feel" touch that eyes see. Nature 391, 756.

Brandt, T., Bartenstein, P., Janek, A., Dieterich, M., 1998. Reciprocal inhibitory visual-vestibular interaction. Visual motion stimulation deactivates the parieto-insular vestibular cortex. Brain 121 (Pt 9, 1749–1758.

Brandt, T., Schautzer, F., Hamilton, D.A., Bruning, R., Markowitsch, H.J., Kalla, R., Darlington, C., Smith, P., Strupp, M., 2005. Vestibular loss causes hippocampal atrophy and impaired spatial memory in humans. Brain 128, 2732–2741. doi:10.1093/brain/awh617

Bresciani, J.P., Blouin, J., Popov, K., Bourdin, C., Sarlegna, F., Vercher, J.L., Gauthier, G.M., 2002. Galvanic vestibular stimulation in humans produces online arm movement deviations when reaching towards memorized visual targets. Neurosci Lett 318, 34–38. doi:S0304394001024624 [pii]

Brooks, J.X., Cullen, K.E., 2014. Early vestibular processing does not discriminate active from passive self-motion if there is a discrepancy between predicted and actual proprioceptive feedback. J. Neurophysiol. 111, 2465–78. doi:10.1152/jn.00600.2013

Canales-Johnson, A., Silva, C., Huepe, D., Rivera-Rei, Á., Noreika, V., Garcia, M.D.C., Silva, W., Ciraolo, C., Vaucheret, E., Sedeño, L., Couto, B., Kargieman, L., Baglivo, F., Sigman, M., Chennu, S., Ibáñez, A., Rodríguez, E., Bekinschtein, T.A., 2015. Auditory Feedback Differentially Modulates

Behavioral and Neural Markers of Objective and Subjective Performance When Tapping to Your Heartbeat. Cereb. Cortex. doi:10.1093/cercor/bhv076

Cardin, V., Smith, A.T., 2010. Sensitivity of human visual and vestibular cortical regions to egomotion-compatible visual stimulation. Cereb. Cortex 20, 1964–1973. doi:10.1093/cercor/bhp268

Carriot, J., Brooks, J.X., Cullen, K.E., 2013. Multimodal integration of self-motion cues in the vestibular system: active versus passive translations. J. Neurosci. 33, 19555–66. doi:10.1523/JNEUROSCI.3051-13.2013

Cavanna, A.E., Trimble, M.R., 2006. The precuneus: a review of its functional anatomy and behavioural correlates. Brain 129, 564–583. doi:awl004 [pii] 10.1093/brain/awl004

Chua, S.E., Lam, I.W., Tai, K.S., Cheung, C., Tang, W.N., Chen, E.Y., Lee, P.W., Chan, F.L., Lieh-Mak, F., McKenna, P.J., 2003. Brain morphological abnormality in schizophrenia is independent of country of origin. Acta Psychiatr Scand 108, 269–275. doi:134 [pii]

Clément, G., Jacquin, T., Berthoz, A., 1985. Habituation of postural readjustements induced by motion of visual scenes., in: Igarashi, M., Black, F.O. (Eds.), Vestibular and Visual Control on Posture and Locomotor Equilibrium. 7th Int. Symp. Int. Soc. Posturography, Houston, Tex., 1983. Karger, Basel, pp. 99–104.

Coltheart, M., 1983. Iconic memory. Philos Trans R Soc L. B Biol Sci 302, 283–294.

Coltheart, M., 1980. Iconic memory and visible persistence. Percept Psychophys 27, 183–228.

Craig, A.D., 2002. How do you feel? Interoception: the sense of the physiological condition of the body. Nat Rev Neurosci 3, 655–666.

Craig, A.D.B., 2004. Human feelings: why are some more aware than others? Trends Cogn. Sci. 8, 239–41. doi:10.1016/j.tics.2004.04.004

Crick, F., 1994. The astonishing hypothesis : the scientific search for the soul. Scribner ; Maxwell Macmillan International, New York.

Crone, J.S., Höller, Y., Bergmann, J., Golaszewski, S., Trinka, E., Kronbichler, M., 2013. Self-related processing and deactivation of cortical midline regions in disorders of consciousness. Front. Hum. Neurosci. 7, 504. doi:10.3389/fnhum.2013.00504

Cullen, K.E., Roy, J.E., Sylvestre, P.A., 2003. Signal processing in vestibular nuclei: dissociating sensory, motor, and cognitive influence, in: Harris, L.R., Jenkin, M. (Eds.), Levels of Perception. Springer Verlag, Berlin, pp. 285–309.

Cyran, C.A.M., Boegle, R., Stephan, T., Dieterich, M., Glasauer, S., 2015. Age-related decline in functional connectivity of the vestibular cortical network. Brain Struct. Funct. doi:10.1007/s00429-014-0983-6

De Graaf, B., Bekkering, H., Erasmus, C., Bles, W., 1992. Influence of visual, vestibular, cervical, and somatosensory tilt information on ocular rotation and perception of the horizontal. J Vestib Res 2, 15–30.

De Ridder, D., Van Laere, K., Dupont, P., Menovsky, T., Van de Heyning, P., 2007. Visualizing out-of-body experience in the brain. N. Engl. J. Med. 357, 1829–1833. doi:10.1056/NEJMoa070010

De Vignemont, F., 2010. Body schema and body image--pros and cons. Neuropsychologia 48, 669–680. doi:S0028-3932(09)00378-9 [pii] 10.1016/j.neuropsychologia.2009.09.022

DeAngelis, G.C., Angelaki, D.E., 2012. Visual-Vestibular Integration for Self-Motion Perception, in: Murray, M.M., Wallace, M.T. (Eds.), The Neural Bases of Multisensory Processes. Boca Raton (FL).

Dehaene, S., Changeux, J., 2004. Neural Mechanisms for Access to Consciousness, in: The Cognitive Neuroscienses. pp. 1145–1158.

Dehaene, S., Changeux, J., 2003. Neural Mechanisms for Access to Consciousness.

Dehaene, S., Changeux, J.-P., Naccache, L., Sackur, J., Sergent, C., 2006. Conscious, preconscious, and subliminal processing: a testable taxonomy. Trends Cogn. Sci. 10, 204–11. doi:10.1016/j.tics.2006.03.007

Dehaene, S., Charles, L., King, J.-R., Marti, S., 2014. Toward a computational theory of conscious processing. Curr. Opin. Neurobiol. 25, 76–84. doi:10.1016/j.conb.2013.12.005

Dehaene, S., Naccache, L., 2001. Towards a cognitive neuroscience of consciousness: basic evidence and a workspace framework. Cognition 79, 1–37. doi:S0010-0277(00)00123-2 [pii]

Della-Justina, H.M., Gamba, H.R., Lukasova, K., Nucci-da-Silva, M.P., Winkler, A.M., Amaro, E., 2015. Interaction of brain areas of visual and vestibular simultaneous activity with fMRI. Exp. brain Res. 233, 237–52. doi:10.1007/s00221-014-4107-6

Dennett, D.C., 2015. Why and How Does Consciousness Seem the Way it Seems ? 10. doi:10.15502/9783958570245

Dennett, D.C., 1991. Consciousness explained, 1st ed. Little, Brown and Co., Boston.

Deshpande, N., Patla, A.E., 2007. Visual-vestibular interaction during goal directed locomotion: effects of aging and blurring vision. Exp Brain Res 176, 43–53.

