REVIEW / SYNTHÈSE

Contribution of sensory feedback to ongoing ankle extensor activity during the stance phase of walking[1]

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Abstract: Numerous investigations over the past 15 years have demonstrated that sensory feedback plays a critical role in establishing the timing and magnitude of muscle activity during walking. Here we review recent studies reporting that sensory feedback makes a substantial contribution to the activation of extensor motoneurons during the stance phase. Quantitative analysis of the effects of loading and unloading ankle extensor muscles during walking on a horizontal surface has shown that sensory feedback can increase the activity of ankle extensor muscles by up to 60%. There is currently some uncertainty about which sensory receptors are responsible for this enhancement of extensor activity, but likely candidates are the secondary spindle endings in the ankle extensors of humans and the Golgi tendon organs in the ankle extensors of humans and cats. Two important issues arise from the finding that sensory feedback from the leg regulates the magnitude of extensor activity. The first is the extent to which differences in the magnitude of activity in extensor muscles during different locomotor tasks can be directly attributed to changes in the magnitude of sensory signals, and the second is whether the enhancement of extensor activity is determined primarily by feedback from a specific group of receptors or from numerous groups of receptors distributed throughout the leg. Limitations of current experimental strategies prevent a straightforward empirical resolution of these issues. A potentially fruitful approach in the immediate future is to develop models of the known and hypothesized neuronal networks controlling motoneuronal activity, and use these simulations to control forward dynamic models of the musculo-skeletal system. These simulations would help understand how sensory signals are modified with a change in locomotor task and, in conjunction with physiological experiments, establish the extent to which these modifications can account for changes in the magnitude of motoneuronal activity.

Key words: walking, sensory feedback, proprioceptors, pattern generation.

Résumé : Au cours des 15 dernières années, de nombreuses recherches ont démontré que la rétroaction sensorielle joue un rôle essentiel dans l'établissement de la synchronisation et de l'amplitude de l'activité musculaire durant la marche. Ici, nous passons en revue des études récentes indiquant que la rétroaction sensorielle joue un rôle important dans l'activation des motoneurones extenseurs durant la phase d'appui. L'analyse quantitative des effets de charge et de décharge des muscles extenseurs de la cheville au cours de la marche sur une surface horizontale a montré que la rétroaction sensorielle peut augmenter jusqu'à 60 % l'activité de ces muscles. Il existe actuellement une incertitude sur l'identité des récepteurs sensoriels à l'origine de cette augmentation, mais les terminaisons des fuseaux secondaires dans les extenseurs de la cheville des humains et les organes tendineux de Golgi dans les extenseurs de la cheville des humains et des chats sont des candidats possibles. La découverte que la rétroaction sensorielle régule l'amplitude de l'activité des extenseurs soulève deux questions importantes. La première est de savoir dans quelle mesure les différences d'amplitude de l'activité des muscles extenseurs durant diverses tâches locomotrices peuvent être directement attribuées aux variations d'amplitude des signaux sensoriels. La deuxième est de savoir si la stimulation de l'activité des extenseurs est déterminée principalement par la rétroaction d'un groupe spécifique de récepteurs ou de nombreux groupes de récepteurs répartis le long de la jambe. Les limitations des stratégies expérimentales actuelles ne permettent pas un résolution empirique précise de ces questions. Une approche potentiellement efficace consisterait à développer des modèles des réseaux neuronaux connus et hypothétiques régulant l'activité des motoneurones et à utiliser ces

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simulations pour réguler des modèles dynamiques directs du système musculo-squelettique. Ces simulations aideraient à comprendre comment les signaux sensoriels sont modifiés lors d'un changement de tâche locomotrice et, conjointement avec des expériences physiologiques, à établir dans quelle mesure ces modifications pourraient expliquer les variations d'amplitude de l'activité motoneuronale.

Mots clés : marche, rétroaction sensorielle, propriocepteurs, génération de patron.

