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Cutaneous afferent regulation of motor function

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Motor systems must be responsive to the environment in which the organism moves. Accordingly, there are many sensory systems that affect intrinsic motor programs. In this mini review, we will discuss the effects that inputs from cutaneous low-threshold mechanoreceptors have on motor function, focusing on locomotion and hand grasp. A mathematical analysis of grip strength is provided to quantify the regulation of the forces required in maintaining the grip of a moving object. These two behaviours were selected because the neural control of locomotion has been primarily studied for hind-limbs in cats and rodents, whereas hand grasp has been primarily studied in fore-limbs in human and non-human primates. When taken together, insight can be gleaned on the cutaneous regulation of movement as well as the role these afferents may play in mediating functional recovery following injury. We conclude that low-threshold mechanoreceptors are critical for normal motor function and for inducing plasticity in motor microcircuits following injury.

Key words: low-threshold mechanoreceptors, locomotion, grasp, interneurons, microcircuits, spinal cord

INTRODUCTION

Although basic patterns of motor activity can be produced in the absence of sensory input, many different types of afferent information continuously sculpt motor output such that the intended movement responds to the environment. One type of sensory input is that derived from the skin. There are several different types of cutaneous receptors and afferents – these have been reviewed elsewhere (McGlone and Reilly 2010, Abraira and Ginty 2013). In this review, we will focus on the integration of the information transmitted by large fibre (i.e. low-threshold mechanoreceptors) cutaneous afferents into motor circuits in the spinal cord. We have selected two movements to discuss: locomotion and hand grasp. In locomotion, neural circuits and their cutaneous regulation have been primarily studied in cats and rodents, with focus on the lumbar spinal cord control of hind limb function. Conversely, cutaneous regulation of hand grasp has been studied primarily in humans and non-human primates, with obvious focus on the cervical spinal cord. Studying both of these motor behaviours may lead to common insight, particularly in relation to recovery of function following central nervous system injury. Therefore, we will focus here on the roles of cutaneous afferent effects on locomotion and hand function, and then briefly discuss the possible role(s) of these low-threshold mechanoreceptors in mediating spinal cord plasticity.

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CUTANEOUS AFFERENTS IN THE CONTROL OF POSTURE AND LOCOMOTION

Cutaneous afferents – or any afferents for that matter – are not necessary for the production of the basic rhythm and pattern of locomotion. This was demonstrated by Brown (1911, 1914), who showed that cats could have bouts of locomotor activity following dorsal rhizotomy and spinal transection, which eliminated all afferent and descending inputs, respectively. This phenomenon was further studied and characterised by many groups over subsequent decades (Grillner 1981, Jordan 1991, Grillner and Jessell 2009). Together, it became evident that the spinal cord has the intrinsic capacity to produce complex rhythmic motor output requiring intra-limb and inter-limb coordination, and

that afferent input is not necessary to produce this fundamental motor output.

On the other hand, a diversity of sensory inputs contributes to posture and locomotion in animals and humans. These include visual (Sherk and Fowler 2001), vestibular (Kennedy et al. 2003), proprioceptive (Pearson 1995), as well as cutaneous (Zehr et al. 1998, Rossignol et al. 2006, Varejão and Filipe 2007) inputs. While elimination of cutaneous input from the hind paws in cats does not compromise their ability to walk overground, the kinematics of their leg movements is altered when compared to intact cats (Bouyer and Rossignol 2003a, Varejão and Filipe 2007). This correlates with findings in humans with peripheral neuropathies affecting cutaneous afferents, in which walking pattern and stability are also disrupted (Lin and Yang 2011). Furthermore, in more challenging environments such as those with unexpected perturbations or obstacles, cutaneous feedback seems particularly relevant (Wutzke et al. 2013). For instance, cats with deafferented hind paws had more significant deficits (Bouyer and Rossignol 2003b, Gregor et al. 2006) when walking on a ladder *versus* on flat overground surfaces (Sherrington 1910, Bouyer and Rossignol 2003b). These data demonstrate that in animals and humans cutaneous input is necessary to modify the fundamental motor output to most appropriately fit the environmental and task related demands.

But how does this cutaneous input integrate into spinal circuits producing motor output? What are the microcircuits involved? And at what level does this interaction take place – at motoneurons, spinal cord locomotor circuits, and/or supraspinal circuits (Fig. 1)? To understand the mechanisms through which cutaneous input affects motor behaviour, it is first necessary to understand the microcircuits involved.

