Review

Bodily illusions in health and disease: Physiological and clinical perspectives and the concept of a cortical ‘body matrix’

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A R T I C L E   I N F O

Article history:
Received 8 November 2010
Received in revised form 22 March 2011
Accepted 25 March 2011

Keywords:
Rubber hand illusion
Body ownership
Cortical representation
Somatotopic representation
Spatial representation
Tactile function
Complex regional pain syndrome
Chronic pain
Spatial neglect
Phantom limb pain
Mirror therapy

A B S T R A C T

Illusions that induce a feeling of ownership over an artificial body or body-part have been used to explore the complex relationships that exist between the brain’s representation of the body and the integrity of the body itself. Here we discuss recent findings in both healthy volunteers and clinical populations that highlight the robust relationship that exists between a person’s sense of ownership over a body part, cortical processing of tactile input from that body part, and its physiological regulation. We propose that a network of multisensory and homeostatic brain areas may be responsible for maintaining a ‘body-matrix’. That is, a dynamic neural representation that not only extends beyond the body surface to integrate both somatotopic and peripersonal sensory data, but also integrates body-centred spatial sensory data. The existence of such a ‘body-matrix’ allows our brain to adapt to even profound anatomical and configurational changes to our body. It also plays an important role in maintaining homeostatic control over the body. Its alteration can be seen to have both deleterious and beneficial effects in various clinical populations.

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1. Introduction

It is over a decade now since Botvinick and Cohen (1998) reignited contemporary research interest in the class of out-of-body illusions of which the rubber hand illusion (RHI) constitutes
but one example. These phenomena are not new (Binet, 1888; Janet, 1898) – Tastevin (1937) published what is commonly acknowledged to be the first study of an out-of-body sensation elicited by an artificial finger. However, the last few years has seen a seemingly exponential growth of research on the phenomenon (see Makin et al., 2008, for a recent review). This burgeoning of research interest can be attributed, at least in part, to scientists’ increased appreciation of disorders of body representation in a number of psychopathologies. In addition, the rapid development of immersive virtual reality environments (e.g., Slater et al., 2009), where the possibility of ‘projecting’ (and controlling) the body into external (or virtual) space is becoming a reality (Gallace et al., in press), have given a far broader context to our understanding of body ownership and awareness than ever before.

The RHI is both subjectively powerful and, at the same time, simple to induce in the majority of participants – it can be elicited in a matter of seconds using nothing more than a joke-shop rubber hand, or even a pair of stuffed washing-up gloves (Ehrsson et al., 2004; Pavani et al., 2000). In the basic RHI (see Fig. 1), a participant is seated at a table with their right hand resting, out-of-sight behind an occluding screen, on the table. The rubber hand is placed directly in front of the participant in their direct view and in an anatomically plausible posture. The participant adopts the same hand posture as that of the rubber hand. The experimenter, sitting on the other side of the table, then starts to stroke both the rubber hand and the participant’s own occluded hand in synchrony. Remarkably, after a few seconds of stroking (approximately 11 s on average; see Ehrsson et al. (2004) and Kammers et al. (2009), although the timing of onset has been shown to be variable both within and between individuals (Zopf et al., 2010)), the majority of participants start to agree with statements such as ‘It seemed as if I were feeling the touch of the paintbrush in the location where I saw the rubber hand touched’, ‘I felt as if the rubber hand were my hand’, and ‘I found myself looking at the dummy hand thinking it was actually my own’ (Botvinick and Cohen, 1998).

2. Behavioural and perceptual aspects of the RHI

The strength of the RHI depends on the crossmodal congruence between what a person feels via the somatosensory pathways and what they see (Tsakiris, 2010). Although some researchers have emphasised the role of visual input in the RHI, describing it as an example of vision ‘overruling’ touch and proprioception (Honma et al., 2009), or ‘visual capture’ of touch and proprioception (Capelari et al., 2009), it is important to note that visual input is not critical either to inducing (Ehrsson et al., 2005a; Giuffra et al., 2010a,b; Pettova and Ehrsson, 2009), or to maintaining, the illusion (Moseley et al., 2008). Undoubtedly, however, the illusion is dependent on multisensory input. It works best when proprioception and touch are involved, when the rubber hand is placed in an anatomically plausible posture (Lloyd, 2007; Pavani et al., 2000; Tsakiris and Haggard, 2005; Zopf et al., 2010); when the same stimulation (visual and tactile) is provided to both the real and rubber hand (although seeing a laser pointer cast on the real or rubber hand can also induce an illusion of touch; see Durgin et al., 2007). That said, the illusion of ownership can still be induced to some extent when various of these criteria are not met. So, for example, when the rubber hand is stroked with a piece of soft cotton and the real hand with rough sponge, the difference in texture is detected, but the RHI is still induced (Schutz-Bosbach et al., 2009).

The precise physical characteristics of the two limbs need not be identical either. In fact, there are even anecdotal reports of volunteers reporting the illusion of ownership over a block of wood, or, remarkably, over a table-top, using the same experimental method (Armel and Ramachandran, 2003). Other researchers though have published contrasting results: The illusion of ownership over a stick (Tsakiris and Haggard, 2005) or a box (Hohwy and Paton, 2010) cannot readily be induced in healthy participants, but it appears relatively easy to transfer the illusion once it is induced, from the rubber hand to another object placed in the same spatial location as the artificial hand (Hohwy and Paton, 2010). What is more, once the illusion has been induced, participants tend to provide irrational and supernatural explanations for sensory phenomena that do not ‘fit’. For example, if the seen stimulus approaches the rubber hand without touching it – and given that the tactile stimulus to the actual hand still occurs in synchrony with the expected touch of the rubber hand – participants’ reports include statements such as: ‘there is an invisible extension of the (stimulating) finger to my arm’ and ‘there is a magnetic forcefield between the finger and the arm’ (Hohwy and Paton, 2010; Nilsen, 1963). Although most participants do not cognitively endorse the reality of the rubber hand, for example stating “… it feels like the rubber hand’s my hand … so I wouldn’t have another hand. Logically, I only have one (right) hand” (Lewis and Lloyd, 2010), the illusion may be sufficient to disrupt what the rubber hand looks like: ‘[the rubber hand] looks like my own!’ (Lewis and Lloyd, 2010).