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Introduction

Animals walk on variable terrain and over long distances with relative ease. This ease, however, belies the underlying complexity. Walking involves the time-varying coordination of a large number of muscles and countless motor units. Indeed, some current models, which capture only a fraction of the complexity of walking, require solution by supercomputers (Anderson and Pandy 2001). The complex physiology underlying the control of walking has both puzzled and excited scientists since the early studies of Sherrington (1910) and Graham Brown (1911) almost a century ago. These and subsequent investigations have established 3 main principles.

The first principle is that walking animals use a combination of feedback and feedforward control. Feedback control uses information about the current state of the animal and the external environment to modify muscle activity. In contrast, feedforward control does not require peripheral receptors, and modifies muscle activity independent of the animal's sensed state. Early last century, Graham Brown (1911) suggested that a central network (now referred to as a central pattern generator or CPG) produced the basic pattern of locomotion. The presence of a CPG in cats was confirmed when investigators demonstrated patterned activity in flexor and extensor motoneurons in the absence of sensory feedback (Jankowska et al. 1967; Grillner and Zangger 1979, 1984). This feedforward control mechanism does not normally act in isolation; feedback extensively modifies the central pattern. From a theoretical standpoint, it is logical to combine feedforward and feedback control; when combined, performance is better than when either strategy is used alone (Kuo 2002). For example, feedback compensates for perturbations and feedforward control reduces degradation of performance when sensory information is imprecise.

The second principle is that feedback control integrates information from many different afferent pathways. The important receptors in walking include the eyes (Sherk and Fowler 2001), the vestibular system (Kennedy et al. 2003), proprioceptors (Pearson 1995), and cutaneous receptors (Bouyer and Rossignol 2003). Integrating information from multiple pathways is sensible because reliance on many afferent sources likely provides a better estimate of the state of the animal, and allows for a robust control strategy in the event of damage to 1 or more pathways.

The third principle is that the strength and sign of feedback pathways are task- and phase-dependent. For example, the force-sensitive afferents that are partially responsible for the increase in ankle extensor activity during walking have the opposite effect during standing (Pearson and Collins 1993). The varying strength of the H-reflex during walking in humans is an example of phase dependence (Capaday and Stein 1986). The dependence of pathway gain on task and phase is theoretically sound, because different conditions typically require different control strategies for optimal performance (Franklin et al. 2002).

