The role of tactile afference in shaping motor behaviour and implications for prosthetic innovation

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Abstract

The present review focusses on how tactile somatosensory afference is encoded and processed, and how this information is interpreted and acted upon in terms of motor control. We relate the fundamental workings of the sensorimotor system to the rehabilitation of amputees using modern prosthetic interventions. Our sense of touch is central to our everyday lives, from allowing us to manipulate objects accurately to giving us a sense of self-embodiment. There are a variety of specialised cutaneous mechanoreceptive afferents, which differ in terms of type and density according to the skin site. In humans, there is a dense innervation of our hands, which is reflected in their vast over-representation in somatosensory and motor cortical areas. We review the accumulated evidence from animal and human studies about the precise interplay between the somatosensory and motor systems, which is highly integrated in many brain areas and often not separable. The glabrous hand skin provides exquisite, discriminative detail about touch, which is useful for refining movements. When these signals are disrupted, such as through injury or amputation, the consequences are considerable. The development of sensory feedback in prosthetics offers a promising avenue for the full integration of a missing body part. Real-time touch feedback from motor intentions aids in grip control and the ability to distinguish different surfaces, even introducing the possibility of pleasure in artificial touch. Thus, our knowledge from fundamental research into sensorimotor interactions should be used to develop more realistic and integrative prostheses.

Keywords: Somatosensory; Efferent; S1; M1; Touch; Rehabilitation

1. Introduction

Sensorimotor integration is the process where peripheral sensory input is used to update and modulate motor output. We receive a continuous stream of sensory afference from multiple senses, and the present review concentrates on tactile somatosensory input and how this shapes our behaviour. Cutaneous, tactile feedback is particularly pertinent for the fine tuning of dextrous movements involving the hands. The afference from mechanoreceptors in the hands allows us to engage in complex tasks, such as writing or playing a musical instrument. It also provides a wealth of information for exploratory and manipulative tactile interactions with objects, allowing us to distinguish between a multitude of surfaces. Thus, for accurate motor control and exploration of the world, sensorimotor integration is essential. This is achieving by comparing motor behaviour and sensory consequences, with the inclusion of cognitive factors such as prior learning, through internal models. The prediction of the sensory outcome of behaviour, especially in feedforward internal models, is key for smooth and precise interactions with the environment. In clinical conditions where sensory afferent feedback is degraded, patients can become progressively unstable during movements: from fine, dextrous control, to more gross control such as walking. Without precise sensory feedback, problems emerge that can cause accidents and make life difficult.

The question of how to approach sensorimotor integration is like the chicken and the egg: which came first? Sensory and motor systems develop in tandem and it essentially depends on the situation as to how we utilise our capabilities. A tactile stimulus may drive behaviour, for example, contact with a sharp object makes you move your hand away. Conversely, a motor intention may drive the behaviour; you may want to pick up a cup, so make a movement that then provides sensory feedback. Presently, we explore how somatosensory signals are relayed to the brain and processed in tandem with motor intentions, with a view to integrating these signals to advance prosthetics. By definition, the term somatosensory refers to any sensory systems providing the brain with information related to the body, including afference from cutaneous, muscle proprioceptive, articular and tendon mechanoreceptors. In the present study, we focus on the cutaneous, tactile system and the term somatosensory will thus be restricted to this sensory channel.

2. Somatosensory pathways

Tactile information is relayed from the periphery to the brain to provide a constant update of object-skin interactions. This is used by the brain to process what is happening on a moment-by-moment basis and shapes how we interact with the external world. Touch is important for controlling how we manipulate objects, but also plays a key role in our social

interactions and our well-being. In the following section, we will explore how and where different types of tactile input are relayed to the brain, where these signals are integrated with motor intentions and behaviour.

2.1 From the periphery to the brainstem

We have learned a great deal about the human touch system from the technique of microneurography: *in vivo*, axonal nerve recordings from single afferents in awake humans (Vallbo & Hagbarth, 1968; Vallbo, Hagbarth, & Wallin, 2004). This has provided a wealth of information about the functioning of the peripheral tactile system across the body, including responses from the skin of the hands, arms, face, legs and feet. A single mechanoreceptive afferent can encode many aspects of a tactile stimulus, such as pressure, vibration and force (Johnson, 2001; Knibestöl & Vallbo, 1980; Knibestöl, 1973, 1975; Ribot-Ciscar, Vedel, & Roll, 1989; Vallbo & Johansson, 1984), as well as more complex facets such as texture and features (Connor, Hsiao, Phillips, & Johnson, 1990; Phillips, Johansson, & Johnson, 1992; Pruszynski & Johansson, 2014; Saal, Vijayakumar, & Johansson, 2009; Weber et al., 2013).

There are many different types of mechanoreceptive afferent in human skin, and these can be classified based on a number of criteria, including whether the mechanoreceptor ending sits in glabrous (non-hairy) or hairy skin, whether it has a fast-conducting myelinated axon (30-75 m/s) or a slowly-conducting unmyelinated axon (~1 m/s), and its adaptation properties to a sustained tactile indentation (slowly-, intermediate- or fast-adaptation). In the glabrous skin of the ventral hands and feet, there are four main types of mechanoreceptive afferent, namely, fast-adapting type 1 (FA1, Meissner corpuscles), slowly-adapting type 1 (SA1, Merkel discs), fast-adapting type 2 (FA2, Pacinian corpuscles) and slowly-adapting type 2 (SA2, Ruffini endings) mechanoreceptive afferents (Figure 1). There are around 17,000 of these myelinated mechanoreceptors in the human hand, where FA1s account for 43%, SA1s for 25%, FA2s for 13%, and SA2s for 19% (Johansson & Vallbo, 1979). The type 1 mechanoreceptive afferents are characterised by having small, point-like receptive fields, whereas the type 2 afferents have larger, more diffuse receptive fields. The large number of mechanoreceptors allows for high discrimination of tactile surfaces with the hands, and particularly the finger tips, where the FA1s are clustered. There have been numerous microneurographical recordings from SA2s from the glabrous hand in humans (Vallbo & Johansson 1984), although histological work shows their presence, yet scarcity (Miller et al., 1958; Paré et al., 2003; Chikenji et al., 2010; Chikenji et al., 2011). The microneurography recordings may over-estimate the numbers of SA2s, as there is an innate sampling bias from spontaneously active units, which the SA2s very often are (see Figure 1).
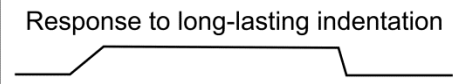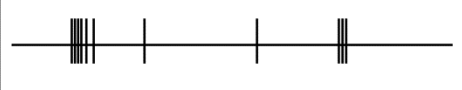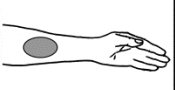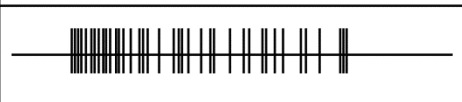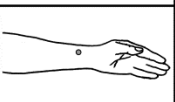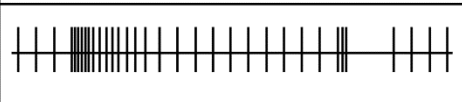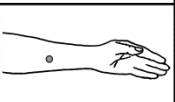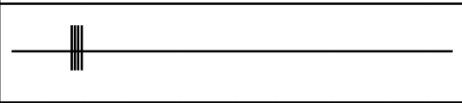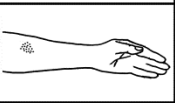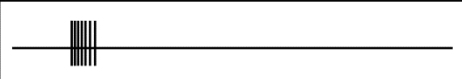
Response to long-lasting indentation	Unit type	Receptive field in: Glabrous skin	Hairy skin	Characteristics
	FA1	(hand)	(Not present)	Small, sharp receptive field Density highest in finger tips
	FA2	(hand)	(arm)	Large receptive field Sensitive to vibration
	SA1	(hand)	(arm)	Small, sharp receptive field Irregular firing to indentation
	SA2	(hand)	(arm)	Often spontaneous firing Regular firing to indentation
	Hair	(Not present)	(arm)	One unit consists of ~20 hairs Sensitive to movement of hairs
	Field	(Not present)	(arm)	Large, irregular receptive field with high-sensitivity spots

Figure 1: Differences between cutaneous myelinated mechanoreceptive afferents that signal discriminative aspects of touch.