Deutschländer, A., Bense, S., Stephan, T., Schwaiger, M., Dieterich, M., Brandt, T., Deutschlander, A., Bense, S., Stephan, T., Schwaiger, M., Dieterich, M., Brandt, T., 2004. Rollvection versus linearvection: comparison of brain activations in PET. Hum Brain Mapp 21, 143–153. doi:10.1002/hbm.10155

Dichgans, J., Brandt, T., 1978. Visual-vestibular interaction: effects on self-motion perception and postural control, in: Held, R., Leibowitz, H.W., Teuber, H.-L. (Eds.), Handbook of Sensory Physiology. Springer-Verlag, pp. 755–804.

Dieterich, M., Bense, S., Stephan, T., Yousry, T.A., Brandt, T., 2003. fMRI signal increases and decreases in cortical areas during small-field optokinetic stimulation and central fixation. Exp Brain Res 148, 117–127.

Downing, P.E., Jiang, Y., Shuman, M., Kanwisher, N., 2001. A cortical area selective for visual processing of the human body. Science (80-.). 293, 2470–2473. doi:10.1126/science.1063414

Duvernoy, H.M., 1999. The human brain. Surface, blood supply, and three-dimensional sectional anatomy. Second edition. Springer-Verlag, Wien.

Ehrsson, H.H., 2007. The experimental induction of out-of-body experiences. Science 317, 1048. doi:10.1126/science.1142175

Eickhoff, S.B., Schleicher, A., Zilles, K., Amunts, K., 2006. The human parietal operculum. I. Cytoarchitectonic mapping of subdivisions. Cereb Cortex 16, 254–267. doi:bhi105 [pii] 10.1093/cercor/bhi105

Fasold, O., von Brevern, M., Kuhberg, M., Ploner, C.J., Villringer, A., Lempert, T., Wenzel, R., 2002. Human vestibular cortex as identified with caloric stimulation in functional magnetic resonance imaging. Neuroimage 17, 1384–1393.

Fernandez, C., Goldberg, J.M., 1971. Physiology of peripheral neurons innervating semicircular canals of the squirrel monkey. II. Response to sinusoidal stimulation and dynamics of peripheral vestibular system. J. Neurophysiol. 34, 661–75.

Ferre, E.R., Bottini, G., Haggard, P., 2012. Vestibular inputs modulate somatosensory cortical processing. Brain Struct Funct 217, 859–864. doi:10.1007/s00429-012-0404-7

Ferrè, E.R., Bottini, G., Iannetti, G.D., Haggard, P., 2013. The balance of feelings: Vestibular modulation of bodily sensations. Cortex 49, 748–758. doi:10.1016/j.cortex.2012.01.012

Ferre, E.R., Lopez, C., Haggard, P., 2014. Anchoring the Self to the Body: Vestibular Contribution to the Sense of Self. Psychol Sci. doi:10.1177/0956797614547917

Ferre, E.R., Sedda, A., Gandola, M., Bottini, G., 2010. How the vestibular system modulates tactile perception in normal subjects: a behavioural and physiological study. Exp Brain Res. doi:10.1007/s00221-010-2450-9

Ferre, E.R., Vagnoni, E., Haggard, P., 2013. Vestibular contributions to bodily awareness. Neuropsychologia 51, 1445–1452. doi:10.1016/j.neuropsychologia.2013.04.006

Fetsch, C.R., Deangelis, G.C., Angelaki, D.E., 2010. Visual-vestibular cue integration for heading perception: applications of optimal cue integration theory. Eur J Neurosci 31, 1721–1729. doi:10.1111/j.1460-9568.2010.07207.x

Fetsch, C.R., Pouget, A., DeAngelis, G.C., Angelaki, D.E., 2012. Neural correlates of reliability-based cue weighting during multisensory integration. Nat Neurosci 15, 146–154. doi:10.1038/nn.2983

Fischer, E., Bülthoff, H.H., Logothetis, N.K., Bartels, A., 2012. Visual motion responses in the posterior cingulate sulcus: A comparison to V5/MT and MST. Cereb. Cortex 22, 865–876. doi:10.1093/cercor/bhr154

Forget, J., Buiatti, M., Dehaene, S., 2010. Temporal integration in visual word recognition. J Cogn Neurosci 22, 1054–1068. doi:10.1162/jocn.2009.21300

Forster, B., Cavina-Pratesi, C., Aglioti, S.M., Berlucchi, G., 2002. Redundant target effect and intersensory facilitation from visual-tactile interactions in simple reaction time. Exp. brain Res. 143, 480–7. doi:10.1007/s00221-002-1017-9

Frank, S.M., Baumann, O., Mattingley, J.B., Greenlee, M.W., 2014. Vestibular and Visual Responses in Human Posterior Insular Cortex. J Neurophysiol. doi:10.1152/jn.00078.2014

Freeman, S., Plotnik, M., Elidan, J., Rosen, L.J., Sohmer, H., 1999. Effect of white noise "masking" on vestibular evoked potentials recorded using different stimulus modalities. Acta Otolaryngol 119, 311–315.

Gentile, G., Petkova, V.I., Ehrsson, H.H., 2011. Integration of visual and tactile signals from the hand in the human brain: an FMRI study. J Neurophysiol 105, 910–922. doi:jn.00840.2010 [pii] 10.1152/jn.00840.2010

Ghaem, O., Mellet, E., Crivello, F., Tzourio, N., Mazoyer, B., Berthoz, A., Denis, M., 1997. Mental navigation along memorized routes activates the hippocampus, precuneus, and insula. Neuroreport 8, 739–744.

Ghazanfar, A.A., Schroeder, C.E., 2006. Is neocortex essentially multisensory? Trends Cogn. Sci. 10, 278–85. doi:10.1016/j.tics.2006.04.008

Glasser, M.F., Van Essen, D.C., 2011. Mapping human cortical areas in vivo based on myelin content as revealed by T1- and T2-weighted MRI. J Neurosci 31, 11597–11616. doi:31/32/11597 [pii] 10.1523/JNEUROSCI.2180-11.2011

Goldberg JM and Cullen KE, W.V.J., 2012. The Vestibular System: A Sixth Sense. Oxford Univ. Press.

Gomez-Alvarez, F.B., Jauregui-Renaud, K., 2011. Psychological symptoms and spatial orientation during the first 3 months after acute unilateral vestibular lesion. Arch Med Res 42, 97–103. doi:S0188-4409(11)00049-X [pii] 10.1016/j.arcmed.2011.03.004

Greicius, M.D., Menon, V., 2004. Default-mode activity during a passive sensory task: uncoupled from deactivation but impacting activation. J. Cogn. Neurosci. 16, 1484–92. doi:10.1162/0898929042568532

Grimm, S., Ernst, J., Boesiger, P., Schuepbach, D., Hell, D., Boeker, H., Northoff, G., 2009. Increased self-focus in major depressive disorder is related to neural abnormalities in subcortical-cortical midline structures. Hum. Brain Mapp. 30, 2617–27. doi:10.1002/hbm.20693

Groen, E.L., Jenkin, H.L., Howard, I.P., 2002. Perception of self-tilt in a true and illusory vertical plane. Perception 31, 1477–1490.

Grossman, E.D., Blake, R., 2002. Brain Areas Active during Visual Perception of Biological Motion. Neuron 35, 1167–75.