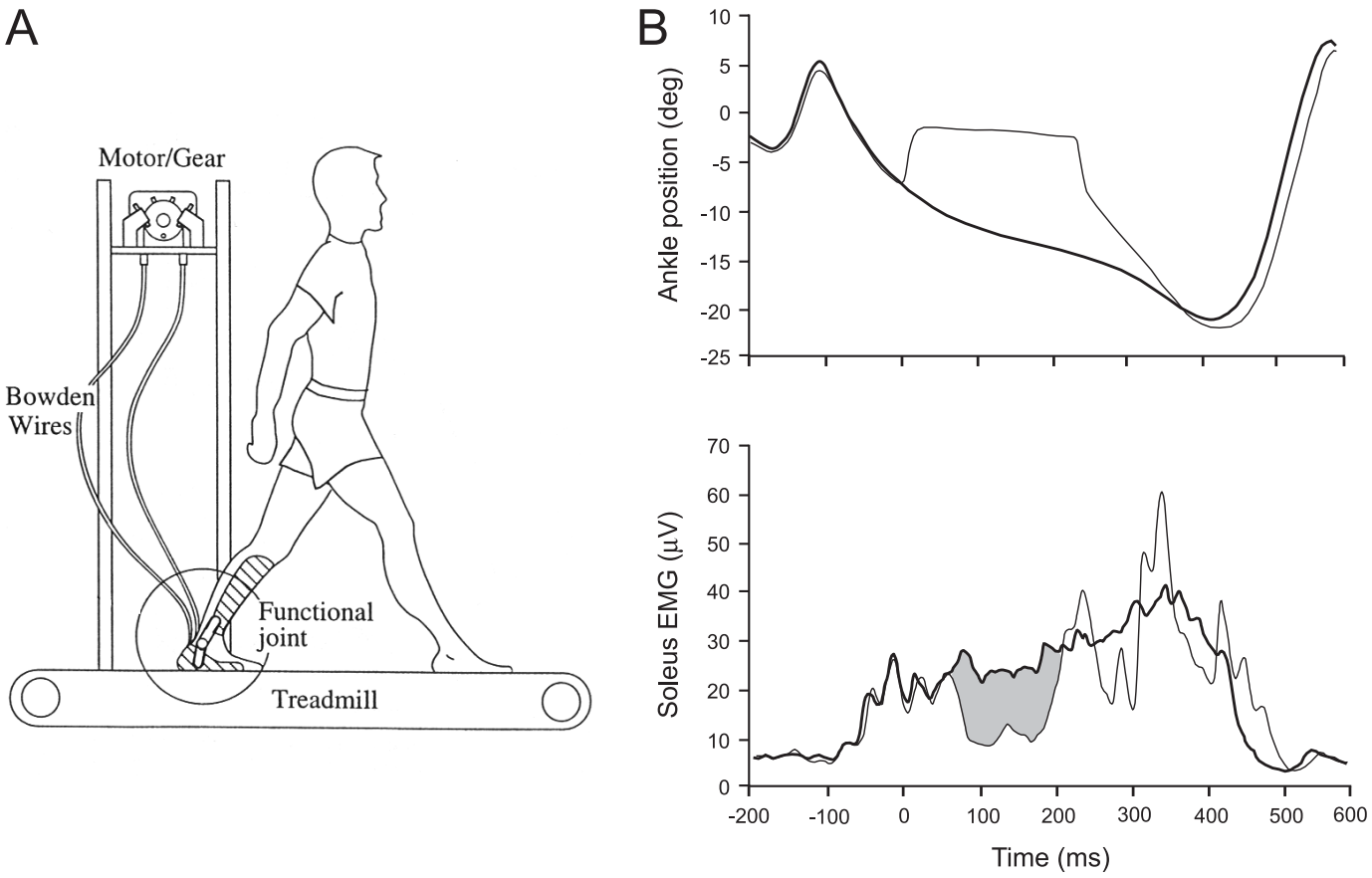
These 3 principles emphasize the importance of afferent feedback to the control of walking. Establishing the functional role of afferent feedback has been a major focus of contemporary research, especially its role in regulating the timing of muscle activity (Grillner and Rossignol 1978; Duysens and Pearson 1980; Conway et al. 1987; Whelan et al. 1995*b*; Hiebert et al. 1995). Perhaps a less appreciated, and certainly less studied, aspect of afferent feedback is its role in modulating the magnitude of ongoing muscle activity.

This review focuses on recent research regarding the contribution of sensory feedback to ongoing extensor activity during walking, with 4 goals in mind. Our first goal is to review the evidence for the afferent regulation of ongoing muscle activity in walking. We have not attempted an exhaustive review, but have restricted ourselves to the most relevant and least ambiguous work in humans and cats. Our second goal is to review work that has focused on understanding the afferent pathways responsible for modulating ongoing muscle activity. Again, we focus on what we consider to be the most relevant work. Our third goal is to outline currently unresolved issues regarding the contribution of sensory feedback to ongoing extensor activity. Our final goal is to suggest future directions that have the potential to provide additional insight into the afferent regulation of muscle activity during walking.

Sensory contribution to extensor activity during stance

The magnitude of activity in leg muscles during walking varies considerably, depending on the task (Pierotti et al. 1989; Carlson-Kuhta et al. 1998; Smith et al. 1998) and the speed (Smith et al. 1993; Kaya et al. 2003). These variations in muscle activity arise from 3 possible sources: modification in central drive to motoneurons (i.e., commands originating in the spinal cord and brain), changes in sensory feedback signals involved in regulating motoneuronal activity, and modification of the strength of transmission in afferent pathways (i.e., pathway gain). To distinguish among these possibilities, it must first be established whether or not sensory signals actually regulate motoneuronal activity during walking, and then determining the magnitude of these regulatory influences under different behavioural conditions must then be determined. In this section, we review evidence from studies on humans and cats demonstrating that ongoing activity in extensor muscles during the stance phase is strongly regulated by sensory feedback. In the next section, we consider which afferents provide this enhancement of extensor activity.