The response to a long-lasting tactile indentation stimulus demonstrates the differences between fast-adapting (FA) and slowly-adapting (SA) afferents. The representative size of the afferent's receptive field (type 1 or type 2) is shown in glabrous and/or hairy skin, with notable further characteristics.

Hairy skin, which covers the vast majority of the body, also contains SA1, SA2 and FA2 mechanoreceptive afferents, as well as myelinated hair afferents and field afferents (Vallbo, Olausson, Wessberg, & Kakuda, 1995) (Figure 1), and unmyelinated C low-threshold mechanoreceptors (CLTMs in animals), so called C-tactile (CT) afferents in humans (Vallbo, Olausson, Wessberg, & Norrsell, 1993; Vallbo, Olausson, & Wessberg, 1999). The tactile information typically used in sensorimotor integration comes from the fast-conducting, myelinated afferents, which provide the brain with high spatial and temporal resolution information about discriminative touch e.g. what, when and where. CT afferents convey gentle touch; however, there is a delay of >1.5 s before the touch information is processed in the brain, due to the slow conduction along the unmyelinated axon (Ackerley, Eriksson, & Wessberg, 2013). These afferents are hypothesised to signal hedonic information about touch such as pleasantness, which is less useful for precise sensorimotor integration, although likely plays a role in the control and motivation of behaviour, such as driving the need to seek pleasurable, interactive social touch (McGlone et al., 2014).

Most research has focussed on investigating touch on the glabrous skin of the hands, partly due to its key role in our everyday lives. The precise responses from these mechanoreceptive afferents have been shown to play an essential role in the prehension needed for the dynamic balance between grip and load forces (Johansson & Westling, 1987; Westling & Johansson, 1987), for example when lifting slippery objects (Johansson & Westling, 1984). This review focuses on the input from the glabrous skin, as it is more pertinent in tactile interactions and manipulations, especially for the recovery of touch in amputees with prosthetic limbs. Hence, a direct, fast pathway is required to signal such important and precise information.

Once a myelinated mechanoreceptor has registered tactile activity, the first-order neurone sends the information up the spinal cord, where second-order neurones in the dorsal column nuclei (trigeminal nucleus for facial input) send projections across the midline, which terminate in the thalamus (Figure 2). Third-order neurones then project from the thalamus to the somatosensory cortex, where tactile information is processed and integrated cortically (Mountcastle, 1957). Although this direct pathway for myelinated tactile information exists, it is likely that the first point of integration for somatosensory input occurs in the dorsal horn (Abraira & Ginty, 2013). This is based on the findings from animal studies that all mechanoreceptive afferents have at least branching terminations in the dorsal horn (Petit & Burgess, 1968), which are somatotopically organised (Li et al., 2011). The local termination of the myelinated afferent information in the cat is mainly in lamina III, although also in lamina VI (Brown, Fyffe, & Noble, 1980; Brown, 1977; Semba et al., 1983, 1984, 1985). The microcircuitry present in the dorsal horn allows for the integration of intra- and inter-modality somatosensory information, therefore tactile input can be influenced by temperature and nociceptive inputs, as well as a top-down, descending drive.
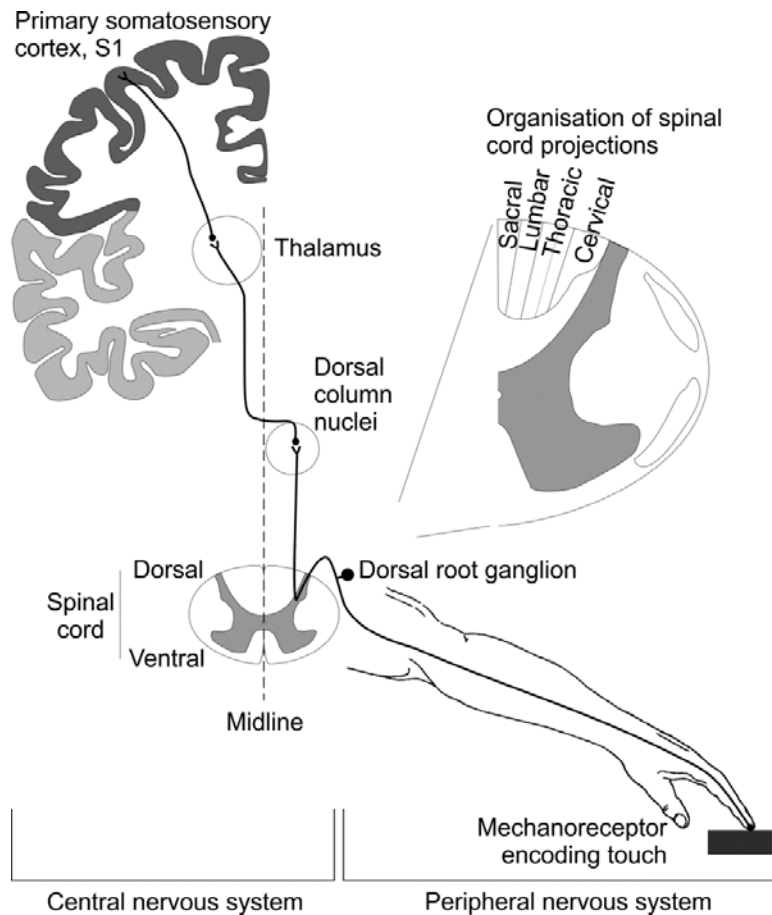
Figure 2: The canonical myelinated discriminative touch pathway from the peripheral mechanoreceptor to the cerebral cortex.

Mechanoreceptors encode when an object comes into contact with the skin; the first-order neurone sends the signal to the spinal cord, which synapses in the dorsal column nuclei. Here, the second-order neurone sends the information to the thalamus, which then projects to the primary somatosensory cortex (S1, in dark grey), as well as other cortical regions. The insert shows somatotopical organisation in the spinal cord projection.

2.2 Cortical processing of tactile somatosensory inputs

A network of cortical areas is involved in tactile processing and classically, the contralateral primary somatosensory cortex (S1), bilateral secondary somatosensory cortices (S2) and the contralateral posterior parietal cortex (PPC) are activated through touch during functional magnetic resonance imaging (fMRI) in humans (Ackerley, Hassan, et al., 2012; Disbrow, Roberts, & Krubitzer, 2000; Francis et al., 2000; Ruben et al., 2001). The somatotopic organisation of the S1 has been known since the historic mapping of the human cortex by Penfield (Penfield & Boldrey, 1937; Rasmussen & Penfield, 1947). The S1 can be further sub-divided into four separate Brodmann areas (BA) 3a, 3b, 1 and 2 (rostral to caudal; see

Figure 3) within the post-central gyrus; however, it has been suggested in monkeys that only BA3 should be referred to as the 'S1' as it receives the bulk of the thalamocortical projections (Kaas, Nelson, Sur, Dykes, & Merzenich, 1984).
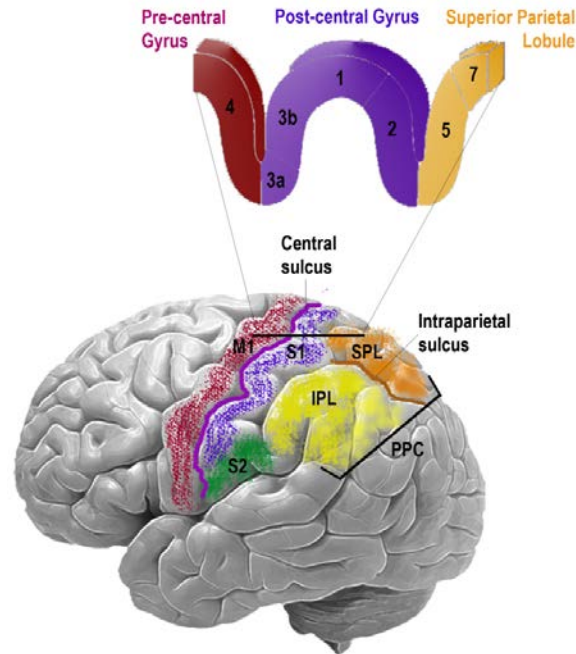
Figure 3: Overview of the main areas of the brain contributing to somatosensation.