Guldin, W.O., Grüsser, O.J., 1998. Is there a vestibular cortex? Trends Neurosci 21, 254–9.

Gusnard, D.A., Akbudak, E., Shulman, G.L., Raichle, M.E., 2001. Medial prefrontal cortex and self-referential mental activity: relation to a default mode of brain function. Proc. Natl. Acad. Sci. U. S. A. 98, 4259–64. doi:10.1073/pnas.071043098

Guterstam, A., Björnsdotter, M., Gentile, G., Ehrsson, H.H., 2015. Posterior Cingulate Cortex Integrates the Senses of Self-Location and Body Ownership. Curr. Biol. doi:10.1016/j.cub.2015.03.059

Guterstam, A., Gentile, G., Ehrsson, H.H., 2013. The invisible hand illusion: multisensory integration leads to the embodiment of a discrete volume of empty space. J. Cogn. Neurosci. 25, 1078–99. doi:10.1162/jocn_a_00393

Guterstam, A., Petkova, V.I., Ehrsson, H.H., 2011. The illusion of owning a third arm. PLoS One 6, e17208. doi:10.1371/journal.pone.0017208

Halligan, P.W., Marshall, J.C., Wade, D.T., 1995. Unilateral somatoparaphrenia after right hemisphere stroke: a case description. Cortex 31, 173–182.

Hanes, D.A., McCollum, G., 2006. Cognitive-vestibular interactions: a review of patient difficulties and possible mechanisms. J Vestib Res 16, 75–91.

Herdman, S.J., Blatt, P., Schubert, M.C., Tusa, R.J., 2000. Falls in patients with vestibular deficits. Am J Otol 21, 847–851.

Hershenson, M., 1962. Reaction time as a measure of intersensory facilitation. J. Exp. Psychol. 63, 289–93.

Heydrich, L., Blanke, O., 2013. Distinct illusory own-body perceptions caused by damage to posterior insula and extrastriate cortex. Brain 136, 790–803. doi:10.1093/brain/aws364

Heydrich, L., Dieguez, S., Grunwald, T., Seeck, M., Blanke, O., 2010. Illusory own body perceptions: case reports and relevance for bodily self-consciousness. Conscious Cogn 19, 702–710. doi:S1053-8100(10)00130-3 [pii] 10.1016/j.concog.2010.04.010

Heydrich, L., Lopez, C., Seeck, M., Blanke, O., 2011. Partial and full own-body illusions of epileptic origin in a child with right temporoparietal epilepsy. Epilepsy Behav 20, 583–586. doi:S1525-5050(11)00011-4 [pii] 10.1016/j.yebeh.2011.01.008

Holmes, N.P., Spence, C., 2005. Multisensory integration: space, time and superadditivity. Curr. Biol. 15, R762–4. doi:10.1016/j.cub.2005.08.058

Howard, I.P., Childerson, L., 1994. The contribution of motion, the visual frame, and visual polarity to sensations of body tilt. Perception 23, 753–762.

Howard, I.P., Hu, G., 2001. Visually induced reorientation illusions. Perception 30, 583–600.

Howard, I.P., Hu, G., Saxe, R., Zacher, J.E., 2005. Visual orientation in a mirror world tilted 90?? Perception 34, 7–15. doi:10.1068/p5151

Huang, J., Gamble, D., Sarnlertsophon, K., Wang, X., Hsiao, S., 2012. Feeling music: integration of auditory and tactile inputs in musical meter perception. PLoS One 7, e48496. doi:10.1371/journal.pone.0048496

Huang, Z., Dai, R., Wu, X., Yang, Z., Liu, D., Hu, J., Gao, L., Tang, W., Mao, Y., Jin, Y., Wu, X., Liu, B., Zhang, Y., Lu, L., Laureys, S., Weng, X., Northoff, G., 2014. The self and its resting state in consciousness: an investigation of the vegetative state. Hum. Brain Mapp. 35, 1997–2008. doi:10.1002/hbm.22308

Indovina, I., Maffei, V., Bosco, G., Zago, M., Macaluso, E., Lacquaniti, F., 2005. Representation of visual gravitational motion in the human vestibular cortex. Science (80-.). 308, 416–419.

Ionta, S., Heydrich, L., Lenggenhager, B., Mouthon, M., Fornari, E., Chapuis, D., Gassert, R., Blanke, O., 2011. Multisensory mechanisms in temporo-parietal cortex support self-location and first-person perspective. Neuron 70, 363–374. doi:S0896-6273(11)00200-5 [pii] 10.1016/j.neuron.2011.03.009

Ionta, S., Martuzzi, R., Salomon, R., Blanke, O., 2014. The brain network reflecting bodily self-consciousness: a functional connectivity study. Soc. Cogn. Affect. Neurosci. 9, 1904–13. doi:10.1093/scan/nst185

Juravle, G., Deubel, H., Spence, C., 2011. Attention and suppression affect tactile perception in reach-to-grasp movements. Acta Psychol. (Amst). 138, 302–10. doi:10.1016/j.actpsy.2011.08.001

Kannape, O.A., Schwabe, L., Tadi, T., Blanke, O., 2010. The limits of agency in walking humans. Neuropsychologia 48, 1628–1636. doi:S0028-3932(10)00049-7 [pii] 10.1016/j.neuropsychologia.2010.02.005

Kelley, W.M., Macrae, C.N., Wyland, C.L., Caglar, S., Inati, S., Heatherton, T.F., 2002. Finding the self? An event-related fMRI study. J. Cogn. Neurosci. 14, 785–94. doi:10.1162/08989290260138672

Keshavarz, B., Berti, S., 2014. Integration of sensory information precedes the sensation of vection: a combined behavioral and event-related brain potential (ERP) study. Behav. Brain Res. 259, 131–6. doi:10.1016/j.bbr.2013.10.045

Kleinschmidt, A., Thilo, K. V, Buchel, C., Gresty, M.A., Bronstein, A.M., Frackowiak, R.S., 2002. Neural correlates of visual-motion perception as object- or self-motion. Neuroimage 16, 873–882.

Knox, J.J., Coppieters, M.W., Hodges, P.W., 2006. Do you know where your arm is if you think your head has moved? Exp Brain Res 173, 94–101. doi:10.1007/s00221-006-0368-z

Kobayashi, H., Hayashi, Y., Higashino, K., Saito, A., Kunihiro, T., Kanzaki, J., Goto, F., 2002. Dynamic and static subjective visual vertical with aging. Auris Nasus Larynx 29, 325–328.

Kording, K.P., Beierholm, U., Ma, W.J., Quartz, S., Tenenbaum, J.B., Shams, L., 2007. Causal inference in multisensory perception. PLoS One 2, e943. doi:10.1371/journal.pone.0000943

Kovács, G., Raabe, M., Greenlee, M.W., 2008. Neural correlates of visually induced self-motion illusion in depth. Cereb. Cortex 18, 1779–1787. doi:10.1093/cercor/bhm203

Lackner, J.R., 1992a. Spatial orientation in weightless environments. Perception 21, 803–812.

Lackner, J.R., 1992b. Sense of body position in parabolic flight. Ann N Y Acad Sci 656, 329–339.

Lackner, J.R., Levine, M.S., 1979. Changes in apparent body orientation and sensory localization induced by vibration of postural muscles: vibratory myesthetic illusions. Aviat Sp. Env. Med 50, 346–354.