Fig. 1. Forcibly extending the ankle during the stance phase of walking decreases ongoing electromyographic (EMG) activity in the soleus muscle in humans. (A) Mechanical device for forcibly extending the ankle using an externally applied extensor moment. The angular position of a flexible ankle brace is controlled by a motor mounted close to the treadmill (adapted from Sinkjaer et al. 1996). (B) Superimposed traces of the ankle position (top) and the rectified/filtered EMG from the soleus muscle (bottom) during normal steps (thick traces) and steps taken when the ankle extensors were shortened (thin traces). Note the large decrease in soleus EMG (shaded area) commencing about 60 ms after the onset of the perturbation. The standing position of the ankle is 0 degrees (adapted from Sinkjaer et al. 2000).



A number of strategies have been used to demonstrate a sensory contribution to the activation of extensor motoneurons during stance: loading and unloading of the body (Harkema et al. 1997; Hiebert and Pearson 1999), stretching or shortening the ankle extensor muscles during the stance phase (Sinkjaer et al. 2000; Stein et al. 2000; Yang et al. 1991), and unexpected removal of the supporting surface (Hiebert et al. 1994; Gorassini et al. 1994). The most compelling evidence for a significant sensory contribution to extensor activity comes from experiments in which the extensor muscles were suddenly and unexpectedly unloaded during the stance phase. The shortcomings of the other approaches are that changes in extensor activity to maintained body unloading or loading could result from modifications in central command signals, and that responses to muscle stretch may be due to the recruitment of afferent pathways not normally involved in regulating motoneuronal activity during unperturbed walking. Nevertheless, data from the former 2 approaches have been consistent with those obtained from the unloading of extensor muscles.

In walking humans, the soleus muscle is active and contributes to ankle torque during most of the stance phase (Fig. 1). By suddenly shortening the ankle extensor muscles through a forced extension of the ankle during the stance phase, Sinkjaer and colleagues (2000) observed a marked reduction in the magnitude of soleus activity (about 50% on average). This reduction commenced, on average, 64 ms after the onset of the extension (Fig. 1B). The reduction in soleus activity is not the result of reciprocal inhibition of the stretched ankle flexors, because it persisted after an anaesthetic block of the common peroneal nerve. This finding is the strongest indication to date that feedback from sensory receptors in the ankle extensor muscles contributes substantially to the generation of burst activity in the soleus muscle during normal walking in humans. The magnitude of this effect is consistent with a previous estimate, derived from the analysis of reflex responses evoked in soleus by unexpected *stretches* of the ankle extensors (Yang et al. 1991). The main conclusion from this study was that the contribution of sensory feedback to soleus activity during the early part of stance was 30% to 60%.

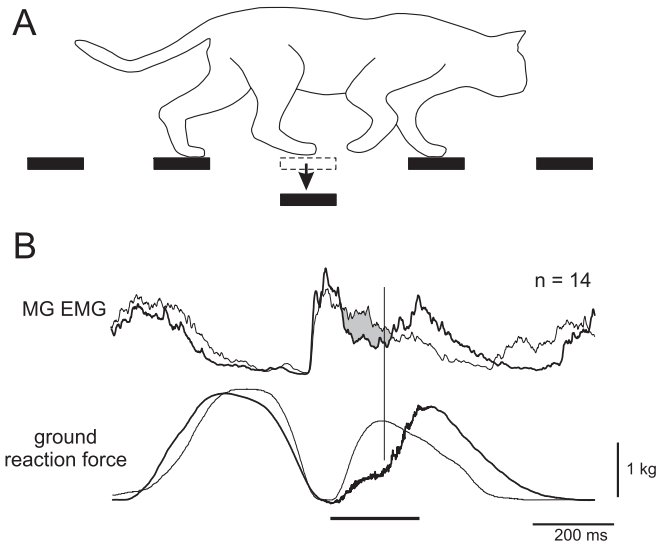
More qualitative data supporting the notion that sensory signals contribute to the activation of extensor motoneurons during stance come from investigations on the effects of unloading leg extensors by partially supporting body weight. Weight support reduces the magnitude of ankle extensor ac-

tivity in normal individuals (Dietz and Colombo 1998) and in patients with complete spinal cord injury (Harkema et al. 1997; Dietz et al. 2002). In spinal-cord-injured patients, this finding is especially important; it reduces the likelihood that the effect in normal individuals is simply the result of changes in the input to motoneurons from rostral structures in the nervous system.