Cutaneous-motor microcircuits and spinal locomotor networks

Aside from muscle spindle afferents – which make direct synaptic connections with motoneurons – the most direct pathway from an afferent to a motoneuron would be through a single internuncial neuron, thus forming a disynaptic reflex pathway (Fig. 1A). Stimulation of low-threshold receptors in the paws of cats can provoke strong short-latency reflexes (Hagbarth 1952, Engberg 1964). A disynaptic pathway

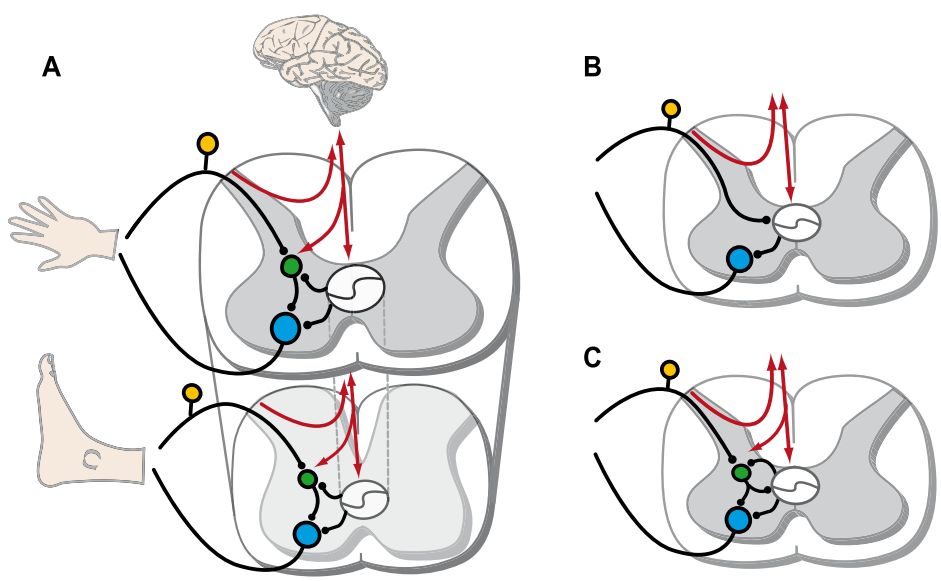

Fig. 1. Integration of cutaneous afferents into spinal cord motor circuits. (A) Disynaptic cutaneo-muscular reflex pathways at the cervical and lumbar levels shape the movement of fore-limbs and hind limbs. Spinal locomotor circuits modulate first order interneurons, which are not part of the cord locomotor network but are modulated by this network. (B) Cutaneous afferents have direct access to spinal locomotor networks. (C) Spinal locomotor networks gate first order interneurons receiving input from cutaneous afferents. These interneurons in turn project to spinal locomotor networks. Note that ascending sensory pathways and descending pathways from supraspinal centres depicted using red arrows are also involved in the integration of cutaneous afferents for motor control.

from cutaneous afferents was suggested in experiments in which the plantar cushion was stimulated in cats (Egger and Wall 1971), and further investigated in the Burke lab, which used this pathway to study differential control of motoneurons during locomotion (Fleshman et al. 1984, Degtyarenko et al. 1996). Some short-latency cutaneous-motor responses have also been reported in the non-human primate (Hori et al. 1986). Evidence for a disynaptic crossed pathway has also been reported (Edgley and Wallace 1989), as well as a trisynaptic pathway linking ipsilateral dorsal horn neurons receiving cutaneous afferents and projecting to last-order commissural interneurons in lamina VIII (Edgley et al. 2003, Jankowska et al. 2003). We recently demonstrated that dI3 interneurons (see below) mediate an ipsilateral, disynaptic, cutaneous to motor reflex (Bui et al. 2013). That is, there is evidence across species of an excitatory reflex involving low threshold cutaneous afferents, a single internuncial neuronal population, and motoneurons.

Furthermore, it is clear that cutaneous-motor microcircuits are not independent of locomotor circuits, as short-latency cutaneo-muscular reflexes are modulated in the locomotor cycle (Forssberg et al. 1977, Andersson et al. 1978, Duysens and Loeb 1980, Van Wezel et al. 1997, Perreault et al. 1999a,b, Burke et al. 2001, Baken et al. 2005, Quevedo et al. 2005a,b). Studies on intact and chronic spinal cats (Forssberg et al. 1975, 1977, Forssberg 1979, Andersson et al. 1978) demonstrated that low-threshold stimulation of the dorsum of the foot during the swing but not the stance phase triggered short-latency knee flexion (Forssberg 1979). In fact, cutaneous stimulation during the stance phase could enhance extensor activity (Duysens 1977). Similarly, modulation of cutaneo-motor reflexes through the step cycle have been reported in man (Duysens et al. 1993, Van Wezel et al. 1997, 2000, Zehr et al. 1998, Komiyama et al. 2000, Baken et al. 2005). These data indicate that interneurons involved in short-latency (likely disynaptic) cutaneo-muscular reflexes receive input from spinal locomotor circuits (Fig. 1A). By modulating cutaneo-muscular reflexes during locomotion, the nervous system ensures an appropriate level of sensory input during different phases of the step cycle.