Lacour, M., Dutheil, S., Tighilet, B., Lopez, C., Borel, L., 2009. Tell me your vestibular deficit, and i'll tell you how you'll compensate. Ann N Y Acad Sci 1164, 268–278.

Lacquaniti, F., Bosco, G., Indovina, I., La Scaleia, B., Maffei, V., Moscatelli, A., Zago, M., 2013. Visual gravitational motion and the vestibular system in humans. Front. Integr. Neurosci. 7, 101. doi:10.3389/fnint.2013.00101

Lamm, C., Decety, J., Singer, T., 2011. Meta-analytic evidence for common and distinct neural networks associated with directly experienced pain and empathy for pain. Neuroimage 54, 2492–2502. doi:S1053-8119(10)01306-6 [pii] 10.1016/j.neuroimage.2010.10.014

Le Chapelain, L., Beis, J.M., Paysant, J., Andre, J.M., 2001. Vestibular caloric stimulation evokes phantom limb illusions in patients with paraplegia. Spinal Cord 39, 85–87.

Lemogne, C., Delaveau, P., Freton, M., Guionnet, S., Fossati, P., 2012. Medial prefrontal cortex and the self in major depression. J. Affect. Disord. 136, e1–e11. doi:10.1016/j.jad.2010.11.034

Lenggenhager, B., Halje, P., Blanke, O., 2011. Alpha band oscillations correlate with illusory self-location induced by virtual reality. Eur J Neurosci 33, 1935–1943. doi:10.1111/j.1460-9568.2011.07647.x

Lenggenhager, B., Lopez, C., 2015. Vestibular Contributions to the Sense of Body , Self , and Others. doi:10.15502/9783958570023

Lenggenhager, B., Lopez, C., Blanke, O., 2008. Influence of galvanic vestibular stimulation on egocentric and object-based mental transformations. Exp. Brain Res. 184, 211–221. doi:10.1007/s00221-007-1095-9

Lenggenhager, B., Tadi, T., Metzinger, T., Blanke, O., 2007. Video ergo sum: manipulating bodily self-consciousness. Science 317, 1096–1099. doi:10.1126/science.1143439

Lestienne, F., Soechting, J., Berthoz, A., 1977. Postural readjustments induced by linear motion of visual scenes. Exp Brain Res 28, 363–384.

Limanowski, J., Blankenburg, F., 2015. Network activity underlying the illusory self-attribution of a dummy arm. Hum. Brain Mapp. 36, 2284–304. doi:10.1002/hbm.22770

Limanowski, J., Lutti, A., Blankenburg, F., 2014. The extrastriate body area is involved in illusory limb ownership. Neuroimage 86, 514–24. doi:10.1016/j.neuroimage.2013.10.035

Lopez, C., 2015. Vestibular Cortex, Brain Mapping: An Encyclopedic Reference. Elsevier. doi:10.1016/B978-0-12-397025-1.00227-X

Lopez, C., 2013. A neuroscientific account of how vestibular disorders impair bodily self-consciousness. Front. Integr. Neurosci. 7, 91. doi:10.3389/fnint.2013.00091

Lopez, C., Bachofner, C., Dieguez, S., Mercier, M., Blanke, O., 2008a. Internal model of gravity influences visual perception of pictures with implied motion (human body postures): a behavioral study in healthy and brain-damaged participants. FENS Abstr., vol.4, 088.7, 2008.

Lopez, C., Bachofner, C., Mercier, M., Blanke, O., 2009. Gravity and observer's body orientation influence the visual perception of human body postures. J Vis 9, 1 1–14. doi:10.1167/9.5.1 9/5/1 [pii]

Lopez, C., Bieri, C.P., Preuss, N., Mast, F.W., 2012a. Tactile and vestibular mechanisms underlying ownership for body parts: A non-visual variant of the rubber hand illusion. Neurosci Lett 511, 120–124.

Lopez, C., Blanke, O., 2011. The thalamocortical vestibular system in animals and humans. Brain Res Rev 67, 119–146. doi:S0165-0173(11)00002-6 [pii] 10.1016/j.brainresrev.2010.12.002

Lopez, C., Blanke, O., Mast, F.W., 2012b. The human vestibular cortex revealed by coordinate-based activation likelihood estimation meta-analysis. Neuroscience 212, 159–179. doi:10.1016/j.neuroscience.2012.03.028 S0306-4522(12)00289-8 [pii]

Lopez, C., Halje, P., Blanke, O., 2008b. Body ownership and embodiment: vestibular and multisensory mechanisms. Neurophysiol Clin 38, 149–161. doi:S0987-7053(08)00018-X [pii] 10.1016/j.neucli.2007.12.006

Lopez, C., Lenggenhager, B., Blanke, O., 2010. How vestibular stimulation interacts with illusory hand ownership. Conscious Cogn 19, 33–47. doi:S1053-8100(09)00189-5 [pii] 10.1016/j.concog.2009.12.003

Mach, E., 1875. Grundlinien der Lehre von den Bewegungsempfindungen. Engelmann, Leipzig.

Malis, D.D., Guyot, J.P., 2003. Room tilt illusion as a manifestation of peripheral vestibular disorders. Ann Otol Rhinol Laryngol 112, 600–605.

Mars, F., Archambault, P.S., Feldman, A.G., 2003. Vestibular contribution to combined arm and trunk motion. Exp Brain Res 150, 515–519. doi:10.1007/s00221-003-1485-6

Mast, F.W., Preuss, N., Hartmann, M., Grabherr, L., 2014. Spatial cognition, body representation and affective processes: the role of vestibular information beyond ocular reflexes and control of posture. Front. Integr. Neurosci. 8, 44. doi:10.3389/fnint.2014.00044

Mazzola, L., Lopez, C., Faillenot, I., Chouchou, F., Mauguiere, F., Isnard, J., 2014. Vestibular responses to direct stimulation of the human insular cortex. Ann Neurol. doi:10.1002/ana.24252

McGurk, H., MacDonald, J., 1976. Hearing lips and seeing voices. Nature 264, 746–8.

Miller, R.L., Pluta, S.R., Stein, B.E., Rowland, B.A., 2015. Relative Unisensory Strength and Timing Predict Their Multisensory Product. J. Neurosci. 35, 5213–5220. doi:10.1523/JNEUROSCI.4771-14.2015

Mitchell, J.P., Banaji, M.R., Macrae, C.N., 2005. The link between social cognition and self-referential thought in the medial prefrontal cortex. J. Cogn. Neurosci. 17, 1306–15. doi:10.1162/0898929055002418

Miyamoto, T., Fukushima, K., Takada, T., de Waele, C., Vidal, P.P., 2007. Saccular stimulation of the human cortex: a functional magnetic resonance imaging study. Neurosci Lett 423, 68–72.

Mohler, B., Thompson, W., 2005. Measuring vection in a large screen virtual environment. Proc. 2nd … 1, 103–109. doi:10.1145/1080402.1080421

Mozolic, J., Hugenschmidt, C., Peiffer, A., Laurienti, P., 2012. Multisensory Integration and Aging. Neural Bases Multisensory Process. Boca Rat. CRC Press Murray MM, Wallace MT, Ed. Front. Neurosci.

Murofushi, T., Iwasaki, S., Takai, Y., Takegoshi, H., 2005. Sound-evoked neurogenic responses with short latency of vestibular origin. Clin Neurophysiol 116, 401–405.