Once the RHI has been established, stimuli presented on, or near to, the artificial hand, elicit behavioural and neural responses that would normally occur if they had been delivered on, or nearby, the participant’s own hand (e.g., Armel and Ramachandran, 2003; Ehrsson et al., 2007). For example, we normally respond more quickly to visual stimuli presented on our own hand than we do to visual stimuli presented in the peripheral space near the hand (Whiteley et al., 2008; see also Whiteley et al., 2004). Short and Ward (2009) recently used a ‘virtual hand’ paradigm, in which participants viewed 3D images of two hands, through a head-mounted visual display. Once a sense of ownership over the virtual hands had been established, the temporal advantage of responding to visual stimuli on the hand over visual stimuli occurring near the hand was replicated (see Hartcher-O’Brien et al., 2010). Thus, the neural mechanisms that subserve the facilitation of processing of body-related stimuli endorse the virtual hand.

Just as stimuli that evoke the desire to interact using the rubber hand increase the strength of the illusion (Giuffra et al., 2010), stimuli that threaten the artificial hand can engage protective responses. Moving a knife or needle toward the artificial hand often induces withdrawal of the actual hand (which, in turn, breaks the illusion). Nevertheless, the perceived threat to the hand is suffi-
cient to result in the activation of brain regions consistent with the preservation of the body (Ehrsson et al., 2007) (see below). That stimuli approaching the rubber hand evoke protective responses demonstrates that the spatial attributes of the stimuli, as well as their somatotopic attributes, contribute to the sense of ownership over the hand (although, notably, ‘image’ attributes do not (Holmes et al., 2006). In fact, Makin et al.’s (2008) recent account of the RHI, emphasizes the dependence of the RHI on multisensory representations of space that appear to be hand-centred (see also Lloyd, 2007). That is, it seems as though we not only own our body parts, but we also in some sense ‘own’ the space around them as well.

These observations in-and-of-themselves raise the interesting question as to whether the body can survive without the mind – certainly the mind-body link is more complex and bidirectional than previously thought, as demonstrated by recent applications of the RHI (see below). As for responses that serve to preserve a rubber hand embodied via the RHI, one might suggest that whether or not such protective responses are dependent on the illusion itself is open to question. Relevant in this regard is a result of a study by Avenanti et al. (2005) in which they reported a modulation of cortically evoked responses of the hand muscles when the participants watched another person’s hand being injured. In that experiment, there was no attempt to induce a sense of ownership over the seen hand. The authors attributed the effect to a kind of ‘motor empathy’, rather than to a sense of ownership over the other’s hand. Similar mechanisms in the sensory domain may underpin synaesthesia for pain, in which seeing someone else being injured evokes pain in one’s own body (see Fitzgibbon et al., 2010, for a review).

The RHI can also induce complex perceptual states that cannot be evoked simply by watching another person. For example, we have recently discovered that feelings that are characteristic of successful acupuncture, collectively called ‘Deqi’, are experienced when acupuncture is given to the rubber hand that is being viewed by the participant, and not to the real hand. This works just as long as the illusion is established beforehand (Bulley et al., 2011). Moreover, in healthy volunteers conditioned to the feeling of transcutaneous electrical nerve stimulation (TENS), subsequent TENS to the rubber hand can evoke tingling sensations and increased pressure pain thresholds on the actual arm (Bulley et al., 2011). These remarkable observations concur with the work of Hohwy and Paton (2010) in that the perceptual responses were logically impossible – that is, participants knew the acupuncture and TENS were only applied to an artificial hand – yet they nonetheless felt the effects.

Perhaps counterintuitively, the RHI appears to be more vivid when there is no actual hand at all. Giummarra et al. (2010a,b) recently induced a variant of the RHI in amputees, by using a mirror and a rubber hand placed on the opposite side of the mirror to the amputated limb. They compared the feelings and proprioceptive drift induced by stroking the rubber hand or the intact limb. Amputees were more likely than healthy controls to report illusory sensations, regardless of whether the rubber hand or the intact hand was stimulated. This finding adds to previous reports of synchiria in amputees (Sathian, 2000). Synchiria is the perception of touch on the phantom at seeing touch on the reflected intact limb. Both amputees and controls were more likely to report illusory sensations when the rubber hand was stroked than when the intact hand was stroked. Moreover, amputees who had sustained an avulsion of the brachial plexus prior to amputation, an injury that leaves the arm paralysed and insensitive, were less likely to report illusory sensations but no less likely to endorse embodiment of the rubber hand. This finding strongly suggests that the illusory sensations that can be evoked by the RHI depend on one’s sensory experience. Consistent with this idea is the finding of dyschiria (Acerra and Moseley, 2005). Dyschiria is the perception of pain, or tingling, when on one hand at seeing touch on the reflected intact hand.

Importantly, pain is evoked when the stimulated area corresponds to an area on the affected limb that would be sensitive to touch (so-called ‘allodynia’) and tingling or paraesthesia is evoked when the stimulated area corresponds to an area on the affected limb that is paraesthetic. The occurrence of dyschiria is reasonably common in people with CRPS (see below), but is uncommon in non-CRPS neuropathic pain states (Kramer et al., 2008). Other accounts of pain being evoked, or indeed relieved, by cross-modal stimuli abound, for example the man who experienced pain when his wife was injured (Bradshaw and Mattingley, 2001) or the amputee who gains pain relief by stimulating the prosthesis at a location corresponding to his pain (Moseley, 2007b; Weeks and Tsao, 2010).