The fact that these reflexes are modulated during locomotion does not mean that the interneuron population involved is an integral part of locomotor circuits (Fig. 1B) – these interneurons may receive input from these circuits, which thus modulate the reflexes. That is, this could result either from the interneurons involved receiving inputs from locomotor circuits (Fig. 1A), or being a fundamental part of the intrinsic locomotor-generating circuits (Fig. 1B).

The next question is whether cutaneous afferent input also has access to spinal locomotor circuits (Fig. 1B). Two main lines of evidence suggest that this is indeed the case. Firstly, stimulation of cutaneous receptors in the paws or in the perineal region (Afelt 1970, Pearson and Rossignol 1991), or electrical stimulation of sacrocaudal afferents (Etlin et al. 2010, Lev-Tov et al. 2010) can trigger locomotion. Conversely, reducing plantar cutaneous afferent activity altered the locomotor cycle (Varejão and Filipe 2007). Secondly, cutaneous afferent stimulation can lead to changes in the phasing of the step cycle, or "resetting" of the locomotor rhythm in cats (Duysens and Pearson 1976, Duysens 1977, Duysens and Stein 1978, LaBella et al. 1992). These data indicate that low-threshold cutaneous afferents have access to spinal locomotor circuits (Fig. 1B).

Combining the above findings, it is clear that cutaneous afferents project – directly or indirectly – to core locomotor circuits, and in turn are modulated by these circuits (or are integral to them; Fig. 1C).

Which cutaneous afferents are responsible for the above effects? There is a large array of cutaneous receptors distributed over the entirety of the skin. The nature and size of cutaneo-muscular reflexes is heavily dependent upon the area of the skin stimulated and the muscle that is observed (Hagbarth 1952). Therefore, it is not surprising that cutaneous signals from different body regions can have dramatically different effects on locomotion. For example, gentle pressure on the dorsal lumbar skin of the rabbit or repetitive electrical stimulation of one of the lumbar skin nerves can inhibit locomotor movements (Viala and Buser 1965, 1974). Similarly, in spinalized cats, cutaneous back stimulation abolished locomotor-like activity and reduced spastic-like activity (Frigon et al. 2012). A similar result has been reported in a human with a motor complete spinal cord injury (Nadeau et al. 2010): pinching the skin of the lower back effectively stopped rhythmic spontaneous synchronous discharges of multiple leg muscles. These results suggest that cutaneous receptors in the back have access to spinal rhythmogenic circuits.

On the other hand, cutaneous mechanoreceptors in the paws or feet are strategically situated to best provide dynamic feedback reflecting the features of the changing surface on which standing or locomotion occurs. Several lines of evidence support the importance of these receptors. Mechanical stimulation of the plantar skin during quiet stance evoked postural sway that was highly correlated with the cutaneous stimuli (Maurer et al. 2001). In addition, plantar cutaneous afferents contributed to determining automatic postural responses following mediolateral perturbations (Ting and Macpherson 2004, Bolton and Misiaszek 2009). Stimulation of cutaneous afferents of the sole of the foot in humans resulted in reflex responses in muscles acting at the ankle, and could thus modulate motoneuron output contributing to stabilization of stance and gait (Aniss et al. 1992). Temporary silencing of cutaneous receptors in the sole of the foot by cold anaesthesia reduces the forces exerted on the sole (Taylor et al. 2004). Along these lines, using microneurography, evidence was provided of coupling between low-threshold mechanoreceptors in the glabrous skin of the foot and motoneurons controlling the ankle (Fallon et al. 2005). It was also shown that people who suffer plantar desensitization (e.g. due to diabetic neuropathy) have compromised gait and stability (Lin and Yang 2011). Therefore, cutaneous reflexes stemming from tactile input to the plantar aspect of the foot are particularly important for maintaining stability, particularly during challenging walking conditions (Zehr and Stein 1999) and are thus critical for normal posture and locomotion.