The primary somatosensory cortex (S1), primary motor cortex (M1), secondary somatosensory cortex (S2), and posterior parietal cortex (PPC) divided by the intraparietal sulcus into the inferior parietal lobule (IPL) and superior parietal lobule (SPL) are shown, with a section shown across the central sulcus. Peripheral cutaneous stimulation can recruit all of these cortical areas; conversely, somatosensory perceptions can be elicited by direct stimulation applied on the post-central (S1), and to a lesser extent, the pre-central (M1) gyri. The numerical notation refers to the respective 1, 2, 3a, 3b, 4, 5 and 7 Brodmann area classifications.

The S1 receives projections from third order neurones originating in the ventral posterolateral nucleus of the thalamus (Figure 2; and ventral posteromedial nucleus for facial input) that terminate in a somatotopic fashion. Thalamic inputs terminate mainly in S1 cortical layer IV and in turn, neurones in this layer project on to other cortical areas. BA3b receives the densest thalamic input and shows specific responsivity to FA1, SA1 and SA2 afference, hence is key in processing discriminative touch. BA1 has inputs from FA1 afferents and BA2 is more sensitive to proprioceptive inputs. BA1 and BA2 receive reciprocal input from BA3b, where texture and size/shape are transmitted, respectively (Randolph &

Semmes, 1974). Each BA in the S1 contains a continuous gross somatotopic body representation, where BA3b and BA1 are mirror representations of the body. However, on closer inspection, the exact representation (e.g. inter- and intra-digital) is more variable and shows differences between individuals in monkeys (Kaas et al., 1979) and in humans during ultra-high field (7 Tesla) fMRI (Sanchez-Panchuelo et al., 2012; Stringer, Chen, Friedman, Gatenby, & Gore, 2011). Overall, the vast amount of myelinated tactile afference that is sent to the S1, coupled with the over-representation of glabrous skin areas, reveals its critical role in the interpretation of discriminative touch information.

The S2 is located in the human parietal operculum (see review by Eickhoff, Grefkes, Zilles, & Fink (2007) and Figure 3), and similarly to S1, was explored by Penfield & Jasper (1954) who reported in detail the somatosensory sensations evoked through electrical stimulation during neurosurgery in the region of the lateral sulcus (Sylvian fissure). There is a long-running debate as to whether incoming tactile information from the thalamus is processed serially from the S1 to the S2, or in parallel. In humans, the opinion is that parallel connections exist, where the first cortical activity is registered in the contralateral S1, ~20-30 ms after electrical nerve stimulation, and at ~90 ms in both the contralateral and ipsilateral S2 (Allison, McCarthy, Wood, & Jones, 1991; Allison, 1982; Hari et al., 1984; Wegner, Forss, & Salenius, 2000).

As well as purposed parallel thalamo-S1 and thalamo-S2 pathways, there is a flow of information between the S1 and S2, where S1 computes differences in firing between SA1 afferents in close proximity and S2 integrates this information to form the basis of texture perception (Hsiao, Johnson, & Twombly, 1993). The S2 contributes to discriminative somatosensory processing, but does not contain the precise somatotopic maps found in S1. Typically, tactile stimulation on one side of the body produces bilateral activations in the S2 during fMRI (Disbrow et al., 2000; Ruben et al., 2001), although with an increased response in the contralateral S2 (Hagen & Pardo, 2002). The receptive fields in the monkey S2 are large and can span many areas on multiple digits (Fitzgerald, Lane, Thakur, & Hsiao, 2006; Sinclair & Burton, 1993; Thakur, Fitzgerald, Lane, & Hsiao, 2006), as well as showing some selectivity for object orientation (Hsiao, Lane, & Fitzgerald, 2002).

Neurones in the S2 have been found to process not just somatosensory information, but also actions in object manipulation, specifically in the stages of motor hand grasping (Ishida et al., 2013), suggesting a role in haptic integration. The S2 also appears to encode more cognitive aspects of tactile processing, such as having representations of present and past sensory information, modulations with attention, comparisons between stimuli, correlations with

behavioural decisions, and tactile discrimination learning (Hsiao et al., 2002; Murray & Mishkin, 1984; Romo, Hernández, Zainos, Brody, & Salinas, 2002; Romo, Hernández, Zainos, Lemus, & Brody, 2002). The overlap of cortical representations and bilateral activation of S2, as well as its role in the cognitive processing of touch, implies this cortical area in the dissection of tactile information, but also in its integration with the current situation, hence may provide the site for a predictive, feedforward internal model of the sensorimotor interaction.

Other cortical areas are activated during discriminative touch, such as BA5 and BA7 in the PPC and the insular cortex, although these are implicated more in the integration and multi-sensory processing of tactile information. In humans, the PPC has been found to integrate visual and motor signals with touch information (Ackerley, Hassan, et al., 2012; Azañón, Longo, Soto-Faraco, & Haggard, 2010; Padberg et al., 2010; Pasalar, Ro, & Beauchamp, 2010), whereas the insula is a hub to functionally connect information from the other senses and regulate homeostatic mechanisms (Augustine, 1996; Craig, 2009), and is more involved in the affective, processing of touch. Brain imaging studies have also shown that gentle, stroking touch on the glabrous skin of the hands, elicits responses in the orbitofrontal cortex (Francis et al., 1999; McGlone et al., 2012; Rolls et al., 2003), which is known for its role in emotion and reward. Together, the input from all afferents provides the brain with a multitude of sensations, which produces positive or negative valence feelings. The experience of touch is not just limited to tactile discrimination, but also includes factors such as temperature, softness, pleasantness, arousal, sharpness, and wetness (Ackerley et al., 2014), which have behavioural consequences in the seeking or avoidance of interactions. If you encounter something that feels pleasant (e.g. a soft piece of clothing) or aids in a social situations (e.g. a pat on the back), you will remember this and the positive (or negative) associated outcomes. This is especially pertinent in the control of behaviour, where internal cognitive mechanisms affect the perception of touch. Positive tactile interactions will hence be favoured, whereas negative tactile interactions will be discouraged.

Since perception is, most of the time, an active process, cortical regions including the S1, S2 and PPC are classically viewed as core components of the somatosensory system, which are closely linked to the motor system for effective exploration and interactions with the environment. In the following sections, we will provide evidence of mutual brain connections between the sensory and motor systems supporting the general assumption that somatosensation and action should not be considered as separable processes (van Ede & Maris, 2013).