Naccache, L., Blandin, E., Dehaene, S., 2002. Unconscious masked priming depends on temporal attention. Psychol. Sci. a J. Am. Psychol. Soc. / APS 13, 416–424. doi:10.1111/1467-9280.00474

Nejad, A.B., Fossati, P., Lemogne, C., 2013. Self-referential processing, rumination, and cortical midline structures in major depression. Front. Hum. Neurosci. 7, 666. doi:10.3389/fnhum.2013.00666

Northoff, G., Bermpohl, F., 2004. Cortical midline structures and the self. Trends Cogn. Sci. 8, 102–7. doi:10.1016/j.tics.2004.01.004

Ohshiro, T., Angelaki, D.E., DeAngelis, G.C., 2011. A normalization model of multisensory integration. Nat. Neurosci. 14, 775–782. doi:10.1038/nn.2815

Palmisano, S., Allison, R.S., Schira, M.M., Barry, R.J., 2015. Future challenges for vection research: definitions, functional significance, measures, and neural bases. Front. Psychol. 6, 193. doi:10.3389/fpsyg.2015.00193

Park, H.-D., Correia, S., Ducorps, A., Tallon-Baudry, C., 2014. Spontaneous fluctuations in neural responses to heartbeats predict visual detection. Nat. Neurosci. 17, 612–8. doi:10.1038/nn.3671

Penfield, W., 1957. Vestibular sensation and the cerebral cortex. Ann Otol Rhinol Laryngol 66, 691–698.

Penfield, W., Faulk, M.E.J., 1955. The insula: further observations on its functions. Brain 78, 445–470.

Petkova, V.I., Bjornsdotter, M., Gentile, G., Jonsson, T., Li, T.Q., Ehrsson, H.H., 2011. From Part- to Whole-Body Ownership in the Multisensory Brain. Curr Biol 21, 1118–1122. doi:S0960-9822(11)00549-5 [pii] 10.1016/j.cub.2011.05.022

Pfeiffer, C., Lopez, C., Schmutz, V., Duenas, J.A., Martuzzi, R., Blanke, O., 2013. Multisensory origin of the subjective first-person perspective: visual, tactile, and vestibular mechanisms. PLoS One 8, e61751. doi:10.1371/journal.pone.0061751

Pfeiffer, C., Serino, A., Blanke, O., 2014. The vestibular system: a spatial reference for bodily self-consciousness. Front Integr Neurosci 8, 31. doi:10.3389/fnint.2014.00031

Philbeck, J.W., Behrmann, M., Biega, T., Levy, L., 2006. Asymmetrical perception of body rotation after unilateral injury to human vestibular cortex. Neuropsychologia 44, 1878–1890.

Philbeck, J.W., Behrmann, M., Levy, L., Potolicchio, S.J., Caputy, A.J., 2004. Path integration deficits during linear locomotion after human medial temporal lobectomy. J. Cogn. Neurosci. 16, 510–520. doi:10.1162/089892904323057254

Phillips-Silver, J., Trainor, L.J., 2008. Vestibular influence on auditory metrical interpretation. Brain Cogn. 67, 94–102. doi:10.1016/j.bandc.2007.11.007

Phillips-Silver, J., Trainor, L.J., 2007. Hearing what the body feels: auditory encoding of rhythmic movement. Cognition 105, 533–46. doi:10.1016/j.cognition.2006.11.006

Phillips-Silver, J., Trainor, L.J., 2005. Feeling the beat: movement influences infant rhythm perception. Science 308, 1430. doi:10.1126/science.1110922

Platek, S.M., Wathne, K., Tierney, N.G., Thomson, J.W., 2008. Neural correlates of self-face recognition: an effect-location meta-analysis. Brain Res. 1232, 173–84. doi:10.1016/j.brainres.2008.07.010

Previc, F.H., Liotti, M., Blakemore, C., Beer, J., Fox, P., 2000. Functional imaging of brain areas involved in the processing of coherent and incoherent wide field-of-view visual motion. Exp Brain Res 131, 393–405.

Prsa, M., Gale, S., Blanke, O., 2012. Self-motion leads to mandatory cue fusion across sensory modalities. J Neurophysiol 108, 2282–2291. doi:10.1152/jn.00439.2012

Qin, P., Northoff, G., 2011. How is our self related to midline regions and the default-mode network? Neuroimage 57, 1221–33. doi:10.1016/j.neuroimage.2011.05.028

Raichle, M.E., Snyder, A.Z., 2007. A default mode of brain function: a brief history of an evolving idea. Neuroimage 37, 1083–90; discussion 1097–9. doi:10.1016/j.neuroimage.2007.02.041

Ramette, P., Onfray, M., 2010. Inventaire irrationnel, Galerie Xi. ed. Editions courtes et longues.

Redfern, M.S., Talkowski, M.E., Jennings, J.R., Furman, J.M., 2004. Cognitive influences in postural control of patients with unilateral vestibular loss. Gait Posture 19, 105–114. doi:10.1016/S0966-6362(03)00032-8 S0966636203000328 [pii]

Ridgway, N., Milders, M., Sahraie, A., 2008. Redundant target effect and the processing of colour and luminance. Exp. brain Res. 187, 153–60. doi:10.1007/s00221-008-1293-0

Riecke, B.E., Väljamäe, A., Schulte-Pelkum, J., 2009. Moving sounds enhance the visually-induced self-motion illusion (circular vection) in virtual reality. ACM Trans. Appl. Percept. 6, 1–27. doi:10.1145/1498700.1498701

Rowland, B.A., Stein, B.E., 2014. A model of the temporal dynamics of multisensory enhancement. Neurosci. Biobehav. Rev. 41, 78–84. doi:10.1016/j.neubiorev.2013.12.003

Roy, J.E., Cullen, K.E., 2004. Dissociating self-generated from passively applied head motion: neural mechanisms in the vestibular nuclei. J. Neurosci. 24, 2102–2111. doi:10.1523/JNEUROSCI.3988-03.2004

Salomon, R., Levy, D.R., Malach, R., 2014. Deconstructing the default: cortical subdivision of the default mode/intrinsic system during self-related processing. Hum. Brain Mapp. 35, 1491–502. doi:10.1002/hbm.22268

Schubert, M.C., Herdman, S.J., Tusa, R.J., 2002. Vertical dynamic visual acuity in normal subjects and patients with vestibular hypofunction. Otol Neurotol 23, 372–377.