Numerous studies in the cat have also revealed a substantial contribution of sensory feedback to the activation of extensor motoneurons during the stance phase of walking. Data have come from investigations of intact (Gorassini et al. 1994), decerebrate (Hiebert and Pearson 1999; Stein et al. 2000; De Serres et al. 2002; Bennett et al. 1996; Angel et al. 1996; McCrea et al. 1995), and spinal (Hiebert et al. 1994) animals. One strategy for demonstrating a significant afferent contribution to the generation of extensor activity has been to unexpectedly remove the supporting surface immediately before ground contact. In intact animals, the unexpected absence of ground contact results in a large reduction in activity of the ankle extensor muscles, with a latency of about 40 ms (Gorassini et al. 1994). The extent to which this reduction in activity is the result of the absence of an expected sensory feedback signal is currently uncertain, because the absence of ground support is often associated with short-latency activation of flexor motoneurons (Hiebert et al. 1994). Thus, the central inhibition of extensors related to flexor-burst generation might contribute to the reduction in extensor activity. However, the effects of central inhibition versus loss of sensory feedback can be dissociated in spinal and decerebrate cats; the activation of flexors after the unexpected loss of ground support is delayed for approximately 100 ms in spinal cats and for more than 500 ms in decerebrate animals. The relevant observation in these preparations is the large reduction in ankle extensor activity preceding the activation of flexors (see Fig. 5 in Hiebert et al. 1994, and Fig. 1 in Hiebert and Pearson 1999). A quantitative analysis of decerebrate walking animals revealed that loss of ground support reduced the magnitude of ankle extensor activity by 50% to 70%.

Because of possible differences of sensory feedback between intact and spinal or decerebrate animals, we reexamined the influence of changes in ground support on ankle extensor activity in intact animals in a situation that did not lead to the short-latency generation of flexor bursts (Fig. 2). Two animals were trained to walk across a series of pegs, 1 of which could be lowered quickly at any time. Measurements of ground-reaction forces taken from 4 of the pegs provided the signals used to initiate peg movement. Fig. 2 shows the average vertical ground-reaction forces and the rectified and filtered electromyograms (EMGs) in the medial gastrocnemius (MG) muscle from trials when the peg was lowered. Superimposed on these records are the same averages for the control step on the preceding fixed peg. In the example shown in Fig. 2, the lowering of the peg was timed to begin immediately after the foreleg left the plate, and the peg was lowered 4 cm over a period of 200 ms. While the peg was accelerating downward, the ground-reaction force was reduced, and there was a corresponding reduction in the magnitude of MG activity, by about 30%. On the other hand, when the peg was decelerating in the latter half of the movement, the ground-reaction force increased to values higher than the control values, and there was a marked increase in MG activity commencing about 20 ms after the onset of the increase in the ground-reaction force. Thus, in intact cats, it is clear that the magnitude of activity in the MG muscle is strongly influenced by sensory feedback during stance, in a manner consistent with the notion that sensory feedback normally contributes substantially to the activation of at least 1 of the ankle extensor muscles (measurements from other ankle extensors have not yet been taken). The close association between the changes in MG activity and the ground-reaction force, which reflects force in the ankle extensor muscles, also supports the hypothesis that one source of the reinforcing feedback signal is the force-sensitive Golgi tendon organs.