3. Neural basis for integration of cutaneous sensory and motor information

The interaction of sensory and motor information is hypothesised through internal models that mimic and predict the output and input, respectively. These allow for the fast, integrative flow of sensorimotor information and combine other cognitive mechanisms, to enhance anticipatory power, thus allow seamless interaction with the world. Of special interest are feedforward models that predict and check the sensory consequences of movements (Wolpert, Ghahramani, & Jordan, 1995). This type of model generates an efference copy of the motor command, which can be used to predict the sensory re-afference (e.g. tactile information from myelinated mechanoreceptors). Differences in the expected and actual tactile input can be used to modify exploratory behaviour. For example, if you run your fingers over a smooth surface and come across an unexpected bump, the change in tactile input (constant firing to increased firing, due to detecting an edge) may be more pertinent as it does not match the expected re-afferent signals. This is especially important in dextrous manipulations using the hands, where we constantly compute and integrate sensorimotor signals very quickly, which is extremely useful when searching for a specific object or feature. Internal models can also be applied to the ongoing valence associated with tactile interactions and motor behaviour.

The question thus arises as to how and where such fine sensorimotor integration processing occurs into the brain. In the following, we provide compelling evidence that the integration of somatosensory and motor signals, which drives active touch, occurs at every level of the brain, from the cortical and cerebellar levels down to sub-cortical areas, and this is supported by a strong link between somatosensory and motor areas, including the primary cortical regions.

3.1 A close link between primary somatosensory and motor cortices

There are well-documented relations between somatosensory and motor cortical areas, especially between the S1 and the primary motor cortex (M1), and an overlap in their function was suggested in the early 1900s (Penfield & Boldrey, 1937). The S1 has been found to contribute to movements and the M1 to sensation; hence these areas are not exclusively sensory and motor, respectively. Stimulation of the M1 has been found to produce pure contralateral sensations with no movement (~a third of all M1 stimulation, the rest gave movements; Penfield & Boldrey, 1937; Rasmussen & Penfield, 1947). Conversely, stimulation of the S1 occasionally produces contralateral movements (~a sixth of the time, compared to sensations the rest). This is especially evident for the hand representation, likely in part due to the large area of sensorimotor cortex dedicated to it. A peripheral stimulation applied on the glabrous hand skin typically activates the S1, S2 and PPC, but

also the contralateral M1, as found in human fMRI studies (Ackerley, Hassan et al., 2012; Francis et al., 2000). It was long-ago suggested that there is an anterior-posterior shift from efferent motor function dominating in the pre-central gyrus, to afferent sensory function dominating in the post-central gyrus, where there is a continuum and no defining boundary between these areas (Lilly, 1956; Polyak, 1932). There is also evidence from animal work for a direct cutaneous input pathway to the monkey M1, via the dorsal column system (Asanuma, Larsen, & Yumiya, 1980).

The physiological findings correspond with the anatomy, where Donoghue & Wise (1982) found a dysgranular area between the granular S1 cortex (which has an abundance of information-receiving neurones in layers II and IV) and the agranular M1 cortex (which has an abundance of information-projecting neurones in layer III and V), in rats. The dysgranular area has a mix of both information-receiving and information-projecting neurones. This partial overlap between the S1 and M1 has been found in many species, to varying extents, and implies that movements are affected by cutaneous signals and vice versa. The specific areas of overlap have been suggested to have a special function, such as overlaps between the hand S1 and M1 may be of importance during the initiation, guidance and execution of movements (Donoghue & Wise, 1982).

The extension of sensation into the pre-central gyrus is more prevalent than motor responses into the post-central gyrus, which has implications for sensorimotor control. However, the S1 also contributes to movements, where Matyas et al. (2010) found a direct role for the S1 in driving exploratory protraction of the whiskers in mice. The excitability of the neurones in the M1 is continuously modulated by somatosensory afference, moreso when precision is required such as during fine motor control in humans (Tamburin, Manganotti, Zanette, & Fiaschi, 2001). This is especially relevant for dextrous manipulations using the hands. As found in animal studies, the spread of somatosensory information to the M1 is also dynamically regulated by behaviour, which is most pertinent in precise and/or slow movements that require continuous somatosensory feedback (Evarts & Fromm, 1977; Ferezou et al., 2007). Lemon (1981) found that input to the monkey hand area produced intense activity during small, precise finger movements and during active tactile exploration without the aid of vision. Of all the neurones sampled, ~50% of M1 hand neurones responded only to cutaneous stimulation and ~40% responded only to movement of the fingers, and their activity was modulated at different phases of manipulation activity. Pyramidal tract neurones preferentially fired during active movements, whereas non-pyramidal tract neurones were modulated similarly during active and passive movements. Ferezou et al. (2007) postulated that tactile processing occurring in the M1 may contribute

specifically to perception in active touch. Activity in the M1 has also been shown to change with both the weight and texture of grasped object (Picard & Smith, 1992), demonstrating the complex interaction between action and sensing.

In humans, precise, slow finger movements require concentration and a pulsatile motor efferent signal at 8-10 Hz has been shown to dominate the response (Vallbo & Wessberg, 1993). These pulsatile discontinuities are coded by muscle afferents during finger movements and are produced by internal mechanisms generated from descending motor commands (Wessberg & Vallbo, 1995). The significance of the pulsatile movement control may be linked to neurones in both the M1 and S1 oscillating continuously in the alpha/mu band (~10 Hz). Neuronal activity in the S1 and M1 oscillates synchronously when there is no afferent or efferent activity, and oscillates desynchronously with input or output, respectively (Nikouline et al., 2000; Pfurtscheller, Stancák, & Neuper, 1996; Pfurtscheller, 1989; Salmelin & Hari, 1994). Oscillatory coupling between the M1 and S1 is proposed to play an important role in integrating proprioceptive and cutaneous signals within motor control (Witham, Wang, & Baker, 2007).

Overall, there appears to be a dynamic and distributed network of sensory and motor streams in the cortex, where the S1 and M1 make multiple contributions simultaneously. This is reinforced by findings showing that the M1 responses better predict the future consequences of the movement, whereas the S1 responses show a better correspondence with past consequences of the movement in monkeys (Fitzsimmons, 2009). The inter-dependence and connectivity between the S1 and M1 demonstrates the complexity and importance of sensorimotor interactions.

3.2 Other somatosensory brain areas contributing to motor integration

Reciprocal connectivity has been found not only between S1-M1 but also between M1-S2, hence these areas operate in a co-ordinated, yet differentiated, way to integrate sensorimotor information (Suter & Shepherd, 2015). Enhancement of sensory reactions to signals from the actively moving limb, but not to those from the opposite limb, indicates a spatial tuning of the S2 neurones to behaviourally-relevant input channels, which also suggests that S2 is important for the integration of sensory information in motor programs (Huttunen et al., 1996).

The cortico-motor pathway is mainly composed (~60%) of pyramidal neurones projecting from M1 or the premotor cortex (PMC) to the spinal cord. Other direct projections to the spinal cord also arise from S1, BA5, and the anterior IPL, as found in the monkey (Galea &

Darian-Smith, 1994). Electrophysiological studies performed in non-human primates have shown that the IPL and PMC play a major role in sensorimotor transformations, for the guidance and control of actions in space (Bremmer et al., 2001; Caspers et al., 2006; Colby & Duhamel, 1996; Rozzi, Ferrari, Bonini, Rizzolatti, & Fogassi, 2008). Interestingly, Rozzi et al. (2008) reported that IPL neurons responsive to tactile stimuli discharge in association with different types of movements performed by the monkey. The PMC has also been found to be sensitive to various kind of sensory stimuli (e.g. area F4; Bremmer et al., 2001) and is known to subserve motor and cognitive functions such as movement co-ordination, motor intentions and the understanding of actions (Bonini et al. 2011; Rizzolatti, Fogassi, & Gallese, 2002). Therefore, these two cortical regions have clear multimodal properties including motor, somatosensory and visual functions, are connected with somatosensory and motor cortices, and contribute to transforming somatosensory information into a motor format.