3. Representations of peripersonal space and body ownership

One might speculate that in addition to an anatomically accurate representation of our body (as supported, for example, by the somatotopic homunculus; Narici et al., 1991; Penfield and Boldrey, 1937) our brains also support other, coarser, neural representations that are responsible for mapping not only the body surface but the space around it as well. In the extant literature on spatial information processing, the term ‘peripersonal space’ has been used to define the visual space around the body (Rizzolatti et al., 1997). It is widely agreed that one of the main functions of such a representation is to provide information about the position of objects in the surrounding environment with respect to the body (Holmes and Spence, 2004; Ladavas et al., 1998a). For some researchers, this occurs with the ultimate aim of planning and executing movements whose purpose is to protect the body from physical threat ( Cooke and Graziano, 2004). Neurophysiological studies suggest that this representation of the space around the body is body part-centred (i.e., it is supported by neurons having their receptive fields centred on the head, face, neck, torso, or shoulder; Holmes and Spence, 2004; Ladavas et al., 1998b). Recently, Makin et al. (2008) suggested that multisensory representations of ‘peri-hand’ space are critical for attributing an artificial hand to the self, which is in line with the finding that the spatial constraints of the RHI are about 30 cm from the participant’s real hand (Lloyd, 2007). Makin et al. (2008) put forward a putative neurocognitive model to explain the RHI in terms of multisensory integration in peri-hand space. They suggested that once the space around a rubber hand is represented as peri-hand space, the seen stroke of the brush on the dummy hand is then represented in reference frames centred on, and defined with respect to, the rubber hand (a process they argue to involve the activation of the intraparietal sulcus). Similarly, the felt touch of the brush stroking the real hand will also activate the same crossmodal mechanisms. This conjunction of visual and tactile sensory events in hand-centred coordinates signals the occurrence of a single bimodal stimulus. As a consequence, the sensation of touch is referred from the hidden real hand to the seen rubber hand (possibly involving the activation in the premotor cortex). While this elegant model appears able to explain the RHI, it cannot explain a number of other more recently reported phenomena related to the representation of the body. In particular, how can this representation of the peri-hand space be involved in the temperature drop observed by Moseley et al. (2009) after the induction of the RHI, or with the effects of crossing the hands in CRPS patients (Moseley et al., 2009)? It is difficult to reconcile the fact that a representation centred on a certain body part (and which is not affected by the position of that body part in space) can be involved in a number of effects that depend on where the body part is actually placed in external space. Certainly, one possibility is that all of these various phenomena are simply not related, and that different mechanisms are needed in order to explain them all. However, that said, a synthesis may still be possible.
This ever-increasing body of literature provides compelling evidence of the behavioural embodiment of artificial body parts and objects, and the pervasive nature of perceptual experiences that are evoked when multisensory inputs are manipulated experimentally. Clearly, somatotopic representations of the inputs are fundamental, as are spatial representations centred on the body part concerned – peripersonal space. One would expect, then, that uncovering the neurological mechanisms involved in bodily illusions such as the RHI might cast light on the relations between our sense of body ownership and other bodily functions, in health and disease.

4. Neuro mechanisms

Neuroimaging studies have started to uncover the neural underpinnings of the RHI. In the first study to be published on this topic, Ehrsson et al. (2004) highlighted the importance of the parietal cortex and the premotor cortex in the initiation of the illusion in a functional magnetic resonance imaging (fMRI) study. Subsequent research by Tsakiris et al. (2007) using positron emission tomography (PET) highlighted the importance of the right insula to the maintenance of the illusion. Tsakiris and his colleagues argued that cortical multisensory areas – the premotor cortex, the superior parietal lobule, and the operculum – seem to be critical to the induction of the RHI, while the right insula, and perhaps the frontal operculum, appear to be important in evoking the sense of ownership that follows. It is notable that damage to the right posterior insula is implicated in post-stroke patients with anosognosia – a disorder in which individuals deny the existence of a disability such as paralysis or sensory impairment (Karnath et al., 2005). Interestingly, although anosognosia has been often considered a disorder in a patient’s awareness of his/her deficits rather than a proper body-ownership disorder, it has been recently suggested that pathological beliefs regarding the functioning of one’s own limbs and disturbed feelings of limb ownership are clinically and anatomically linked (Karnath and Baier, 2010a; see also Karnath and Baier, 2010b; Karnath et al., 2005, for the involvement of the right insula in both the sense of limb ownership and of its functioning).

Schaef er et al. (2007) used an artificial hand and arm that appeared visually to be connected to the participant’s own body in order to give their participants the impression that they had a supernumerary third arm (positioned in a central location between their actual hands; see also Newport et al., 2010). The behavioural data, obtained by means of questionnaire responses, demonstrated that six out of the eight participants tested felt as if they had three arms (yet another impossible notion!). Even more interesting is that the activation of primary somatosensory cortex (SI), as measured by magnetoencephalography (MEG), was modulated by the perceived presence of the supernumerary limb (i.e., the cortical representation of the thumb shifted to a more medial and superior position). This modulation was found to be positively related to the strength of the feeling that the third arm actually belonged to the participant. That is, the modulation of bodily awareness seems to correlate with changes in activity at the level of the somatosensory cortex – a finding consistent with earlier work in which artificially induced referred sensations occurred with concomitant changes in S1 responses (Schaef er et al., 2006). That sensory input can be used to induce impossible configurations of the perceptual representation of one’s body is not new. In older experiments using tendon vibration (e.g., Craske, 1977), participants were reported to experience their hand moving through their head, or their nose growing to an unnatural length (the so-called ‘Pinocchio illusion’), or their waist shrinking (Ehrsson et al., 2005b). However, recent work has also established that entirely novel bodily schema can also be generated without the need to manipulate the sensory input: For instance, in one recent study, Moseley and Brugger (2009) encouraged upper limb amputees to learn a movement of their phantom limb that would be impossible to perform in a real limb because of anatomical constraints. Remarkably, those who reported success also reported fundamental changes in the structure of their phantom limb – for example, the wrist joint was transformed into a wheel and axle type joint (see Fig. 2). Crucially, all of the participants’ reports (which, of course, might be subject to experimenter expectancy effects) were corroborated by performance on an implicit motor imagery task.