There is a particular set of reflexes elicited by cutaneous stimulation to the dorsal aspect of the foot that is involved in responses to unexpected physical obstacles. In intact or spinalized cats walking on a treadmill, contact of the foot dorsum with a mechanical obstacle triggers a set of stereotyped reflexes involving flexors and extensors of the hind limb that allow the contacted limb to clear the obstacle (Forssberg et al. 1975, 1977, Forssberg 1979). This stumbling corrective response has also been observed in the fore-limbs of cats (Drew and Rossignol 1987), and in response to low-threshold electrical stimulation of the superficial peroneal nerve (Quevedo et al. 2005b). In humans, it was demonstrated that electrical stimulation of the superficial peroneal nerve during the swing phase of the step cycle can elicit reflex activity in the leg consistent with a "stumble corrective response," which may assist in maintaining stability during walking (Van Wezel et al. 1997, Zehr et al. 1997). Thus, cutaneo-motor responses are key to short-latency recovery mechanisms associated with obstructions.

These corrective mechanisms involve a whole body response which presumably results, at least in part, from inter-limb cutaneous reflexes (Marigold and Patla 2002). It is noteworthy, that in cats, cutaneous denervation of the hind paws affected the trajectories of all four limbs. Therefore the loss of cutaneous sensation from the hind paws has a clear impact on body position and stability (Bolton and Misiaszek 2009).

Inter-limb cutaneous reflexes are important for limb position in cats, rodents, and humans (Nakajima et al. 2013). Cutaneous stimulation of the hand evoked reflexes in leg muscles which changed the ankle trajectory (Haridas and Zehr 2003), and cutaneous stimulation of the hand and foot during arm and leg cycling produced convergent reflex effects, suggesting that reflex pathways from hands and legs activated common, as yet unidentified, interneurons (Nakajima et al. 2013). Convergent cutaneous pathways between the hands and feet were also demonstrated in humans during treadmill walking (Haridas and Zehr 2003), stair climbing (Lamont and Zehr 2006), and at rest (Nakajima et al. 2013). Together, these data demonstrate that the effects of cutaneous afferents are not confined to their limb of origin, but rather are distributed to affect upper and lower limb movement.

Taken together, these observations support the notion that cutaneous signals from low-threshold mechanoreceptors in animals and humans are integrated with spinal locomotor circuits, and although they are not necessary for the generation of locomotor activity, they play a critical modulatory role.

Integration of cutaneous afferents into supraspinal locomotor centres

The effects of cutaneous afferents on movement are not confined to the spinal cord, but a full discussion of supraspinal roles in integrating cutaneous input to motor circuits is beyond the scope of this brief review. There are three distinct ways that these systems can interact: (1) cutaneous afferents can affect supraspinal motor circuits; (2) supraspinal neurons can act at pre-

synaptic cutaneous boutons in the spinal cord; and (3) supraspinal neurons can modulate cutaneo-motor reflex pathways in the spinal cord.

In addition to affecting pyramidal tract neurons in a task- or phase-dependent manner (Palmer et al. 1985), cutaneous input can also affect reticulospinal neurons. These neurons are critical for locomotion, and may respond to cutaneous stimulation of each of the four limbs (Drew et al. 1986). Drew and coworkers (1996) suggested that one mechanism through which locomotion is affected by low-threshold cutaneous mechanoreceptors is through modulation of reticulospinal neurons involved in limb movement.

Supraspinal neurons can also affect the output of cutaneous afferents in the spinal cord via presynaptic inhibition (Rudomin and Schmidt 1999, Fetz et al. 2002, Baken et al. 2006). This was nicely demonstrated in monkeys performing voluntary movements, in which presynaptic inhibition of cutaneous afferents was shown to be task-dependent, and thus likely part of the motor command, ensuring appropriate movement (Seki et al. 2003).

Spinal cutaneous-motor circuits can also be directly affected by descending inputs. For example, Pinter and colleagues (1982) demonstrated that both corticospinal and rubrospinal systems can facilitate low-threshold cutaneous-motor post-synaptic potentials. During locomotion, motor cortical stimulation also facilitated or depressed various cutaneo-muscular reflexes in the intact cat (Bretzner and Drew 2005). In humans, transcranial magnetic stimulation of the motor cortex facilitated cutaneous reflexes evoked by sural nerve stimulation during swing (Pijnappels et al. 1998, Christensen et al. 1999).

Together, these studies demonstrate the granular interaction between cutaneous inputs and motor output, with interactions occurring at many levels in different tasks, including locomotion.

CUTANEOUS MODULATION OF HAND FUNCTION

In the previous section, we highlighted the role of cutaneous feedback in shaping locomotion. In this section, we will briefly discuss the key role that cutaneous afferents play in shaping motor commands necessary for basic hand function during tasks such as grasp.