Besides its traditional role in spatial body representations and sensorimotor transformation during visuo-guided motor activities (Colby & Duhamel, 1996; Kalaska, Scott, Cisek, & Sergio, 1997), the PPC is also involved in object recognition based on haptic sensing. Posterior parietal and premotor neurones were shown to generate anticipatory activity preceding tactile responses during active touch (Gardner, Ro, Babu, & Ghosh, 2007). This suggests that the there is a predominance for predictive and planning components during active touch, which are processed mostly in the PPC and PMC, whereas S1 and M1 handle the more immediate components of performance and feedback.

3.3 Cerebro-cerebellar connections for somatosensory-motor integration
The cerebro-cerebellar pathway is one of the largest in the mammalian brain and the cerebral cortex influences the cerebellum via relays in both of its main inputs, the mossy fibres and the climbing fibres. There is a dense projection from both the S1 and the M1 to the pons (Leergaard et al., 2000; Leergaard et al., 2004; Leergaard, Lillehaug, De Schutter, Bower, & Bjaalie, 2006), which is the primary source of the mossy fibre projection. Topographical relations have been found between the somatotopic continuous bodily found in the S1 and M1 and the more fractured cerebellar representations (Leergaard et al., 2006; Odeh, Ackerley, Bjaalie, & Apps, 2005). The pons has been shown to be a key area of sensorimotor integration, where there is correspondence between the cerebro-pontine input and ponto-cerebellar output. In each pontine nucleus, lamella-like internal-to-external bodily representations have been found for the projections from S1, S2 and M1, where the face is represented centrally and the legs are on the outer borders of the pons (Leergaard et al., 2004; Odeh et al., 2005). Furthermore, the output representation of mossy fibres to climbing

fibre zones is in close correspondence with the topography of the cerebral pontine representation (Leergaard et al., 2006; Odeh et al., 2005).

The difference between the bodily representations in the cerebral cortex, pons and cerebellum shows the complexity and potential for interaction and integration along this pathway. The spatial organisation of bodily representations in the pons is of particular interest, where there is a mass convergence of sensory and motor efference (as well as from other areas, such as visual cortical regions), as well as a combined afference signal that is representative of this integration for specific body areas. The mossy fibre signal sent to the cerebellum has the capacity to relay specific timing information about sensorimotor occurrences, which is combined with the climbing fibre information. The cerebellum also has the capacity for the mass integration of a variety of sensory, motor and cognitive inputs.

Brodal (1979) suggested that cerebro-ponto-cerebellar projections were organized to bring about convergence in the cerebellum from many cerebral cortical areas, and that the integration in the pons takes place in an organised manner, so that specific cerebellar cortical targets receive 'characteristic' sets of inputs. This may explain the differences between the continuous body map representations in the cerebral cortex, compared to the more fractured and complex maps found in the cerebellum (for an overview of cerebellar maps, see Apps & Hawkes (2009)). An example of this is the finding, during human fMRI, that a single finger movement can be paired with a range of possible sensory outcomes, represented by a number of small and fractured areas in the cerebellum (Wiestler, McGonigle, & Diedrichsen, 2011). The cerebellum is often viewed as a structure with uniform cytoarchitecture; however, there are great variations in its anatomy and physiology, where Cerminara, Lang, Sillitoe, & Apps (2015) suggest that distinct cerebellar cortical microcircuits exist to provide diverse information processing capacities.

The cerebellum has been implicated in predicting the sensory consequences of an active movement, through generating a feedforward internal model to compare the predicted and actual sensory feedback, with the motor feedback (Bastian, 2006; Wolpert, Miall, & Kawato, 1998; Wolpert et al, 1995). This prediction and fine-tuning aids in the smooth control of fine movements, where cerebellar lesions typically present as deficits in coordination and accuracy (Bastian, 2006). However, cerebellar processing is not restricted to just the integration of somatosensory and motor signals, but rather the cerebellum receives input from prefrontal, temporal, parietal and limbic systems, suggesting a distinct role in the integration of cognitive and emotional information (D'Angelo & Casali, 2012).

3.4 Other sub-cortical areas involved in somatosensory-motor integration

Dense connections exist between cortical and sub-cortical levels, which also provide the neural bases for sensorimotor control. S1 receives projections from thalamic nuclei, but conversely, it sends projections to the thalamus, as found using tract tracing methods in rodents (Aronoff et al., 2010; Bourassa, Pinault, & Deschênes, 1995; Veinante, Lavallée, & Deschênes, 2000) and non-human primates (Cappe, Morel, Barone, & Rouiller, 2009; Darian-Smith, Tan, & Edwards, 1999).

In addition to its connectivity with S1, the thalamus is also widely connected with other brain regions including the primary auditory cortex, M1, PMC and PPC, making this sub-cortical structure a suitable candidate as an integrative relay between distant cortical sensorimotor areas (Cappe et al., 2009; Rouiller et al., 1998; Sherman, 2007). S1 also sends excitatory inputs to the striatum, which influence basal ganglia processes (Alloway et al 1999; Aronoff et al 2010; Hoover et al 2003; Wright et al 1999). Neurones in the caudate-putamen interact, in turn, with neurones in the globus pallidus, and the pallidal neurones finally project to the thalamus. This sub-cortical loop connects S1 to other sensory areas via the thalamus and forms the substrates underlying motor control and action selection based on the effective processing of multisensory information.

4. Self perception driven by cutaneous afferents

Any movement of the body produces deformations of the skin. The glabrous skin on the human hand includes a wide range of cutaneous receptors sensitive to oriented skin stretch (Edin, 2004; Grill & Hallett, 1995), as well as to oriented pressure (Birznieks, Macefield, Westling, & Johansson, 2009; Vallbo & Johansson, 1984) and superficial brushing (Essick & Edin, 1995) applied to their receptive fields. These physiological properties make the mechanoreceptors efficient movement direction and velocity transducers (Gardner & Sklar, 1994). The contribution of cutaneous afferents to self-motion coding is demonstrated by the illusory sensation of movements that are easily evoked by stretching the skin of the fingers of motionless participants (Cordo et al., 2011) or scrolling a texture disk under participants' hands (Kavounoudias et al., 2008). The finding that cutaneous afferents can drive motor perception is shown by the activation of the whole cortical motor network during tactile-induced illusory movements including in the M1, PMC, cingulate gyrus, striatum and cerebellar regions, in fMRI (Kavounoudias et al. 2008).

Numerous studies have also reported the importance of cutaneous afferents in the sense of body ownership, which refers to the ability to feel our body as belonging to us. Initially reported by Botvinick & Cohen (1998), the rubber hand illusion is observed when a

synchronous cutaneous stimulation is applied over a participant's unseen hand, while they view the same stimulation on a nearby rubber hand, leading the participant to wrongly attribute the rubber hand to their own body. Since the rubber hand illusion does not occur when the rubber hand and the actual unseen hand are stimulated asynchronously, the general assumption is that embodiment of the rubber hand results from the multisensory processing of visual, cutaneous and proprioceptive information (Tsakiris, 2010). By taking advantage of the bottom up influence of somatosensory information, augmented sensory feedback included in prosthetic limbs may help amputees to assimilate this external extension as a part of their body schema (Ehrsson et al., 2008; Shokur et al., 2013).