Fig. 2. Reducing the vertical ground-reaction force decreases the magnitude of ongoing EMG activity in the medial gastrocnemius (MG) muscle during the stance phase of walking in the cat. (A) Experimental arrangement. Adult cats walk across a series of pegs, one of which is lowered just prior to hind paw contact. (B) Superimposed averaged rectified/filtered EMGs (top) and vertical ground-reaction forces (bottom) when the hind paw stepped onto the moving peg (thick traces) and during the immediately preceding step on a fixed peg (thin traces). The horizontal bar indicates the period over which the peg was moving (also indicated by the noise on the ground-reaction force). During the acceleration of the downward movement of the peg, the ground-reaction force was reduced and, correspondingly, the ongoing MG EMG decreased (shaded area). The ground-reaction force increased (onset indicated by thin vertical line) as the peg commenced decelerating, and about 20 ms later the MG EMG increased above control values.



Another strategy for investigating the potential role of sensory feedback in the activation of the ankle extensor has been to modify sensory signals from the muscles, either by stretching or vibrating the isolated muscles in decerebrate walking animals, or by electrically stimulating the nerves of these muscles (Hiebert and Pearson 1999; Stein et al. 2000; De Serres et al. 2002; Bennett et al. 1996). This strategy has clearly demonstrated that large afferents, arising from primary muscle spindles and from Golgi tendon organs, exert an excitatory action on ongoing activity in ankle extensor

motoneurons, suggesting that both length and force signals from these muscles contribute to motoneuronal activation. However, a major difficulty in interpreting these types of studies, in terms of functional importance, is that the experimental leg is either extensively or completely denervated and not moving rhythmically. Thus, there is uncertainty about whether the state of the pathways mediating the excitatory actions is the same as that in a stepping leg because of the loss of sensory signals that may be involved in establishing appropriate gains in these pathways. Another problem is that, in many instances, the perturbations are quite artificial, as in electrical stimulation of nerves and high-frequency muscle vibration. This may increase the role of pathways that are normally not effective during walking, when the same afferents are activated in a more natural manner and at a lower intensity (Morita et al. 1998; Enriquez-Denton 2002). In addition, the abnormal patterns produced by artificial activation may recruit high-threshold excitatory interneuronal pathways that are normally not open. Nevertheless, a consistent feature of all studies is that stimulation of large-muscle afferents from ankle extensors excites extensor motoneurons when applied during the extensor bursts. Because these afferents are known to be active during the stance phase of walking (Prochazka and Gorassini 1998), this general finding is consistent with the data found using other strategies. Afferent feedback enhances activity in ankle extensors during stance.

Afferent pathways responsible for increasing extensor activity during stance

The previous section reviewed the evidence for the contribution of feedback to ongoing ankle extensor activity during the stance phase of walking in humans and cats. In this section, we focus on the afferent pathways responsible for this effect. Determining the relative contribution of different feedback pathways is not a simple task, because of the difficulty in selectively activating or silencing individual groups of receptors during walking. Instead, the roles of different pathways are determined by inference, relying on the results of experiments that involve a number of techniques. These methods include comparing walking biomechanics with change in muscle activity (Wisleder et al. 1990), directly measuring afferent activity (Prochazka and Gorassini 1998), electrically stimulating afferents (Guertin et al. 1995; Whelan et al. 1995*a*; Whelan and Pearson 1997), transecting nerves (Bouyer and Rossignol 2003), blocking transmission in sensory afferents (Grey et al. 2001), and applying perturbations (Yang et al. 1991; Sinkjaer et al. 1996). These various techniques have different strengths and limitations, and no single method should be considered the gold standard. What follows is a brief review of our understanding of the contribution of different afferent pathways from the summed knowledge gained by investigations using these techniques.

For their contributions to ongoing activity, the most studied feedback pathways are proprioceptive pathways. Of these, the group Ia afferents, which arise from velocity-sensitive primary-spindle endings, have been most thoroughly investigated. Interestingly, the evidence suggests a reduced role of monosynaptic group Ia pathways during walking. Bennett et al. (1996) applied sinusoidal stretches to an ankle extensor in walking spinal cats and found that, because of a change in gamma drive, the sensitivity of Ia afferents was lower than it was when the cat was standing. Compounding this reduction in sensitivity, Gosgnach et al. (2000) demonstrated that monosynaptic group I connections to motoneurons receive presynaptic inhibition during walking in the decerebrate cat. Similarly, in humans, the magnitude of the H-reflex is lower during walking than when standing, probably because of the action of presynaptic inhibition (Capaday and Stein 1986).