There is a high density of cutaneous mechanoreceptors in the hands reflecting the high demand for afferent sensation in generating specialized motor commands required for grasping. Low-threshold mechanoreceptors of the hand signal contact with an object and contribute to the development of appropriate muscle forces (McNulty and Macefield 2001). Both spinal and transcortical pathways linking low-threshold mechanoreceptors in the hand and hand muscles have been identified (Jenner and Stephens 1982, Bui et al. 2013). Experiments with local anaesthesia confirmed that signalling from cutaneous receptors is required for appropriate force control (Johansson and Westling 1984, 1987) and movement kinematics of reaching and grasping trajectory (Gentilucci et al. 1997). In addition to adjustments for slip, cutaneous sensation was also shown to be important in setting and maintaining a background level of input to motoneurons in order to set the appropriate force (Augurelle et al. 2003). The activity of these pathways has been found to be task-dependent (Evans et al. 1989). Thus, cutaneous receptors in the hand play an important role both in the tonic setting of grip force as well as in its adjustment in the case of slippage, in a task-dependent manner.

To grip an object, a number of forces must be balanced. In the simplest scenario of holding a stationary unsupported object, two main components come to play: the load force (equal to the object weight) and friction, which can be changed for a given textured object by altering grip force (see Appendix). Thus,

$$F_{grip} \geq \frac{m * g}{\mu} \quad (1)$$

where F_{grip} = grip force, m = mass of object, g = acceleration due to gravity, and μ = coefficient of static friction. This shows that the grip force is proportional to the weight of the object (m*g). Furthermore, the more slippery the object is – thus having a lower coefficient of friction – the greater the force must be. But during arm movement, grip force is dynamically modulated in parallel with changes in the acceleration of the object (Flanagan et al. 1993, Flanagan and Wing 1995). In an accelerating vertical unsupported object, F_{grip} may need to change such that

$$F_{grip} \geq \frac{m * (g + a)}{\mu} \quad (2)$$

where a = the acceleration (in an upward direction) of the object. That is, if accelerating the object upward

(positive 'a' value), a greater force is needed, but if the acceleration is downward (negative 'a' value), less force is required. If the object is not vertical, and thus at least partly supported (for example by the palm), then this becomes

$$F_{grip} \geq \frac{m(\vec{a}_{x'} - g\sin\theta)}{\mu} - m(\vec{a}_{y'} + g\cos\theta) \quad (3)$$

where θ is the constant angle of the palm in relation to the horizontal plane. While these equations determine the minimum force to prevent the object from slipping, there is also a maximum force determined by the object, such that the object is not damaged. In healthy individuals, the grip forces generated are only slightly larger than the smallest forces needed to lift the object (Cole and Abbs 1988). The key question, therefore, is how is grip force regulated to maintain this balance of forces?

Much of our knowledge about the role of cutaneous afferents in hand function comes from experiments with digital anaesthesia, which either blocks or attenuates cutaneous information such as pressure and direction of tangential force vectors (Monzée et al. 2003). Anaesthesia that led to blocking of cutaneous reflex responses in human subjects impaired their hand performance (Collins et al. 1999). Moreover, the grip response adjustments to changing load forces was either delayed and attenuated or totally abolished (Johansson et al. 1992). A number of studies confirmed that impairment of cutaneous feedback was associated with an increased "safety margin" in the grip force vs. load force balance where generally the grip forces were elevated (Nowak and Hermsdörfer 2003). Surprisingly, despite the compensatory increase in applied grip force, anaesthetizing the index finger and thumb reduced the maximum pinch force by 25% (Rossi et al. 1998). On the other hand, the precise anticipatory temporal coupling between grip force vs. load force (i.e. feed-forward component) was not affected by the anaesthesia (Nowak et al. 2001). Together, these studies demonstrate that grip function relies on descending or feed-forward control (anticipatory or predictive) coupled with cutaneous feedback (reactive).

Clearly, feed-forward input and feedback regulation must integrate within the central nervous system to ensure appropriate grip function. Feed-forward strategies are proposed to dominate in performing fast grasping tasks, whereas feedback control mechanisms dominate in unpredictable movements such as in sudden perturbations or in handling novel objects (Blakemore et al. 1998, Quaney et al. 2005, Nowak et al. 2013). Also, there is evidence suggesting that the relative roles of feed-forward and feedback mechanisms are task-dependent, and change during development. For example, in young children, the scaling of motor commands relies mainly on reactive rather than predictive commands, and this changes with age (Forssberg et al. 1991, Paré and Dugas 1999, Bleyenheuft and Thonnard 2010). Therefore, the neural circuits mediating integration of these commands are plastic in both short-term (task-dependence) and long-term (developmental) domains.