Another supporting argument in favour of the inseparable processing of somatosensory and motor information comes from resting state fMRI. Compelling evidence demonstrates that brain regions are not silent during rest, i.e. in absence of any specific cognitive activity, such as the continuous alpha rhythm found in the sensorimotor cortex. In fact, temporal correlations exist between the spontaneous low frequency blood-oxygenation level dependence signal fluctuations recorded in anatomically separated brain areas, suggesting ongoing information transfer between these functionally connected regions. In the pioneering study by Biswal, Yetkin, Haughton, & Hyde (1995), the authors reported strong co-activation between the M1 and S1, M1, S2, PMC, supplementary motor area and cingulate motor areas of the two brain hemispheres in relaxed participants, who were not engaged in any motor task. Later studies have further confirmed that this sensorimotor network is one of eight resting networks and is the most robustly observed network during rest (Damoiseaux et al., 2006; van den Heuvel, Stam, Boersma, & Hulshoff Pol, 2008; Xiong, Parsons, Gao, & Fox, 1999).

5. Interactions with other sensory and cortical functions

Perception is by nature multimodal. The brain relies on multisensory sources of information to build a unified representation of our own body and its interactions with the environment. Somatosensory information is thus combined with information from other sensory modalities (e.g. visual, proprioceptive, olfactory, auditory, gustatory) and with cognitive mechanisms (e.g. previous experience, learning, memory, expectations, predictions, assumptions) to produce a percept that can be interpreted and acted upon quickly.

Over the last two decades, there has been growing interest in neural mechanisms underlying multisensory integration. Heteromodal neurones, sensitive to tactile, visual and auditory stimuli, have been found in the superior colliculi of the cat (Stein, Meredith, & Wallace, 1993; Wallace, Meredith, & Stein, 1993). Bimodal neurones sensitive to both visual and tactile

stimuli applied on the hand have also been found in the premotor and parietal areas of the monkey (Graziano & Gross, 1998; Grefkes & Fink, 2005), among which some responded in a supra-additive manner when spatially congruent stimuli from different origins are simultaneously presented to the animal. These are strong candidates for neural substrates of multisensory integrative processing. Neuroimaging studies provide support that heteromodal brain regions are specifically activated in the presence of different sensory inputs (Calvert, 2001; Downar, Crawley, Mikulis, & Davis, 2000; Gentile, Petkova, & Ehrsson, 2011; Kavounoudias et al., 2008; Macaluso & Driver, 2001). By applying coincident visual and tactile stimuli on human hands, Gentile et al. (2011) used fMRI to show the involvement of the PMC and intraparietal sulcus in visuo-tactile integration processing, supporting observations previously reported in monkeys. The co-processing of cutaneous and muscle proprioceptive information from the hand within the IPL, superior temporal sulcus, insula and the cerebellum may account for the improvement of hand movement perception observed when these two sensory inputs are combined in a congruent fashion (Kavounoudias et al., 2008).

Recently, the traditional hierarchical idea of brain organisation has been challenged by anatomical and electrophysiological data from non-human primates showing that some neurones in primary sensory areas respond to various kinds of stimuli (Ghazanfar & Schroeder, 2006; Schroeder & Foxe, 2005) and that cortico-cortical connections exist between several primary sensory areas (for a see review Cappe et al., 2009). Structural findings of direct projections between the striate cortex and S1 were described by Cappe & Barone (2005) using retrograde tracing in monkeys. In human fMRI studies, tactile stimuli can modulate activity in the occipital lobe, which is traditionally regarded as a purely visual area (Amedi, Malach, Hendler, Peled, & Zohary, 2001; Beauchamp, Yasar, Kishan, & Ro, 2007; Hagen et al., 2002; Helbig et al., 2012; Merabet et al., 2008; Pietrini et al., 2004). For instance, after a five day period of visual deprivation, a reading Braille task performed by healthy participants activated the primary visual cortex, as typically observed in blind patients (Merabet et al., 2008). A simple brush stroking the arm or a vibrotactile stimulus applied at several body levels can result in activation in visual MT and/or MST areas (Beauchamp et al., 2007; Blake, Hsiao, & Johnson, 1997; Hagen et al., 2002).

Conversely, the modulation of the S1 by a visual signal has been shown in circumstances where the visual input implies touch (Meyer, Kaplan, Essex, Damasio, & Damasio, 2011; Pihko, Nangini, Jousmäki, & Hari, 2010). However, the influence of visual information on somatosensory areas has mainly been demonstrated during social human touch situations (Ebisch et al., 2011; Rossetti, Miniussi, Maravita, & Bolognini, 2012), for example during

perspective taking during inter-personal touch (Schaefer, Xu, Flor, & Cohen, 2009). Regardless of human social touch interactions, Ebisch et al. (2008) found different modulations in the S1 when touch was accidental or intentional. Recently, Helbig et al. (2012) reported that during a task of shape identification, the S1 was modulated by congruent visual inputs according to the reliability of the visual information. These studies have mainly found a cognitive or emotional aspect to the modulation of somatosensory areas by visual signals, demonstrating the multimodal connectivity and important relationship between touch and vision, which can be manipulated to the benefit of amputees (e.g. by having a realistic-looking and -feeling prosthetic to enhance congruent sensory signals).

Many behavioural studies reveal that the brain takes advantage of temporally coincident and spatially congruent signals coming from different sensory sources, stressing the need to integrate convergent inputs to properly assess body configuration and any changes that may occur. However, this does not imply that these sensory sources contribute equally to these integrative mechanisms. The general assumption is that the brain may compute the various sensory signals according their relative reliability to code the actual event (Ernst & Banks, 2002). Accordingly, it has been proposed that cutaneous afferents from the human hands may override muscle proprioceptive information in the perception of relatively slow hand movements (Blanchard, Roll, Roll, & Kavounoudias, 2011).

Hand localisation in space may also be optimally determined on the basis of a direction-weighting of visual and somatosensory information: visual cues may be preferred to somatosensory ones when the hand is located straight in depth, and vice versa when the hand is located in an angular azimuth direction (van Beers, Sittig, & Gon, 1999). Of course, sensory weights are context-dependant and may change after the transient or definitive loss of one sensory channel. As an example, visual-dependency is known to increase dramatically in deafferented patients who have completely lost any afferent feedback due to large-fibre sensory neuropathy (Cole & Sedgwick, 1992; Rothwell et al., 1982; Sanes, Mauritz, Dalakas, & Evarts, 1985). Such adaptive multisensory processes should be used proficiently for rehabilitation purposes.

6. Applications of research into sensorimotor integration

One of the main applications of the fundamental research into sensorimotor functioning is the development of prosthetics, typically for lost limbs. Research can aid developments both from a motor perspective (how to move a prosthetic) and a sensory perspective (how to regain feedback). Amputations of limbs are common: 1 in 190 Americans are currently living with the loss of a limb, and this figure is set to increase (Ziegler-Graham, MacKenzie,

Ephraim, Travison, & Brookmeyer, 2008). The removal of a body part entails a loss of peripheral afference, which has a clear detrimental effect on tactile feedback, but will also lead to more complex difficulties, such as issues with body image and social relationships. Amputations arise for a variety of reasons, including tumours, war injuries or vascular disease, and almost always lead to a phantom sensation, which can occur with or without pain; however, phantom limb pain affects the vast majority of patients (Flor, Denke, Schaefer, & Grüsser, 2001). There are two main issues in treating amputations: how to combat phantom limb pain and how to best fit and use a prosthetic.

6.1 Somatosensory recovery and reduction of phantom limb pain

The experience of phantom limb pain is thought to originate from various cortical mechanisms, including neighbouring somatosensory cortical regions entering the former area of the amputation site due to a loss of afferent input, and plastic structural and/or functional changes in the cortical representation of the amputation (Flor, Diers, & Andoh, 2013; Flor, Nikolajsen, & Staehelin Jensen, 2006). Understanding cortical organisation in healthy participants, and in the intact limb of amputees, are vital comparisons in diagnosing and treating phantom limb pain. Cortical reorganisation due to amputation can even lead to changes in sensibility in the intact limb (Kavounoudias, Tremblay, Gravel, Iancu, & Forget, 2005), which must be taken into account.