There are, however, strong oligosynaptic pathways from group Ia afferents that potentially contribute to ongoing extensor activity during locomotion. In a fictive preparation, McCrea and colleagues found that the stimulation of extensor nerves at group I strength, as well as the selective activation of group Ia afferents using small-amplitude vibrations, produced a short-latency widespread increase in ipsilateral extensor activity (Guertin et al. 1995). Intracellular recordings indicated that this feedback was mediated by a disynaptic pathway that is open only during the extensor phase of the locomotor cycle, and not open at all in the absence of locomotor activity (McCrea et al. 1995; Angel et al. 1996).

Although group Ia afferents have the potential to contribute to ongoing activity, it is not yet certain that their contribution is substantial. Ensemble averaging of triceps surae–afferent activity, measured during the stance phase of normal walking in cats, indicates that group Ia activity is only slightly elevated near the beginning of the stance phase, and is relatively low, relatively constant, and has poor covariance with ongoing muscle activity throughout the remainder of stance (Prochazka and Gorassini 1998). Furthermore, a strong indication that group Ia afferents do not contribute substantially to ongoing extensor activity in humans comes from the forced ankle extension experiments of Sinkjaer et al. (2000) (Fig. 1). The imposed shortening of the ankle extensors decreased ongoing muscle activity, and this reduction remained after an ischemic nerve block, designed to reduce feedback from group Ia afferents. On the other hand group Ia afferents were found to contribute to a short-latency activation of the soleus muscle in response to imposed length increases (Grey et al. 2001). This demonstrates the importance of Ia feedback for generating a rapid response to a perturbation during the stride cycle. However, evidence that group Ia afferents normally contribute to ongoing muscle activity in the unperturbed stride cycle is not compelling; imposed rapid stretches may recruit pathways normally not effective. One possible mechanism for regulating the contribution of group Ia afferents during the normal and perturbed gait cycle is presynaptic inhibition. In humans and cats, presynaptic inhibition appears to reduce motoneuron excitatory postsynaptic potentials (EPSPs) evoked by low-rate Ia activity to a greater degree than EPSPs evoked by high-rate Ia activity (Morita et al. 1998; Enriquez-Denton 2002). Ankle extensor muscle velocity during normal walking is slow (Fukunaga et al. 2001) relative to the imposed velocity in Grey et al. (2001), suggesting that group Ia afferent pathways may not be effectively recruited during normal human walking.

There is a growing body of evidence suggesting that group Ib afferents, arising from force-sensitive Golgi tendon organs, contribute substantially to ongoing muscle activity.

Pearson and Collins (1993) found that electrical stimulation of an extensor nerve (plantaris) at group I strength during walking in the spinal cat substantially increased ongoing activity in other extensor muscles (medial and lateral gastrocnemius). Activating group Ia afferents by vibration produced much weaker excitation than stimulation of both group Ia and Ib afferents, demonstrating group Ib afferents exert an excitatory action on ankle extensor motoneurons during walking. Our recent findings also support the importance of group Ib feedback in modulating ongoing muscle activity (Donelan and Pearson 2004). In a preparation that isolates feedback from Golgi tendon organs during treadmill walking in decerebrate cats, we found that increased group Ib feedback from an ankle extensor caused a substantial increase in ongoing homonymous and heteronymous extensor activity. This corresponds well with the ensemble averaging of triceps surae–afferent activity measured during normal walking in cats, which demonstrated a high modulation of group Ib activity and a strong covariation with ongoing muscle activity (Prochazka and Gorassini 1998).

In human walking, the work of Sinkjaer and colleagues suggests that group Ib feedback may contribute to ongoing ankle extensor activity. Little effect on the reduction in muscle activity with forced extension was observed after lidocaine was injected into the common peroneal nerve to reduce reciprocal inhibition, after an ischemic block on the thigh to reduce feedback from large proprioceptive and cutaneous afferents, and after tizanidine was administered to selectively depress group II feedback. Although not conclusive, these observations suggest that the large decrease in muscle activity was primarily due to a reduction of activity in group Ib afferents, which is caused by a reduction in force within the ankle extensor muscles (see Grey et al. 2004).