Recently, researchers have been using event-related potentials (ERPs) in order to investigate the role of early and late neural processing in the integration of seen and felt tactile stimulation, thought to be at the core of the RHI. Watching someone else being touched activates secondary somatosensory cortex in the same manner as being touched – a kind of tactile empathy (Keysers et al., 2004). Press et al. (2008) extended this to the RHI. They demonstrated increased N140 amplitudes, which are thought to reflect the early sensory processing of the stimuli, after a training period in which participants were exposed to synchronous tactile and visual stimuli presented on a rubber hand or a non-corporeal rubber object. Surprisingly, this effect did not change as a function of whether the participants were viewing a rubber hand or another object. This would seem consistent with Armel and Ramachandran’s observation that they were able to induce the illusion of ownership over a table-top (Armel and Ramachandran, 2003; though see Tsakiris and Haggard, 2005; Hohwy and Paton, 2010, for contradictory findings). Press et al. (2008) also reported that later ERP components (i.e., those occurring more than 200 ms post-stimulus) were modulated by the ‘spatial’ compatibility between the real hand and the visible rubber hand/object. That is, an enhanced sustained negativity was found following stimulation of the left hand when participants viewed a left rubber hand or object. These findings can be taken to suggest that: (1) Early levels of sensory information processing (e.g., the secondary somatosensory cortex, SII) are modulated by the synchronous presentation of visual and tactile stimuli, but not by the anatomical compatibility between higher order representation(s) of the body and the position (or nature) of the objects in external space; (2) Later levels of information processing are affected both by the spatial compatibil-
ity between the position of the stimuli in external space and by the actual position of the body in space; and (3) These later changes in neural activity seem to be related to the physical similarity between the object placed in that part of space (i.e., a neutral object or rubber hand) and the participant’s own body. Press and her colleagues went on to conclude that higher order body representations affect later but not early stages of tactile information processing. It is relevant to note here that disrupting activity in higher order areas such as the right temporo-parietal junction (rTPJ) by using TMS impairs the process that compares the compatibility between the visual aspect of a stimulus and a mental representation of the body. That is, TMS over rTPJ reduced the extent to which an artificial rubber hand was incorporated into the mental representation of a person’s own body, while it increased the incorporation of a neutral object (Tsakiris et al., 2008; see also Tsakiris, 2010).

5. Body-centred spatial representations and bodily illusions – lessons from the clinic

On the basis of the large body of empirical evidence that is now available, it has been suggested that spatial rather than solely anatomical representations might play a major role in the awareness of tactile stimuli presented on the body surface (Gallese and Spence, 2008, 2010; Kitazawa, 2002). One source of evidence in support of such a claim comes from the study of those patients affected by spatial neglect. In fact, neurological damage to those areas of the brain involved in the processing and selection of the spatial aspects of stimulation, such as in neglect or extinction, is often associated with disorders of body ownership. So, for example, neglect patients may show the presence of somatoparaphrenia, a form of delusion whereby the patient denies ownership of a limb or an entire side of their body. That is, patients with this condition might affirm (even if no evidence of psychiatric disorders is present) that their contralesional arm belongs to the doctor or to another patient who they believe may have left it behind (Vallar and Ronchi, 2009). It is worth noting here that this deficit has also been reported in patients with spared somatosensory processing (e.g., Berthier and Starkstein, 1987). This suggests that peripheral mechanisms are unlikely to constitute the main cause of disrupted body disownership disorders such as somatoparaphrenia.

Emerging data suggest that tactile neglect-like pathologies, disrupted bodily awareness and body ownership can also result from neurological disease triggered by musculoskeletal injury. Anecdotal accounts exist, for example Sacks’ (1991) reflections of limb disownership after a fracture. One condition in which disrupted bodily awareness is common is complex regional pain syndrome (CRPS), which is most common after wrist fracture (occurring in about 2% of cases). CRPS is characterised by severe pain and sensitivity, swelling, and motor disturbance. Disrupted thermal regulation, with the affected arm most often cooler than the healthy one, is a cardinal sign of the disorder. Signs and symptoms are usually confined to a single limb or occasionally to one side of the body (see Janig and Baron, 2002, and Moseley, 2007a, for reviews).

Although usually triggered by minor tissue injury, CRPS has also been reported after stroke (Petchkrau et al., 2000) and psychogenic cases have also been reported too (Grande et al., 2004). Acute CRPS is sometimes still considered a peripheral disorder (Oaklander and Fields, 2009), but chronic CRPS is now widely established to be a central nervous system disease (Janig and Baron, 2002). Behavioural evidence of neglect and disruption of bodily awareness, including disownership of the limb, were first reported in people with CRPS almost 150 years ago in seminal work by Mitchell (1864). However, only recently have these phenomena been formally investigated using more robust empirical/psychophysical methods.

We now know that in those suffering from CRPS one limb, the limb is perceived to be bigger than it actually is (Moseley, 2005), a phenomenon known as ‘macrosomatognosia’ (Podoll and Robinson, 2000). As might be predicted, CRPS is also associated with increased two-point discrimination threshold on the affected limb (Moseley et al., 2008b; Moseley and Wiech, 2009). This perceived enlargement of a specific body part occurs clinically with the use of local anaesthesia – think of the feeling of a fat lip after the anaesthetic wears off following a dental procedure – and has been induced experimentally by topical anaesthetic applied to a single digit, non-noxious electrical stimulation of one digit, and painful cooling of one digit (Gandevia and Phegan, 1999, see Fig. 3).

Amputees often report that their phantom limb is very large, twisted, heavy, or floating above them (Melzack, 1989). The wide range of perceptual distortions that are reported by amputees has been comprehensively studied (Giummarra et al., 2010a,b) and such distortions are usually attributed to bottom-up mechanisms, namely disrupted somatosensory input from the body-part concerned. The common observation that people with CRPS often report feeling as though the affected limb no longer belongs to them has also been attributed to bottom-up mechanisms (Lewis et al., 2007).