Various methods have been trialled to alleviate phantom limb pain, but few can be implemented practically. Visual signals can modulate phantom limb pain: using a mirror to view the healthy arm in place of the amputation can reduce pain (Ramachandran, Rogers-Ramachandran, & Cobb, 1995), and combining visual signals and motor feedback is also effective (Lotze et al., 1999; Ortiz-Catalan, Sander, Kristoffersen, Håkansson, & Brånemark, 2014). These therapeutic strategies relay on how the brain combines sensory and motor information, to trick it into believing sensory signals are present. However, due to the variability of the observed effects, the beneficial impact of mirror therapy to promote recovery is still debated and some authors suggest that it is the bimanual coupling in the mirror paradigm rather than visual information, per se, that might be the key factor in rehabilitation (Metral et al., 2014; Rothgangel, Braun, Beurskens, Seitz, & Wade, 2011). Sensory discrimination training (stimulating the stump) has also been shown to help with pain and also affect cortical reorganisation (Flor et al., 2001), showing that nearby tactile feedback can have a positive influence.

Lotze et al. (1999) found that using a myoelectric prosthesis correlated negatively with cortical re-organisation, and positively with the reduction of phantom limb pain. They suggest

that the ongoing use of a prosthesis, with multi-sensory integration, regulates cortical signals due to the provision of congruent visual and proprioceptive feedback. This can be linked to the re-establishment of sensory feedback in an internal model, thus from a neural perspective, seeing a realistic and movable prosthetic limb closes the sensorimotor loop. However, somatosensory signals from touch, pain and temperature are nevertheless absent, which decreases the amount of sensory information available to the brain and makes movements with the prosthetic less precise. Therefore having a prosthesis that feels as natural as possible is a great advantage in recovery from amputations. It seems that the addition of sensory feedback to a prosthesis is advantageous, not only to provide the missing tactile feedback, but to help with body image, pain issues and in engaging in social interactions.

6.2 Towards a promising "sensory" prosthesis

Improving prosthetics increases quality of life, as well as decreasing the rate of prosthetic rejections. Even with modern advances in prosthetic design and the addition of some tactile sensory feedback, prosthetic limbs nevertheless lack the full sensory awareness that healthy limbs provide. Recent research into prosthetics has developed rapidly and we are at a stage where the prosthetic itself is advanced (e.g. it looks and feels realistic, it provides the user with increased motor control), as well as the technology utilised in the prosthetic (e.g. long-life batteries, pattern recognition of muscular activity for precise control). A major issue with standard prostheses is that they are often unstable, especially when the stump left over from amputation is short. The technique of osseointegration offers a stable and reliable way of attaching prostheses to the body. It involves a fixture that is implanted directly into the bone, with an extension that exits the body and serves as an anchor for the prosthesis.

Limb osseointegration has been carried out since 1990; the technique has a low rejection rate and can be used long-term (>10 years) (Hagberg & Brånemark, 2009; Palmquist, Windahl, Norlindh, Brånemark, & Thomsen, 2014). Osseointegrated limbs have been found to be resilient to myoelectric and motion artefacts, and provide a full and naturalistic range of movement (Figure 4; Ortiz-Catalan, Håkansson, & Brånemark, 2014). Bone-anchored limbs prostheses have also been found to give better perception and integration of the body part, than socket prostheses, where the prosthesis feels more like the unaffected body part (Jacobs et al., 2000), which could help in body image issues and phantom limb pain.
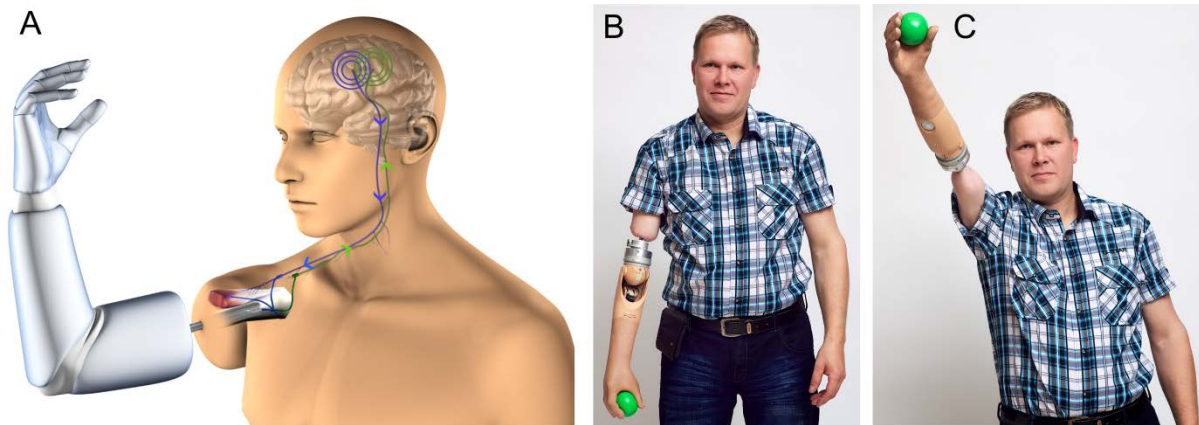
Figure 4: Illustration and use of an osseointegrated arm prosthesis.

(A) Diagram of the osseointegration process, where the fixture is implanted directly into the bone with an extension exiting the distal stump, for attaching the prosthesis. Here, epimysial electrodes are implanted in the upper arm muscles for movement control of the prosthetic hand and a cuff electrode is implanted around the ulnar nerve to provide sensory feedback (for more information see Ortiz-Catalan, Håkansson, & Brånemark (2014)). (B) A patient wearing the osseointegrated prosthetic limb, which is attached directly to the skeleton and neuromuscular system. (C) The patient has an unrestricted range of movement and robust prosthetic control, regardless of position. Illustrations used with permission from Integrum AB.

Typical prostheses do not offer any kind of somatosensory feedback, thus degrading the sensory experience, as this feedback is essential in fine-tuning motor control (e.g. in internal models). It has been proposed that patients with osseointegrated prostheses can develop a special sensory perception skill, so called 'osseoperception', where they can 'feel' through the prosthesis. This has been particularly encountered in oral prosthetics, where osseointegrated tooth implants are commonly used. A true sense of sensory perception in dental implants is not widely acknowledged due to the loss of input from periodontal mechanoreceptive afferents, on removal of the tooth (Trulsson, 2005). However, in osseointegrated limb prostheses, patients often report better awareness of the prosthetic limb, an example being the ability to recognise the type of soil walked on through a leg prosthesis (Jacobs & van Steenberghe, 2006). Osseoperception has been investigated through measuring pressure and vibration thresholds, where these stimuli were delivered through bone- and socket-anchored prostheses, and to the contralateral control limb. Although the thresholds for detection were increased for both types of prosthesis, the osseointegrated prosthesis gave better detection thresholds than the socket-anchored prosthesis (Jacobs et al., 2000). A further study found a similar result using vibration, but

additionally found that detection thresholds in osseointegrated prostheses were better for higher frequencies (>100 Hz) (Häggström, Hagberg, Rydevik, & Brånemark, 2013). Clinical observations have also found that patients can feel and judge mechanical loadings through osseointegrated prosthetics (Häggström et al., 2013).