Schurger, A., Sarigiannidis, I., Naccache, L., Sitt, J.D., Dehaene, S., 2015. Cortical activity is more stable when sensory stimuli are consciously perceived. Proc. Natl. Acad. Sci. U. S. A. 112, E2083–92. doi:10.1073/pnas.1418730112

Seilheimer, R.L., Rosenberg, A., Angelaki, D.E., 2014. Models and processes of multisensory cue combination. Curr. Opin. Neurobiol. 25, 38–46. doi:10.1016/j.conb.2013.11.008

Sergent, C., Dehaene, S., 2004. Is consciousness a gradual phenomenon? Evidence for an all-or-none bifurcation during the attentional blink. Psychol. Sci. a J. Am. Psychol. Soc. / APS 15, 720–8. doi:10.1111/j.0956-7976.2004.00748.x

Shulman, G.L., Corbetta, M., Fiez, J.A., Buckner, R.L., Miezin, F.M., Raichle, M.E., Petersen, S.E., 1997a. Searching for activations that generalize over tasks. Hum. Brain Mapp. 5, 317–22. doi:10.1002/(SICI)1097-0193(1997)5:4<317::AID-HBM19>3.0.CO;2-A

Shulman, G.L., Fiez, J.A., Corbetta, M., Buckner, R.L., Miezin, F.M., Raichle, M.E., Petersen, S.E., 1997b. Common Blood Flow Changes across Visual Tasks: II. Decreases in Cerebral Cortex. J. Cogn. Neurosci. 9, 648–63. doi:10.1162/jocn.1997.9.5.648

Slobounov, S., Wu, T., Hallett, M., Shibasaki, H., Slobounov, E., Newell, K., 2006. Neural underpinning of postural responses to visual field motion. Biol Psychol 72, 188–197. doi:S0301-0511(05)00164-X [pii] 10.1016/j.biopsycho.2005.10.005

Smith, A.T., Wall, M.B., Thilo, K. V., 2012. Vestibular inputs to human motion-sensitive visual cortex. Cereb. Cortex 22, 1068–1077. doi:10.1093/cercor/bhr179

Smith, P.F., 1997. Vestibular-hippocampal interactions. Hippocampus 7, 465–471.

Smith, P.F., Zheng, Y., Horii, A., Darlington, C.L., 2005. Does vestibular damage cause cognitive dysfunction in humans? J Vestib Res 15, 1–9.

Spence, C., Pavani, F., Driver, J., 2004. Spatial constraints on visual-tactile cross-modal distractor congruency effects. Cogn Affect Behav Neurosci 4, 148–169.

Stein, B.E., Stanford, T.R., 2008. Multisensory integration: current issues from the perspective of the single neuron. Nat. Rev. Neurosci. 9, 255–66. doi:10.1038/nrn2331

Stein, B.E., Stanford, T.R., Rowland, B.A., 2014. Development of multisensory integration from the perspective of the individual neuron. Nat. Rev. Neurosci. 15, 520–35.

Stephan, T., Deutschländer, A., Nolte, A., Schneider, E., Wiesmann, M., Brandt, T., Dieterich, M., 2005. Functional MRI of galvanic vestibular stimulation with alternating currents at different frequencies. Neuroimage 26, 721–732.

Sugiuchi, Y., Izawa, Y., Ebata, S., Shinoda, Y., 2005. Vestibular cortical area in the periarcuate cortex: its afferent and efferent projections. Ann N Y Acad Sci 1039, 111–123.

Tiliket, C., Ventre-Dominey, J., Vighetto, A., Grochowicki, M., 1996. Room tilt illusion. A central otolith dysfunction. Arch Neurol 53, 1259–1264.

Todd, N.P., Cody, F.W., 2000. Vestibular responses to loud dance music: a physiological basis of the "rock and roll threshold"? J. Acoust. Soc. Am. 107, 496–500.

Tong, F., 2003. Out-of-body experiences: from Penfield to present. Trends Cogn Sci 7, 104–106.

Trainor, L.J., Gao, X., Lei, J., Lehtovaara, K., Harris, L.R., 2009. The primal role of the vestibular system in determining musical rhythm. Cortex. 45, 35–43. doi:10.1016/j.cortex.2007.10.014

Trutoiu, L.C., Mohler, B.J., Schulte-Pelkum, J., Bülthoff, H.H., 2009. Circular, linear, and curvilinear vection in a large-screen virtual environment with floor projection. Comput. Graph. 33, 47–58. doi:10.1016/j.cag.2008.11.008

Uddin, L.Q., Iacoboni, M., Lange, C., Keenan, J.P., 2007. The self and social cognition: the role of cortical midline structures and mirror neurons. Trends Cogn. Sci. 11, 153–7. doi:10.1016/j.tics.2007.01.001

Urgesi, C., Berlucchi, G., Aglioti, S.M., 2004. Magnetic stimulation of extrastriate body area impairs visual processing of nonfacial body parts. Curr Biol 14, 2130–2134.

Väljamäe, a., Soto-Faraco, S., 2008. Filling-in visual motion with sounds. Acta Psychol. (Amst). 129, 249–254. doi:10.1016/j.actpsy.2008.08.004

Van Atteveldt, N., Murray, M.M., Thut, G., Schroeder, C.E., 2014. Multisensory integration: flexible use of general operations. Neuron 81, 1240–53. doi:10.1016/j.neuron.2014.02.044

Van Hulle, L., Juravle, G., Spence, C., Crombez, G., Van Damme, S., 2013a. Attention modulates sensory suppression during back movements. Conscious. Cogn. 22, 420–9. doi:10.1016/j.concog.2013.01.011

Van Hulle, L., Van Damme, S., Spence, C., Crombez, G., Gallace, A., 2013b. Spatial attention modulates tactile change detection. Exp. brain Res. 224, 295–302. doi:10.1007/s00221-012-3311-5

Ventre-Dominey, J., 2014. Vestibular function in the temporal and parietal cortex: distinct velocity and inertial processing pathways. Front Integr Neurosci 8, 53. doi:10.3389/fnint.2014.00053

Vilares, I., Kording, K., 2011. Bayesian models: the structure of the world, uncertainty, behavior, and the brain. Ann. N. Y. Acad. Sci. 1224, 22–39. doi:10.1111/j.1749-6632.2011.05965.x

Wall, M.B., Smith, A.T., 2008. The Representation of Egomotion in the Human Brain. Curr. Biol. 18, 191–194. doi:10.1016/j.cub.2007.12.053

Wang, Z., Chen, M., Gong, X., Huang, W., Xu, L., Zhou, C., 2008. Why cold water delays the onset of vestibular vertigo--an functional MRI study. Eur. J. Radiol. 67, 459–65. doi:10.1016/j.ejrad.2007.08.021

Wardman, D.L., Fitzpatrick, R.C., 2002. What does galvanic vestibular stimulation stimulate? Adv Exp Med Biol 508, 119–128.

Warren, W.H., Kay, B. a, Zosh, W.D., Duchon, a P., Sahuc, S., 2001. Optic flow is used to control human walking. Nat. Neurosci. 4, 213–216. doi:10.1038/84054

Wiest, G., Zimprich, F., Prayer, D., Czech, T., Serles, W., Baumgartner, C., 2004. Vestibular processing in human paramedian precuneus as shown by electrical cortical stimulation. Neurology 62, 473–475.

Witten, I.B., Knudsen, E.I., 2005. Why seeing is believing: merging auditory and visual worlds. Neuron 48, 489–96. doi:10.1016/j.neuron.2005.10.020

Yaoi, K., Osaka, N., Osaka, M., 2009. Is the self special in the dorsomedial prefrontal cortex? An fMRI study. Soc. Neurosci. 4, 455–63. doi:10.1080/17470910903027808

Yokota, J., 2000. [Click-evoked myogenic potential as a new diagnostic tool for the vestibular disorders]. No To Shinkei 52, 691–699.