How does this integration occur (Fig. 2)? According to these theories, sensory information – visual, proprioceptive, cutaneous – would lead to the formation of an internal model of the physical properties of an object. This internal model would serve as a template for the behaviour controlled by feed-forward pathways (Augurelle et al. 2003, Monzée et al. 2003). Feedback from cutaneous afferents would also play a role in the maintenance and adaptation of the model (Monzée et al. 2003, Nowak et al. 2013). In other words, unsuccessful or unplanned experiences when grasping an object would lead to adaptations of the internal model.

Where might this integration occur? We recently demonstrated that spinal glutamatergic neurons derived from the pd3 progenitor domain, dI3 interneurons, mediate disynaptic cutaneo-motor reflexes (Bui et al. 2013). Animals in which the vesicular glutamate transporter used by these neurons, vGluT2, was genetically removed from dI3 interneurons have an inability to grasp, demonstrating the necessity of this population for normal hand function. We proposed that these spinal neurons are ideally situated and connected to mediate the integration of feed-forward and feedback commands regulating grip function.

ROLE OF CUTANEOUS AFFERENTS IN MOTOR FUNCTIONAL RECOVERY

The degree of motor functional recovery following injury to the central nervous system affecting movement can be variable. Our current understanding of the

mechanisms of such recovery is incomplete. Here, we briefly review the role of cutaneous afferents in effecting plasticity of the nervous system that leads to improvement in motor function.

Motor function is generated through the interaction between supraspinal centers, spinal motor networks, and peripheral sensory inputs (Fig. 2). These three networks need to stay in relative balance in order to adapt ongoing motor behaviour to current demands as dictated by both intrinsic (body) and extrinsic (environment) factors. Injury or disease affecting any of these networks and hence motor function would consequently require compensatory changes, or plasticity to recover motor function. Plasticity could potentially occur in all three networks. These changes could be generated spontaneously (intrinsic network reorganization) and/or triggered by extrinsic factors (i.e. by training).

Recovery of locomotor function following spinal cord injury

Following spinal cord transection in animals or spinal cord injury in humans, treadmill training can lead to improvement of locomotor function (Rossignol and Frigon 2011, Harkema et al. 2012). Locomotor training can enhance the recovery of stepping (Edgerton et al. 2001, 2008) after a spinal cord injury in mice (Fong et al. 2005, Cai et al. 2006), rats (Timoszyk et al. 2005, Cha et al. 2007), cats (Lovely et al. 1986, 1990, Barbeau and Rossignol 1987, de Leon et al. 1998, 1999), and human subjects (Harkema et al. 1997, Van de Crommert