In fact, disruption of body-related representations is widespread in painful disorders. For example, in phantom limb pain, to the extent of S1 reorganisation, as measured by the shift in the peak S1 response to stimulation of the lip, is positively related the magnitude of usual phantom limb pain (Flor et al., 1995). S1 reorganisation has also been documented in people with chronic low back pain (Flor et al., 1997) and CRPS (Maihofner et al., 2003). In CRPS, the somatotopic representation of the affected limb in primary sensory cortex is altered such that the peak cortical evoked response to stimulation of the 5th digit is about 1 cm closer to the peak cortical evoked response to 1st digit stimulation than in healthy controls (Maihofner et al., 2003); tactile stimuli are often mislocalised and proprioceptive acuity is reduced (Frettloh et al., 2006; Maihofner et al., 2006). When asked to judge whether a picture represents a left or right hand, a task that has been thoroughly investigated in healthy controls (see Parsons, 2001, for review), people with CRPS of one hand take longer to make this judgment if the pictured hand corresponds to their own affected limb (Moseley, 2004a,b). Previously, this effect has been attributed to pain (Schwoebel et al., 2001). However, experiments in healthy controls suggest that it probably reflects an information processing
bias instead, such that visual stimuli relevant to the healthy hand are prioritised over those relevant to the painful hand (Hudson et al., 2006; Moseley et al., 2005). A similar effect has also been observed in spatial neglect (Coslett, 1998). Thus, it is clear that the body-related cortical maps of the affected body-part are disrupted in patients suffering from CRPS. What is more, the response profile of SI neurons is altered as well. However, some of these findings may equally relate to disruption of higher level representations, such as those responsible for the functional engagement of body parts (e.g. Blasing et al., 2010) or for the mapping of external space.

Relevant to this possibility is the recent finding that CRPS is associated with spatially defined deficits in sensory processing. For example, in one recent study, individuals with unilateral CRPS resulting from tissue trauma to one arm made temporal order judgments (TOJs) concerning pairs of tactile stimuli, one delivered to either hand (Moseley et al., 2009). When the arms were positioned to either side of the body midline (i.e., in their normal space), the vibrotactile stimulus delivered to the affected hand had to be presented before the stimulus to the other hand in order for them to be perceived as simultaneous. However, when the participant’s arms were crossed over, such that the affected hand was now situated on the opposite side of the body midline and the healthy hand was placed on the affected side of space, the order of the stimuli had to be reversed in order for them to appear simultaneous (see Fig. 4). This pattern of results is also characteristic of post-stroke neglect (Aglioti et al., 1999; Berberovic et al., 2004; Rorden et al., 1997).

6. Spatial representation and autonomic control

The link between these higher order representations and signs and symptoms of CRPS seems to be even closer than was previously thought. Hard though it might be to believe, patients with CRPS involving autonomic dysfunction of one hand have a cold side of external space (Moseley et al., unpublished data). That is, when these patients hold their affected, cool, hand on the opposite side of the midline, it becomes warmer. Even more remarkably, when the participants held their unaffected, healthy hand on the opposite side of the midline, it became somewhat cooler and slightly less painful, although the extent of pain relief was too small to be clinically meaningful. The extent of the temperature change was positively related to how far across the midline the hand was positioned. These observations clearly beg for further investigation in order to address questions such as: How are the disruption of body ownership, tactile processing, and thermal regulation related to one another and to pain? Relevant to this is the finding that phantom limb pain is negatively related to stump temperature (Nikolajsen and Jensen, 2001) – perhaps they too have a cold side of space.

One is inclined to ask then, to what extent are higher order spatial representations responsible for these phenomena? The answers to such questions might have implications that extend well beyond our understanding of those individuals with chronic pain – indeed, many psychiatric and neurological conditions are also characterised by both distortions of bodily awareness or ownership and disrupted thermal regulation (see Supplementary Table S1).

7. The ‘body matrix’

Here, we suggest that a multisensory representation of peripersonal space, and, in particular, of the space directly around the body – what we call a ‘body matrix’ – might be involved in some aspects of the phenomena described in this review (see Fig. 5). This representation is likely to receive inputs from areas of the brain that code for visual, tactile, and proprioceptual input. An important difference between the body matrix and other representations of peripersonal space is that the body matrix is aligned with a body-centred rather than hand-centred frame of reference. That is, stimuli arising from the left side of external space and within the body-matrix are always mapped as ‘left’, regardless of the fact that they arise from the left hand, or from the right hand being placed in the left space (and regardless of their sensory modality). Note, however, that under those conditions in which the hands are crossed over the midline, the strength of the connections from somatotopically organized areas might change (Gallace et al., in press). Given that a body-centred frame of reference does not depend on the position of the body parts in space (e.g., whether the arms are crossed or uncrossed over the body midline), results such as those obtained with CRPS patients become more easily explained. Of course, it remains to be established whether this midline effect is centred on the head or the torso, so that this representation is rather coarse, and extends beyond the boundaries of the body surface, allows external objects, such as rubber hands (or indeed two rubber hands, see Petkova and Ehrsson, 2009), to be perceived as part of the body (but perhaps it is also responsible for phenomena such as tactile completion: Gallace and Spence, in press; Kitagawa et al., 2009). Given the multisensory nature of such representations, synchronous cross-modal stimulation of the external object would seem most likely to modulate ownership. Of course, any ‘assumption of unity’ that the participant has (i.e. a top-down belief that what the participant sees genuinely belongs together with what they feel), may help to facilitate the illusion (see Helbig and Ernst, 2007; Spence, 2007).

We propose that this body-centred representation might be altered (or the amount of neural activation involved in the representation be decreased; Maialofner et al., 2003) by abnormal feedback from other areas of the brain, just as is seen following direct neurological damage. A malfunctioning in the part of this representation responsible for mapping one side of the space around the body might, for example, be caused by altered input from the side of the body that more often occupies that part of space. In the case of CRPS, this altered input might result from musculoskeletal injury, while, in the neglect syndrome, this might be caused by direct damage or lack of feedback from other higher order spatial representations. The presence of an alteration that is spatially, rather than somatotopically driven, would then help to explain why it is that tactile processing in both neglect and CRPS patients varies whenever their hands are crossed over the body midline.