Zhu, Y., Zhang, L., Fan, J., Han, S., 2007. Neural basis of cultural influence on self-representation. Neuroimage 34, 1310–6. doi:10.1016/j.neuroimage.2006.08.047

zu Eulenburg, P., Baumgärtner, U., Treede, R.D., Dieterich, M., 2013. Interoceptive and multimodal functions of the operculo-insular cortex: Tactile, nociceptive and vestibular representations. Neuroimage 83, 75–86. doi:10.1016/j.neuroimage.2013.06.057

zu Eulenburg, P., Caspers, S., Roski, C., Eickhoff, S.B., 2012. Meta-analytical definition and functional connectivity of the human vestibular cortex. Neuroimage 60, 162–169. doi:10.1016/j.neuroimage.2011.12.032

Glossary

ACC	anterior cingulate cortex
AG	angular gyrus
AH	autoscopic hallucination
BA	Brodmann area
Csv	cingulate sulcus visual area
CVS	caloric vestibular stimulation
EBA	extrastriate body area
FBI	full body illusion
FEF	frontal eye fields
fMRI	functional magnetic resonance imaging
GCS	galvanic cutaneous stimulation
GVS	galvanic vestibular stimulation
HAS	heautoscopy
hMSTd	human homologue of MSTd, the anterior part of MST
IL	intralaminar nuclei
IPL	inferior parietal lobule
IPS	intraparietal sulcus
LGN	lateral geniculate nucleus
LP	lateral posterior nucleus
MGN	medial geniculate nucleus
MIP	medial intraparietal area
MST	medial superior temporal
MT	middle temporal
NCC	neural correlates of consciousness
OBE	out-of-body experience

PET	positron emission tomography
PFC	prefrontal cortex
PIVC	parieto insular vestibular cortex
PMC	premotor cortex
RHI	rubber hand illusion
S1	primary somatosensory cortex
S2	secondary somatosensory cortex
SMG	supramarginal gyrus
STG	superior temporal gyrus
TPJ	temporo-parietal junction
VA	ventro anterior nuclear complex
VIP	ventral intraparietal area
VL	ventro lateral nuclear complex
VPL	ventral posterior lateral nucleus
VPM	ventral posterior medial nucleus
VPS	visual posterior sylvian area
VR	virtual reality

Acknowledgments

I first thank my wife Jung Soo - *kamsahamnida* to you - for being the best support I could ever find, whether it is with direct help with my scientific work or simply for her presence. I thank my two children Lucas Kim and Jiah Lior for giving me the force to have many projects to succeed in the next decades.

I thank my co-directors: Pr Reto Meuli, for giving me the chance to become a radiologist, with a very special mention to the care he gave me in his neuroradiology teaching, together with Prs Philippe Maeder and Dr Patrick Hagmann. Their presence was very important. Pr Olaf Blanke, for the chance that he gave me to come in Switzerland, study at EPFL and learn new approaches in cognitive psychology, that fascinated me since I met him in a conference eleven years ago.

I met Olaf Blanke at a conference in Porto. I heard more for the first time about bodily self-consciousness and out-of-body experiences. This conference was kind of strange, as a community of, let's say, "parapsychologists", was also present amongst major cognitive scientists, who were somehow my rock stars of the moment. This was a wonderful opportunity for me, as a student finishing his master degree, to develop my critical thinking. Some of the people in Porto's conference were proposing irrational explanations but claiming the use of scientific methods that could be confusing for a naïve observer; looking like science but being something else. I choose my way quite easily, while I was already quite inspired by major thinkers such as the impressive Daniel Dennett; I was craving for learning new things, and my wish to

continue demystifying issues related to consciousness, without being resigned to dualistic beliefs, was quite strong, and I hope it continues like this in the future. I thank again Pr Stanislas Dehaene for all what I learnt with him in Paris when he hired me in his lab when I was 19 years old and fascinated by his work, and Pr Philippe Ascher who coached me to follow the good scientific pathways. I do not want to forget my dear Henry D. Plée, that I try to keep alive inside of me since he left us too early, and thanks to whom I learnt so rich details about ethology applied to human beings, and who still inspire me from my childhood. The chain of union with those remarkable people made all this possible. Finally I thank the MD-PhD Commission in Lausanne and the Swiss National Found for their financial support and the INSERM School program in France, who allowed me to pursue a double curriculum in medicine and science. I would like to add some special "thank you" to Dr Roberto Martuzzi for teaching me fMRI, to Dr Michiel van Elk for teaching me cognitive psychology methods, and to Dr Christophe Lopez for the huge knowledge he tried to transmit me on vestibular research. And I will not forget my lab mates: Mariia Kaliuzhna, Christian Pfeiffer, Lukas Heydrich, Bruno Herbelin, and more particularly *hvala lepa* to Polona Požeg. *Toda raba* to my colleague in radiology Dr Steven Hajdu who helped to polish the final version of my thesis. Thank you Pierre Naftule, for giving me the recent chance to "pay" my candidacy exam fees with my first official job as an actor in your theatre play. It was highly symbolic as I always kept as a target to manage medicine/science and my artistic projects equal in terms of personal investment. This opens me the opportunity to thank my professor of harpsichord Olivier Beaumont, who gave me the chance with his wonderful teaching to learn a lot, and to inspire me drawing lines between my academic interests and my

way of practicing music. Keeping the balance between science and music was a challenge during my all life, and I could continue to discern it was possible, thanks to Olivier, as he was always positive on my abilities to go further. Thank you Sebastian Dieguez, great master of irony and satire, for your very special way of thinking, out of the mediocre frames. My final intention goes to the wonderful, modest and bright Philippe Ramette, who knows everything so deeply about body, self and otherness.

Lausanne, April 15th 2015

Curriculum Vitae

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QUALIFICATIONS

2015	AIRP radiology course validated
2011	FMH1 Radiology
2009	FMH 1 Surgery
2008-2009	Federal Diploma of Medicine (MD), Swiss Public Health Office, Switzerland
2005	Master's Degree (MSc), with honours - mathematics and cognitive science Ecole Normale Supérieure, France
2004	Minor in Cognitive Science Ecole Normale Supérieure, France
2003	Selected for French MD-PhD Program – Ecole de l'INSERM, France
2002	Selected for medical studies –Dijon, France: rank 77/666
2000	Baccalauréat - Science section

EMPLOYMENT

2010-2015	Medical Doctor - Radiology Department University Hospital of Lausanne, Switzerland
	PhD candidate Center for Neuroprosthetics - Ecole Polytechnique Fédérale de Lausanne Research topics: “Neural mechanisms of bodily self consciousness, role of the vestibular and visual system in multisensory integration”
2009-2010	Resident in neurosurgery and surgical emergencies, Lausanne
2008-2009	Resident in general surgery, University Hospital, Geneva 1 month of volunteer experience in abdominal surgery unit, Prishtina, Kosovo
2003-2008	Intern, INSERM-CEA Cognitive Neuroimaging Unit, Neurospin center, Paris Supervision: Pr Stanislas Dehaene - Collège de France Research Topics: Neural correlates of consciousness and reading expertise
2002-2008	Working as nurse’s aide, stretcher-bearer, nurse and surgery assistant
1999	Workman in foundry

PUBLICATIONS

Science and Medicine

The effect of limb crossing and limb congruency on multisensory integration in peripersonal space for the upper and lower extremities. Van Elk J, Forget J, Blanke O, Consciousness and Cognition, in press

Temporal integration in visual word recognition, Forget J, Buiatti M and Dehaene S, 2010 May;22(5):1054-68.Impact Factor: 4.867

What and where in word reading: ventral coding of written words revealed by parietal atrophy, Vinckier F, Naccache L, Papeix C, Forget J, Hahn-Barma V, Dehaene S, Cohen L, J Cogn Neurosci, 18(12): 1998-2012, December 2006

Association between HIV infection and lymphoepithelial cyst of the pancreas. Forget J, Genevay M, Dumonceau JM, Morel P, Berney T. Société Suisse de chirurgie Viscérale, Zurich, september 2009 (published in Swiss Medical Weekly)

Association between HIV infection and lymphoepithelial cyst of the pancreas. Bedat, Morel, Dumonceau, Genevay, Forget, Berney, Pancreatology 2012

Political science

Book chapter in: Kosovo, Récits sur la construction d'un Etat. Publication on Kosovo statebuilding by french military officers, international workers, political analysts and diplomats. Introduction by Pr Jacques Rupnik. Coordinated by S Gricourt and G Pernet. Editions Non Lieu, Paris, 2014. Albanian version published by Koha group, Prishtina, Kosovo.