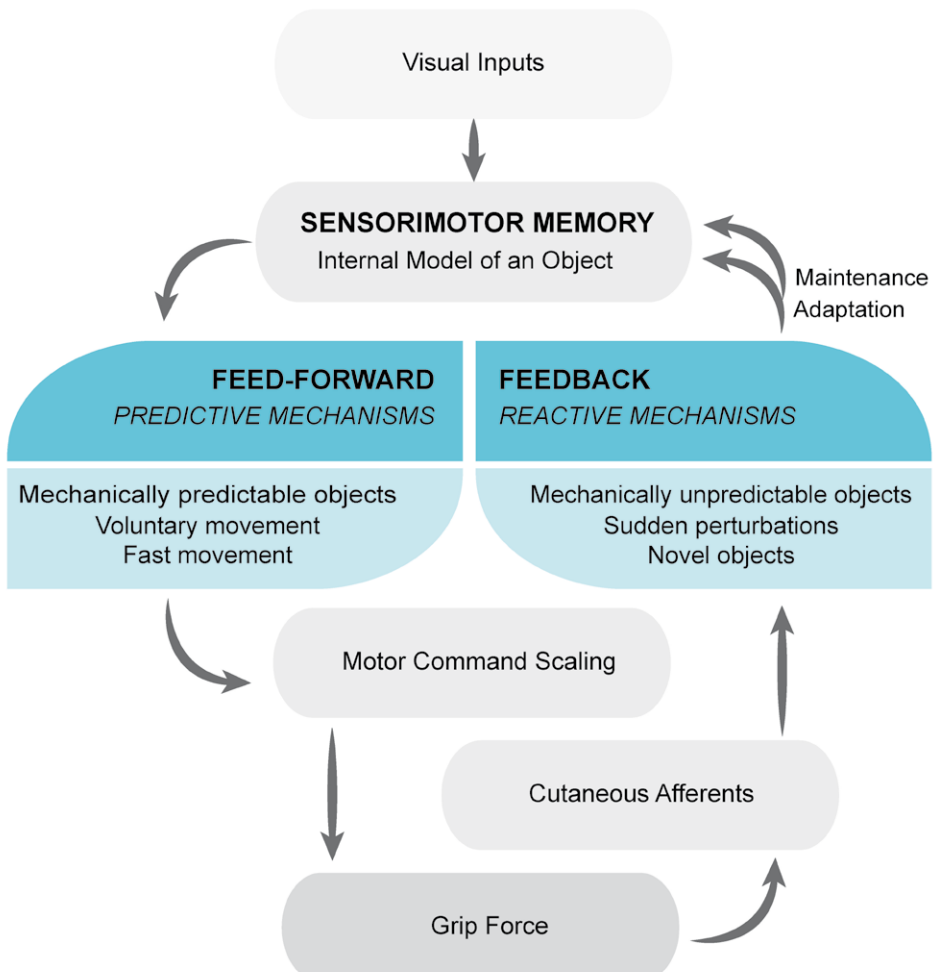

Fig. 2. Sensorimotor Control of grip force. The control of grip force includes both feed-forward (predictive) and feedback (reactive) mechanisms that rely upon sensory inputs to create an internal model of an object and then to adapt grip force in order to maintain hold of the object. Amongst the sensory modalities that shape the control of grip force are visual inputs and low-threshold cutaneous afferents.

et al. 1998, Dietz and Harkema 2004). The mechanisms underlying plasticity of spinal locomotor networks are incompletely understood, but cutaneous afferents can play a role in rats (Multon et al. 2003, Smith et al. 2006, Sławińska et al. 2012a), chicks (Muir and Steeves 1995), and humans (Harkema et al. 1997, Abel et al. 1999, Hicks et al. 2003). This has perhaps best been studied in cat: following spinal transection, cutaneous deafferentation of the hind paws prevented recovery of locomotor function that was normally seen as long as one cutaneous nerve was intact (Bouyer and Rossignol 2003a). Furthermore, even in the absence of training, cutaneous afferents play an important role in enabling rodents to walk upright on a treadmill following spinal transection. Input from hind limb load receptors is critical for recovery of stepping (Sławińska et al. 2012b). Injection of lidocaine into the hind paws to inactivate low-threshold cutaneous receptor critically strips away all recovery, reducing coordination between fore-limbs and hind limbs and between left and right limbs, increasing cycle duration, and altering individual electromyograms (Sławińska et al. 2012a). The importance of cutaneous transmission to the recovery of locomotion by locomotor training may partially involve normalization of cutaneous neurotransmission (Côté and Gossard 2004). These studies highlight the importance of cutaneous afferents in reorganizing spinal circuitry after injury.

Cutaneous afferent contribution to hand motor functional recovery

Studies on human subjects and monkeys have been instrumental in demonstrating the role of cutaneous afferents in recovery of hand function following injury. Several groups have investigated mechanisms underlying recovery of hand function in people with stroke and spinal cord damage (e.g. Wade et al. 1983, Lang and Schieber 2004, Wenzelburger et al. 2005). A number of studies demonstrated reorganization of corticospinal function following chronic lesions such as limb amputation (Cohen et al. 1991, Fuhr et al. 1992, Pascual-Leone et al. 1996), spinal cord injury (Levy et al. 1990, Topka et al. 1991), hemiplegic cerebral palsy (Farmer et al. 1991), and subacute stroke (Traversa et al. 1997). Interestingly, even minor changes in sensory inputs such as those induced by finger anaesthesia, were shown to induce short-term enlargement of the cortical representation of the unanaesthetized fingers (Rossini et al. 1994) and changes in corticospinal activity accompanying voluntary movements (Kristeva-Feige et al. 1996). Following such injuries in animals, training induces changes in somatotopic maps of the somatosensory and motor cortices (Friel et al. 2000, Weidner et al. 2001, Cai et al. 2006, Ramanathan et al. 2006). In rats spinalized in the neonatal period, exercise increased both the percentage of somatosensory cortical neurons responding to cutaneous fore-limb stimulation as well as the amplitude of their responses (Kao et al. 2009, 2011). Such changes correlated with behavioural outcomes (Kao et al. 2009). Thus it would seem that cutaneous input plays a role in cortical reorganisation following injury.