What is the role of this body matrix? We contend that the body matrix serves to maintain the integrity of the body at both the homeostatic and psychological levels, and to adapt to changes in our body structure and orientation (from both an ontogenetical and phylogenetic point of view; see Bremner et al., 2008). By incorporating regulatory functions such as tempera-
ture control and the prioritisation of tactile inputs, the body matrix contrasts with previous dichotomous distinctions between a posturo-sensorimotor body 'schema' and a conscious and evaluative 'body image' (e.g., Gallagher, 2005). Rather, the body matrix integrates these constructs by proposing a direct inter-relationship between cognitive representations such as ownership over a body part and homeostatic function such as thermoregulation. Not that such an inter-relationship necessitates a single cortical representation that is, one body in the brain. We instead propose that many cortical representations contribute to this interrelationship, much in the manner elegantly proposed by Berlucchi and Aglioti (2010), that is, many bodies in the brain. The precise mechanisms responsible for these inter-relationships certainly need to be investigated further, including by means of neuroimaging studies. However, we believe that an important role might be played here by the connections between the posterior parietal cortex (where spatially based information is processed and integrated) and the insular cortex (see Fechir et al., 2010, for the report of inhibitory connections between the insula and autonomic brain stem structures). In addition to its apparent role in the sense of ownership imparted by the RHI (Tsakiris et al., 2007), the insular is also important in interoceptive awareness (Craig, 2002; Critchley et al., 2004) and homeostasis (Oppenheimer et al., 1992). Interestingly, as a paralimbic cortex, the insular cortex can be considered a relatively old neural structure (Tucker, 1992). Following on from these considerations, it is not implausible to think that the body matrix (seen as a coarse representation of the body and of the space around it) might be evolved within this structure. In fact, from an evolutionary point of view, it seems more economical to have a unique structure (a sort of proto-representation of the body space) that can endorse different body shapes (given a small number of constraints) rather than having a larger number of more specific structures for more specific body shapes. Moreover, most mammals have a broadly similar body structure (Darwin, 1859) and a ‘body matrix’ such as that proposed here would accommodate this wider range of broadly similar structures.

Also relevant to this idea of a body matrix is the rapidly expanding literature on empathy. Empathy usually refers to understanding the emotional state of another, within the context of oneself (Decety and Jackson, 2006). Empathy is thought to be critical for social function, allowing us to interpret and predict the behaviours of others and to respond to them in a functional manner. Indeed, empathy may involve the active simulation of another person’s state, via activation of so-called cortical mirror systems (Fitzgibbon et al., 2010). A multisensory body matrix as proposed here would accommodate variability in body dimensions in the capacity to mirror the physical configuration and behaviour of another. Moreover, theories of embodied cognition (e.g., Damasio, 1996; Seitz, 2000) would suggest that the homeostatic and regulatory role of the body matrix might also give it a role in emotional empathy.

8. What happens to the disowned/replaced part?

Myriad studies have focused on how a foreign limb, or indeed object, can be ‘owned’. Researchers now know a lot about embodiment of artificial or even virtual body parts (and indeed entire bodies, e.g., Ehrsson, 2007; Lenggenhager et al., 2007), but far less is currently known about what happens to the limb that is ‘replaced’, if indeed it is. Even in the absence of the clinical observations outlined above, it would seem a sensible consideration because, with the exception of a small proportion of upper limb amputees (see Giummara et al., in press), neurocognitively normal participants never report the sensation of having three arms when they experience the RHI (Longo et al., 2008; Schaefer et al., in press). This observation suggests that either (1) The rubber hand and the actual hand become unified, that is, there is some sense of disownership of the intact, actual hand; or else (2) Maybe the dominant hand representation simply extinguishes the other representation as happens in the Colavita effect (see Hartcher-O’Brien et al., 2008, 2010).

The question related to the destiny of the disowned or replace body part was recently investigated by Moseley and his colleagues in a series of six RHI experiments, each conducted on a different
group of healthy volunteers (Moseley et al., 2008b). In their first experiment, they showed that the RHI was associated with cooling of the ‘replaced’ hand. Subsequently, it was demonstrated that that the drop in temperature was limited to the experimental hand – the opposite hand does not cool, nor for that matter does the ipsilateral leg. This result demonstrates that the effect is not simply a general effect of arousal (i.e., a body-wide sympathetic response). The drop in temperature was clearly dependent on the illusion of ownership over the rubber hand, not on tactile stimulation of the hand, nor on simultaneous visual and tactile input, and it was equally apparent no matter whether the RHI was induced in the left or right hand. Finally, the stronger the illusion of ownership over the rubber hand, the greater the drop in temperature of the intact hand (see Fig. 6). This cooling effect has since been replicated using a similar protocol (Kammers et al., in press) and using a protocol that does not involve the spatial disparity between any artificial and actual hand (Hohwy and Paton, 2010). We suggest here that this drop in the temperature of the hand might arise from the dynamic changes in neural activity across the body matrix. That is, following synchronous visuo-tactile stimulation, neural activation increases across the representation of the space that is now occupied by the rubber hand. As a result, that space starts to be considered more as an actual part of the body (generating protection, body ownership and homeostatic control). By contrast, the neural activation of the representation of the space where the real hand is placed decreases. As a consequence, that degree to which a space or body part is ‘owned’ is decreased, and thus homeostatic control and sensory processing from these areas decreases. Consistent with this idea is a recent finding of tactile processing deficits induced by visual-proprioceptive incongruence using prism glasses (Folegatti et al., 2009). In that study, participants performed a tactile detection task under a control condition in which visual and proprioceptive information were aligned and when prism glasses shifted the visual perspective so that it was no longer aligned with the proprioceptive input. In that condition, tactile processing was disrupted in the same manner as that observed during the RHI. That finding seems consistent with the idea that the perceived spatial coordinates of the limb are important. As such, one might predict, that the reduction in homeostatic control and sensory processing observed during the RHI would be reduced or eliminated if the rubber hand and the real hand were to be located in exactly the same location in space.