Le Coluche 'kosovar' fait son entrée en scène, Tribune on a satiric party in Kosovo, Marianne, November 2013

Votation, piège à cons, Tribune on Minder initiative and its applicability in France, Forget J and Richard Molard G, Marianne, mars 2013

The wealth of our differences – the story of an intercountry adoption – Forget J Monthly Review June 2012 - International Social Service - International Reference Centre for the Rights of Children Deprived of their Family (ISS / IRC)

Opinion on Swiss elections, La Tribune de Genève, October 2011

TV and RADIO SHOWS

Interview for medical activities at CHUV, Lausanne and in Bern meeting with François Hollande's official visit. April 15th 2015 (RTS la première, TV5 Monde, Canal plus, la nouvelle edition)

Interview France Culture, Documentaire Sur les docks, Les voies royales du club 21ème siècle, Claire Pouly; février 2015

Interviews at the radio show on Radio Television Suisse la première," En ligne directe" Debate on French government actions October 31st 2013 and "Forum", January 9th 2014

Interview for KTO channel and France 5: scientific explanation of Out of Body experiences and Near-Death experiences phenomena TV reportage "Le commun des mortels", 2011

Finalist at TV show 'Questions pour un Champion', University Edition, 2008

INVITED SPEAKER

Société Suisse de Radiologie, Luzern (CH), June 2013

'The irrational body'

a collaboration with the French visual artist Philippe Ramette, Paris, 2012

Ecole de l'INSERM – Fondation Liliane Bettencourt Schueller, Paris, 2012

Ecole de l'INSERM – Fondation Liliane Bettencourt Schueller, Paris, 2011

Brain Meeting, LREN, University Hospital, Lausanne, December 2011

Rotary Club Prishtina, Prishtina, May 2011

Brain and Cognition Seminar, University Hospital, Geneva, May 2011

Brain Meeting, LREN, University Hospital, Lausanne, May 2011

LNCO lab meeting, EPFL, Lausanne, 2011

Guest at recent International conferences

5th Israeli Presidential Conference Jerusalem 2013 – Shimon Peres 90th birthday

POSTER PRESENTATIONS

Société Suisse de Radiologie, 2014 (Educational Topics : Temporal encephalitis, CADASIL)

Ecole Lémanique de Neuroscience, Les Diablerets, Switzerland, september 2011

MD PhD scientific Day, University of Lausanne, November 2011

Cognitive Neuroscience Society, Montreal, May 2010

IPSEN foundation, Characterizing Consciousness seminar, Paris May 2010

Alpine Human Brain Mapping, Champéry, Switzerland, January 2010

Journées de l'institut de Biologie, Collège de France, Paris, November 2009

Société Suisse de Chirurgie Viscérale, Zurich, September 2009

Ecole de l'INSERM, Journées de rentrée, Paris, September 2007

GRANTS

MD-PhD grant awarded by Swiss National Foundation, total amount 180.000 CHF)

Musical project composition and creation “Entre-Deux”, 2016, City of Geneva, Department of Culture, 8000 CHF

MEMBERSHIPS AND OTHER FUNCTIONS

Political advisor to Balkans in Kosovo, Albania and ex-Yougoslavia region

Vice President of Kaori Ito association “Hime”, for the development of Contemporary dancer and choreographer Mrs Kaori Ito

Member of Club XXIème siècle and Les entretiens de l’excellence, Paris

Member of FMH number 079364-83 (Swiss Federal Medical Association)

Member of Swiss MD-PhD Association

Junior member of Swiss Society of Radiology

Student of Ecole de l’INSERM program

Past mandates

President, Music Club, Bureau des Elèves, Ecole Normale Supérieure, Paris 2005-2006

Delegate for students at Burgundy University Council (Dijon), 2001-2004

LANGUAGES

French mother tongue

English fluent

Albanian fluent Standard language and Geg dialect

Slovenian, Croatian, Serbian, Bosnian, basics to intermediate level

Hebrew Basics

Korean Basics

TEACHING EXPERIENCE

Bachelor students (EPFL), 2013-2014: teaching assistant in biochemistry, cellular biology, genetics. **2011-2012:** practical works in electroencephalography and evoked related potentials

Science & medicine: High-field MRI functional neuroimaging, electroencephalography, sonography, CT-scan imaging, MRI imaging, X-Ray imaging, Medical Imaging processing tools

IT: Environments: Windows, Linux, MacOsX. **Softwares:** Office, Photoshop, Matlab, Eprime, SPSS, R, SPM, Brain Voyager

OTHER INTERESTS AND ACTIVITES

Musician performer

Harpsichord – student of Olivier Baumont, Professor at CNSM Paris

Piano – Certificate of superior studies in piano, Mulhouse 1998

Pipe Organ & clavichord

Jazz and electric guitar

Concerts and other events:

Upcoming events:

- Music creation of show "Entre-Deux", with the participation of Philippe Ramette, and harpsichordist Jean Rondeau, January 2016
- Concert du midi , Espace Fusterie Genève, Clavecin solo. October 2015

Selected past events:

- Role in theatre play by Pierre Naftule, Lausanne, June 4th 2015, Swiss Convention Centre
- Role in music clips for artist MEI, Dijon, France, March 2015
- Piano Solo Concert for the French National Day: celebration by the French embassy in Prishtina, Kosovo, on behalf of her Excellency Mrs Maryse Daviet, July 14th 2013, in the presence of Kosovo government and presidency.
- Harpsichord solo concert / Conference with art exhibition by Olivier Morel, Red Zone art Gallery, April 22th 2013, Links between European baroque music and philosophical principles in Medieval Japan

- Harpsichord solo concert, Geneva March 1st 2013, in the presence of the French general consul and French ambassador to Switzerland
- Private harpsichord solo concert, Paris, February 19th 2013
- Clavichord: “Verklarte Nacht,” November 2012, Geneva, Creation by Brice Catherin
- Chamber music trio with Mrs Drita Dida (violinist –Philarmonic orchestra, Kosovo) for festival “Flute Sounds”, 2009, Prishtina, Kosovo
- Non exhaustive lists of past solo piano recitals: Château de la Robertsau, Strasbourg 1998, Théâtre de Langres, 1998, diverse recitals for charities from 1997 to 2000 (Kosovo war, associations in Senegal, Thailand orphans)

Records:

Piano - Works of Chopin: Polonaise opus 19nr1, Posthumous nocturnes in C# minor and in C minor, Posthumous waltz in A minor, 1998

Sport interests

kung fu, taijiquan, karate