Recovery of hand function, however, results from spinal plasticity as well as cortical plasticity. Unilateral lesions of the dorsal column in monkeys led to impaired reaching and grasping, with the degree of impairment related to the number of axons damaged (Qi et al. 2013). Interestingly, however, there was still considerable recovery even when lesions were near complete, suggesting that recovery was mediated by plasticity in spinal circuits. Hand functional recovery was also observed in mice with combined cortical and spinal lesions, reinforcing the importance of plasticity in spinal circuits for hand function (Blanco et al. 2007). In conclusion, cutaneous afferent-mediated plasticity of spinal motor circuits plays a critical role in motor functional recovery following injury.

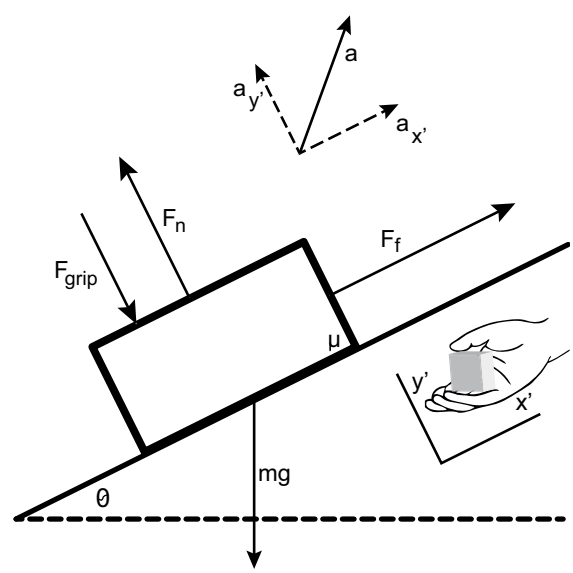

Fig. 3. Free body diagram illustrating forces for grip. See appendix.

CONCLUSIONS

In summary, low-threshold cutaneous mechanoreceptors play critical roles in mediating normal motor function, and ensuring that motor systems adapt to their environment. Furthermore, afferents from these receptors are important in ensuring plastic changes to central nervous system microcircuits following injury. Studies comparing and contrasting circuitry responsible for fore- and hind limb motor functions as well as their supraspinal and sensory modulation would be necessary to better understand inter-limb relationships, that could be necessary in devising more efficient training paradigms promoting recovery following spinal cord injury.

APPENDIX

It is critical that appropriate force is used to grasp an object. How much force is needed? In order to determine the amount of grip force needed (Fig. 3), we assumed that the hand grips an object of constant mass, m, and that the coefficient of friction between the mass and the hand is μ, and the force of friction F_f. We also assumed that the coefficient of friction is constant, although this is not always the case, particularly with low normal forces (André et al. 2009). Furthermore, the hand is held at angle Θ from the horizontal plane. We defined axes x' and y' to be parallel and perpendicular, respectively, to the plane defined by the palm (at angle Θ). The normal force, F_n, would then be in direction y', and the grip force, F_{grip}, in the negative y' direction. Finally, we assumed movement of the hand with acceleration, a, in an arbitrary direction that could be represented by the sum of vectors in x' and y' directions, represented as $\vec{a}_{x'}$ and $\vec{a}_{y'}$ respectively. The force in the x' direction is therefore:

$$m\vec{a}_{x'} = F_f - mg \sin\theta$$

which can be rearranged to:

$$F_f = m(\vec{a}_{x'} - g \sin\theta)$$

Substituting $F_f = \mu F_n$, we get:

$$\mu F_n = m(\vec{a}_{x'} - g \sin\theta) \qquad \text{(Eq. A)}$$

Similarly, in the y' direction, one can see that:

$$m\vec{a}_{y'} = F_n - F_{grip} - mg \cos\theta$$

or

$$F_n = m\vec{a}_{y'} + F_{grip} + mg \cos\theta \qquad \text{(Eq. B)}$$

If we now substitute Eq. B into Eq. A, we can see that:

$$\mu(m\vec{a}_{y'} + F_{grip} + mg \cos\theta) = m(\vec{a}_{x'} - g \sin\theta)$$

$$\mu m(\vec{a}_{y'} + g \cos\theta) + \mu F_{grip} = m(\vec{a}_{x'} - g \sin\theta)$$

$$\mu F_{grip} = m(\vec{a}_{x'} - g \sin\theta) - \mu m(\vec{a}_{y'} + g \cos\theta)$$

$$F_{grip} = \frac{m(\vec{a}_{x'} - g \sin\theta)}{\mu} - m(\vec{a}_{y'} + g \cos\theta)$$

But this defines the minimum grip force. Therefore the equation could be written as:

$$F_{grip} \geq \frac{m(\vec{a}_{x'} - g \sin\theta)}{\mu} - m(\vec{a}_{y'} + g \cos\theta)$$

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