That the strength of the illusion and limb-specific cooling are positively related might lead one to wonder if the effect is in some way linked to Damasio’s (1996) somatic marker hypothesis; According to Damasio’s oft-cited theory, our reasoning and decision-making is influenced by our body’s internal state. That theory would predict that cooling of the limb would occur before the illusion. In contrast, the illusion clearly occurs before the limb begins to cool (see Figs. 6 and 7). Of further interest, with regards to the effects of the RHI on the replaced or disowned hand, were the results of a series of TOJ experiments performed by healthy volunteers who either were, or were not, experiencing the illusion (Moseley et al., 2008b). During the RHI, a vibrotactile stimulus had to be delivered to the ‘disowned’ hand before an identical stimulus was delivered to the opposite hand, for the two stimuli to be perceived as simultaneous (see Fig. 6). One might wonder if this effect could have resulted from the drop in skin temperature, but the magnitude of the cooling effect was too small to induce such a change (see von Bekesy, 1963). Thus, the simplest interpretation is that inducing the illusion of ownership over a rubber hand also induced a type of tactile neglect of the real hand, similar in magnitude to that observed in people suffering from CRPS of one hand (Moseley et al., 2009). Moreover, the sense of ownership over the rubber hand was positively correlated with the extent of the tactile processing bias as measured by stimulus onset asynchrony at which stimuli were perceived as simultaneous. A similar relation between the extent of the tactile processing bias away from the affected hand, and the reported sense of disownership of the arm, has been observed in people with CRPS of one arm (Moseley et al., unpublished data). The integration of ownership and regulatory loops was recently highlighted by Kammers et al. (in press), who demonstrated that cooling the experimental arm during the RHI increased the vividness of the illusion and warming it decreased the vividness of the illusion.

**Fig. 6.** Mean (bold line) and standard deviation (grey line) vividness of the rubber hand illusion (RHI) (panel a), foot skin temperature (b) and hand skin temperature (c) during control (Ctl) and RHI conditions. Scatterplots of the decrease in hand skin temperature vs the vividness of the RHI (d) and of the point of subjective simultaneity (PSS, R = 0° away from experimental hand) vs the vividness of the RHI. Asterisk denotes significant effect p < .02. Adapted from Moseley et al. (2008b).

**Fig. 7.** Infra-red thermographic images taken after 10 min of asynchronous stroking of the rubber hand and the actual hand, which does not induce the rubber hand illusion (RHIS) (left image) and after 25 min of a sustained rubber hand illusion (right image). Time course of the change in temperature at each of two locations on the hand is shown.
9. Other distortions of bodily perception induced by misleading visual cues

While the majority of studies have utilized an artificial (rubber) hand in order to induce intersensory conflict and distortions of body image, one might ask what happens if such an intersensory conflict is introduced by distorting the veridical visual input of one’s own limb? Moseley et al. (2008c) recently investigated the effect on pain of viewing one’s body through a magnifying or minifying lens (see also Kennett et al., 2001; Rock and Victor, 1964). In that study, participants with chronic pain in their arm made a set of ten stereotypical movements while viewing their affected limb. They simply watched their affected arm, or viewed it through (i) a pair of binoculars that had had their lenses removed (control condition), (ii) through binoculars (magnification condition), or (iii) through reversed binoculars (minification condition). The results showed that the increase in pain caused by movement was lower when the patients looked at their limb through a minifying lens than during any of the other conditions. By contrast, the increase in pain was greater when patients looked at their limb through a magnifying lens than in any of the other conditions (see Fig. 8). Crucially, because motion analysis demonstrated that the movements themselves were very similar during each condition, it can be concluded that the psychological illusion itself led to physiological consequences, namely more swelling of the fingers on the affected limb during magnification and less during minification.

That distorting the visual appearance of a limb can affect swelling demonstrates the bidirectional nature of the link between the body matrix and the body itself. However, one might ask how this effect could occur? There are at least three possibilities here: First, the representational state of the body probably has direct projections to descending modulatory neurons within the nociceptive system. In chronic pain patients, sensory cues that imply that the limb is more swollen than it actually is, likely activate these modulatory neurons. This possibility would be predicted by our modern understanding of pain as a protective output of the brain that depends on the implicit perception of threat to body tissue, not on the actual threat to body tissue (see Butler and Moseley, 2003, and Moseley, 2007a, for reviews).

The neural hardware that would be capable of mediating a top-down effect on swelling, should the brain seek to protect a specific body part, is also well-established – descending projections work both to facilitate and inhibit activity of spinal nociceptive neurons (Pertovaara, 2000; Vanegas and Schaible, 2004) and antidromic activation of C fibres has been shown to induce peptidergic inflammation and thus swelling (e.g., Wang et al., 1997). It is also possible that the effect is less about protection of the painful arm and, instead, just a legacy of the visual enhancement of touch, which is thought to be mediated by visuotactile cells in the parietal cortex (Kennett et al., 2001; Schaefer et al., 2005a,b, in press). Perhaps magnifying the visual image of the limb increases activity of these cells sufficiently to induce activation in sensitive neural networks subserving pain, and upregulating descending facilitation and subsequent peptidergic inflammation in a manner similar to that described above (Butler and Moseley, 2003).

Perhaps magnifying the image simply introduces conflict between vision and proprioception. Such incongruence has been proposed to cause phantom limb pain (Harris, 1999; Ramachandran et al., 1995), although it should be noted that this explanation would predict similar effects during both minification and magnification. There are also anecdotal reports that viewing oneself through a minifying lens reduces one’s sense of ownership over a body part (Ramachandran and Rogers Ramachandran, 2007), which would seem, in part, consistent with the idea that decreasing ownership over a limb serves to reduce provocation of pain in that limb. In any case, the remarkable observation that bodily illusions in which higher order representations of the body are cognitively distorted, modulates swelling at a tissue level, clearly implicates a top-down mechanism that extends to the bodily tissues.

In neurologically normal individuals, merely seeing a body part reduces pain evoked by a noxious stimulus (Longo et al., 2009) and seeing a magnified view of the body has a larger analgesic effect (Mancini et al., 2011). That a magnified visual image is algesic in patients with CRPS but analgesic in healthy controls is consistent with findings from somatosensory stimuli – proprioceptive when the central nervous system is in a sensitised state and antinoceptive when it is in a normal state (Fields et al., 2006). Indeed, it is well established that neural mechanisms that subserve nociception and pain undergo profound changes in sensitivity as pain persists (see Butler and Moseley, 2003), so much so that visual input of touch can evoke pain without any sensory input from the body part (Acerca and Moseley, 2005). This result would seem similar at first glance to recent reports that the RHI can be induced using noxious stimuli such that pain is felt in the rubber hand (Capelari et al., 2009).