These osseoperceptions must be transduced by mechanoreceptive afferents, which may include those from the skin, muscles, joints and periosteum (Klineberg et al., 2005). As the amputated body part has been removed, there is a significant decrease in cutaneous input from the affected area; however, the remaining cutaneous mechanoreceptive afferents proximal to the amputation may provide some sensory feedback in relation to the use of the prosthetic. The myelinated low-threshold mechanoreceptive afferents in glabrous (FA1, FA2, SA1, SA2) and hairy (FA2, SA1, SA2, hair and field units) skin may provide varying degrees of tactile feedback. It is likely that distal touch to a prosthesis would need to be quite forceful to generate impulses in most proximal cutaneous receptors, where actual skin vibrations may evoke afferent firing. A potential candidate for tactile signalling may be the FA2 afferents, which are extremely sensitive to touch (especially vibration) and have large receptive fields (see Figure 1). FA2 afferents respond to remote touch, for example, tapping on the hand may be sensed by FA2s in the arm, and they have been implicated in coding the roughness of remote surfaces. This effect has been demonstrated by the ability to make roughness judgements using a probe (Klatzky & Lederman, 1999; Yoshioka, Bensmaïa, Craig, & Hsiao, 2009) and when the nerve to a finger is blocked or damaged (Libouton, Barbier, Berger, Plaghki, & Thonnard, 2012). Furthermore, vibrations have been found to travel up the arm that relate to rough surface being touched by the finger (Delhaye, Hayward, Lefèvre, & Thonnard, 2012). These authors postulated that the vibrations are conducted proximally by the bone, tendons and/or skin and it is likely that these vibrations can be sensed during prosthetic use, making it feasible to sense roughness with a prosthesis.

In an attempt to assess the tactile feedback in osseointegration, touch was applied to a single patient's osseointegrated prosthetic right thumb and to the patient's healthy left thumb, during fMRI. As expected, strong activity was found in the contralateral S1 from touch to the healthy thumb; touch on the prosthetic thumb produced bilateral activity in lateral and parietal somatosensory areas, but not the strong activity seen in the S1 to actual touch (Lundborg, Waites, Björkman, Rosén, & Larsson, 2006). The obvious difference is the lack of mechanoreceptive information sent to the S1, but the clear activation of sensory areas showed a potential neural correlate of tactile osseoperception.

Other non-cutaneous afferents may contribute to osseoperception, including muscle and joint afferents, and mechanosensitive afferents innervating the bone. These types of deep afferent may have the capability to transmit tactile signals, for example, muscle afferents can follow vibration of the tendon, especially Ia muscle afferents (up to 180 Hz) (Roll, Vedel, & Ribot, 1989; Roll & Vedel, 1982). Therefore, when an amputation occurs, a range of afferents may be able to provide some sensory feedback during prosthetic use, primarily based on proximally conducted vibrations. However, the ideal situation would be to restore much more sensory feedback than this, to provide sensory feedback from tactile interactions of the prosthesis in real-time. Achieving this would be a major step forward in prosthetics and enhancing the lives of amputees.

Visual information can provide some feedback for prosthesis use and systems have also been developed to provide some feedback during touch (e.g. stimulation of the stump) (Schofield, Evans, Carey, & Hebert, 2014). However, these are not as precise as the potential offered from peripheral nerve stimulation and there have been few attempts at providing closed-loop, real-time sensory nerve feedback during prosthetic use. A first-attempt was made in the 1970s, where median nerve stimulation during prosthetic use gave sensations of paresthesia, moreso, patients reported being able to use these sensations to gain a sense of pressure during grasp (Clippinger, Avery, & Titus, 1974). In the last 10 years, various nerve implants have been used successfully to provide sensory feedback, although these have only been used in the short-term (< 6 weeks) (Dhillon, Lawrence, Hutchinson, & Horch, 2004; Dhillon & Horch, 2005; Horch, Meek, Taylor, & Hutchinson, 2011; Raspopovic et al., 2014; Rossini et al., 2010). These studies use electrical nerve stimulation to elicit sensations that can be used as feedback, for example, during grip; however, these sensations typically consist of paresthesia, rather than actual touch.

Tan et al. (2014) demonstrated that naturalistic sensations could be generated from implanted electrodes, for over a year. When they applied constant-intensity, square-wave electrical pulses, patients reported paresthesia; however, when they applied patterned electrical stimulation, the sensation felt much more like touch (e.g. tapping, pressure, vibration, light movement). This represents major progress towards implementing real tactile feedback in prostheses, where subjects may be able to distinguish between different surfaces and even gain pleasure through prosthetic touch. A further study has shown the longevity and stability of implanted epimysial electrodes for prosthetic control, combined with peripheral nerve stimulation for sensory feedback, where an osseointegrated prosthetic has been used for >2 years (Figure 4; Ortiz-Catalan, Håkansson, et al., 2014). Here, the patient has reported consistent pressure and tapping sensations to nerve stimulation over time. The

electrical stimulation of peripheral nerves through implanted electrodes opens up the possibility of specificity in afferent stimulation. Through technique of microneurography, peripheral axonal intraneural microstimulation can be used to electrically activate individual mechanoreceptive afferents. For example, an FA1 gives a small, distinct sensation of tapping, whereas an SA1 feels like a small area of pressure (Vallbo, Olsson, Westberg, & Clark, 1984). Therefore, it may be possible to selectively excite different types of mechanoreceptive afferent, in different locations.

The stimulation of individual afferents may provide the basis to reconstruct normal tactile interactions. For example, providing an artificially-generated signal from electrically-stimulating myelinated tactile afferent axons during prosthetic touch may allow the person to know when an object is in contact with the skin and how much force is being applied (e.g. from SA1 afferent firing), to distinguishing edges and textures (e.g. from FA1 afferent firing). Even these basic sensations from touch would have an impact on how the prosthetic is used, where delicate grip would be achievable (e.g. to pick up a glass), as well as the dextrous manipulation of objects (e.g. when searching for an object in a bag). These things are possible with the aid of visual signals, such as if the person sees their prosthetic picking up a glass and can vary their grip; however, the touch feedback allow for a much faster, precise, integrated movement that is natural to perform. Research into how mechanoreceptive afferents fire under natural tactile interactions and the modulation of these responses through intraneural microstimulation may help in recreating a true sense of touch for amputees.

Currently, there is no way to selectively reproduce thermal or nociceptive inputs, which are essential in normal cutaneous sensing. Touch without temperature can be restrictive, for example, it may be difficult to sense wetness without coherent tactile and temperature signals (Ackerley, Olausson, Wessberg, & McGlone, 2012; Filingeri, Fournet, Hodder, & Havenith, 2014; Filingeri, Redortier, Hodder, & Havenith, 2013). Furthermore, nociception and the sense of pain are unpleasant, yet play a fundamental role in alerting us to potential injuries. This may be different in the case of a prosthesis, but having nociceptive feedback may prevent prosthesis damage. Conversely, the positive affective side of somatosensation would be advantageous to recapture in a prosthesis, where pleasantness could be felt in tactile interactions, thus adding to the realism of the device and providing a higher cognitive integration for more realistic interactions, especially in the social domain. Thermal and affective sensations are so far not feasible feedback in a prosthesis due to the complexity in reconstructing these types of sensations, yet advances in nerve stimulation and increasingly sophisticated interfaces may make this achievable.

7. Conclusions

Diverse touch information from all over the body provides continuous feedback to the brain for both active tactile manipulations (e.g. writing with a pen) to ongoing interactions (e.g. the knowledge that you are wearing clothes). This combination of cutaneous somatosensory signals intertwined with motor intentions underpins the everyday interactions that we take for granted. The somatosensory and motor systems are often viewed as separate entities; however, we present compelling evidence that there is considerable overlap in their structure-function relations, which is essential in the everyday integration of sensorimotor interactions. This is relevant in the integration of prosthetic body parts, especially the hands which provide a mass of afferent information to the large areas of the brain dedicated to this. It is hoped that for true sensorimotor integrations of prostheses, precise and useable tactile feedback will allow closed-loop functioning that may one day provide a true range of sensations, in turn, improving motor action precision.

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