Of course, many questions remain unanswered and the use of minification lenses to treat those in chronic pain, or magnifying lenses to treat acute procedural pain, are not yet warranted. However, that visual distortion can modulate tissue function adds to a growing body of evidence that illusions of body ownership and bodily awareness can have clinical applications.

10. Other bodily illusions in patients – can it all be done with mirrors?

That a minifying lens can reduce pain (at least in the short term) in patients with arm pain has now also been demonstrated with regards to phantom limb pain, albeit in a single case report (Ramachandran et al., 2009). Nonetheless, those familiar with research in this area cannot help but see the parallel between the use of minifying lenses to reduce pain and swelling utilized by Moseley et al. (2008c), and the more widespread use of mirrors to reduce the phantom limb pain, an approach popularized by Ramachandran et al. (1995). Although the peculiar perceptual effects that can be induced using mirrors have been of interest for well over a century (Stratton, 1899), Ramachandran’s observations sparked much interest in its potential clinically. In short, one places the affected arm or leg behind a mirror and uses the reflected image of the healthy arm or leg to ‘trick’ the brain to concluding that the affected limb is ‘magically’ better, or, as in the case of phantom limb pain in amputees – that the phantom has ‘come alive’ (Ramachandran et al., 1995).

With regard to phantom limb pain and CRPS, anecdotal observations are numerous and usually report complete resolution of pain and of other distressing symptoms during mirror therapy (Altschuler and Hu, 2008; Giraux and Sirigu, 2003; Karmarkar and Lieberman, 2006; MacLachlan et al., 2004; Ramachandran et al., 1995, 2009; Rosen and Lundborg, 2005; Tichelaar et al., 2007). However, case studies of little or no effect are typically unattractive to journal editors (Hubbard and Armstrong, 1997), and even the most benign of treatments can seem powerful on a one-off basis, so, to assess the efficacy of mirror therapy, we must rely on the usual scientific methods – randomised controlled trials. A full review of the evidence lies beyond the scope of this paper, but it has been covered in some detail elsewhere (Moseley et al., 2008a; Ramachandran and Altschuler, 2009). Perhaps the most parsimonious conclusion of the robust scientific data published to date would appear to be that mirror therapy decreases phantom limb pain and CRPS-related pain (Chan et al., 2007; McCabe et al., 2003), particularly if it constitutes part of a wider graded program of motor imagery (Moseley, 2006).
It remains unclear as to whether the analgesic effect of mirror therapy is greater than that offered by motor imagery alone (Brodie et al., 2007). Motor imagery paradigms that include visual feedback of a virtual limb (Mercier and Sirigu, 2009) report similar effects on phantom limb pain to those that do not include visual feedback (Maclver et al., 2008), although some reports suggest motor imagery alone can actually exacerbate pain in some patients (Moseley, 2004a,b; Moseley et al., 2008d). A head-to-head comparison remains to be undertaken. Mirror therapy seems promising in post-stroke rehabilitation, where it is known as mirror ‘training’, not ‘therapy’. Again, most case studies are very positive (Beis et al., 2001; Lum et al., 2004; Sathian et al., 2000; Stevens and Stoykov, 2004; though see Huffman, 1978, and Stevens and Stoykov, 2003), but in this randomised controlled trials also seem encouraging, particularly if mirror therapy is undertaken in the first months after the stroke (Altschuler et al., 1999; Cacchio et al., 2009; Subeyzay et al., 2007; Yavuzer et al., 2008).

That mirror feedback and motor imagery both seem to have some beneficial effects in patients with chronic pain, or post stroke, is consistent with the idea that the body matrix is disrupted in these conditions. Indeed, it remains possible that a key mechanism of the effect is the higher level of interest and engagement in therapy that such illusions might entail. Our group introduced 36 patients with arm pain to the mirror box and to motor imagery and told them that the effect of both was the same. Most (32/36) said they would prefer to use the mirror box and expected to do it more often (Moseley, 2010). We contend that, thus far, the available clinical trials have not clearly demonstrated that it is the reflected image of the other hand mediates the effect of mirror therapy, but more research into this possibility certainly seems warranted.

Regardless of whether mirror therapy offers any benefit over and above that offered by motor imagery, it is reasonable that both reinstate aspects of a disrupted body matrix. Motor imagery might work to reinstate the body matrix by activating previously established motor and behavioural representations and mirror therapy might have its effect via visual pathways. That the body matrix integrates spatial as well as somatotopic representations lends itself to explaining the beneficial effects of movement-based therapies that rely on across-midline movements rather than movement alone, such as Tai Chi and Feldenkrais (Lundblad et al., 1999).

11. Conclusions

That we own our body and can sense it is taken for granted. Experiments that have utilized bodily illusions, most notoriously the RHI, have been very important in these developments. The cortical mechanisms that underpin the RHI have now been elucidated, at least in part, and the utility of bodily illusions for investigating the representation of our body and the space around it, has been demonstrated. Indeed, psychological illusions revealed complex relationships between our sense of ownership over a body part, tactile processing, and autonomic control, relationships that seem to become disrupted in those individuals suffering from chronic pain and other neurological and psychiatric disorders. In order to explain these relationships, we have introduced the concept of ‘body matrix’, a body-centred coarse neural representation of our body and of the space around it. We propose that such a multisensory representation is involved in maintaining the integrity of the body (at both the homeostatic and psychological levels), and to adapt to changes in our body structure, and orientation. Damage, malfunctioning or altered feedback from and toward this structure might be one of the causes of certain symptoms of neurological syndromes involving body-ownership disorders, such as neglect and CRPS. Finally this review has highlighted the fact that multisensory illusions such as the mirror box, can be used to treat people with phantom limb pain and to aid recovery after stroke, but more work is still required to clarify the effects and to elucidate the mediating mechanism underlying them.

Acknowledgements

GLM is supported by the National Health & Medical Research Council of Australia ID 571090. We would like to thank Dr. Norimichi Kitagawa for drawing Fig. 1.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.neubiorev.2011.03.013.

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