The contribution of group II afferents, arising from length-sensitive secondary muscle-spindle endings, to ongoing activity in ankle extensors is not yet clear. In the cat, a few experimental results suggest that group II feedback is not of primary importance. During fictive locomotion in spinal cats, Gossard et al. (1994) found that increasing the strength of electrical stimulation to an ankle extensor nerve increased the size of EPSPs in extensor motoneurons as group I afferents were recruited, but higher stimulus strengths that recruited group II afferents produced no additional increase in EPSPs. Similarly, Perreault et al. (1995) failed to observe any effect of electrically stimulating extensor group II afferents on the magnitude of extensor activity during fictive locomotion in decerebrate cats, a result we have confirmed in our recent work on decerebrate walking cats (Donelan and Pearson 2004). Corresponding to these negative findings are the observations from ensemble averaging of triceps group II activity, which demonstrated relatively low and constant activity, as well as poor covariance with ongoing muscle activity, during walking in the cat (Prochazka and Gorassini 1998). Thus, in the cat, there are currently no indications that feedback from extensor group II afferents has a significant influence on extensor-burst activity.

This is in contrast with recent conclusions, drawn from a series of experiments in walking humans, that suggest that group II afferents may be an important source of afferent input to ankle extensor motoneurons during stance (Grey et al. 2001, 2002). The relevant findings of these experiments are that the medium-latency reflex evoked by imposed ankle flexion is not influenced by the ischemic blocking group Ia afferents, or by altering the loading conditions, but they are reduced by ingested tizanidine, a drug that selectively suppresses transmission in group II pathways. On the other hand, the large reduction in soleus activity evoked by imposed ankle extension (Fig. 1) is not influenced by tizanidine or the ischemic blocking of group Ia afferents (Grey et al. 2001). These observations are more consistent with a contribution of group Ib afferents to ongoing soleus activity. Thus, it appears that group II afferents contribute to soleus activation when the ankle extensors are rapidly stretched during walking, but it remains uncertain whether these afferents provide substantial excitatory input to soleus motoneurons during the normal stance phase.

Although the main focus of recent research has been on the role of large-muscle afferents in regulating extensor activity, contributions from other afferent pathways have not been excluded. Electrical stimulation of cutaneous afferents from the foot can increase ankle extensor activity in intact walking cats (Duysens and Stein 1978) and in humans (Duysens et al. 1996), but whether these afferents actually have a significant influence on extensor activity during normal walking is unknown. The fact that the removal of all cutaneous signals from the cat's paws has virtually no effect on ankle extensor activity (Bouyer and Rossignol 2003) suggests that the role of cutaneous signals in regulating ongoing ankle extensor activity is minor. However, it is quite possible that increased activity in other afferent pathways, such as increased feedback from Golgi tendon organs in the extensor muscle, compensates for the loss of cutaneous feedback in these instances.

Conclusions

The primary conclusion from this review is that numerous studies over the past decade on the neurobiology of walking in humans and cats have unambiguously demonstrated that sensory feedback contributes significantly to the activation of extensor muscles during the stance phase. The quantitative value of this contribution has not been established with certainty, but for ankle extensor muscles it appears to be within the range of 30 to 60%. In other words, sensory signals from leg receptors contribute approximately half of the suprathreshold excitatory input to ankle extensor motoneurons. The contribution relative to the absolute value of central drive to the motoneurons must be lower, because a fraction of the excitatory input (from whatever source) is used to depolarize motoneurons to threshold. Regardless of the exact values, it is clear that sensory receptors provide a drive to the ankle extensor motoneurons during the stance phase, and therefore have the capacity to regulate the magnitude of activity in response to the biomechanical parameters monitored by the receptors.

What parameters are monitored? Not all have been identified, but 1 important parameter in the cat appears to be the force in the ankle extensors signalled by feedback from the Golgi tendon organs (McCrea 2001; Lam and Pearson 2002). Similarly, indirect evidence from muscle-unloading experiments indicates that force feedback is involved in the regulation of ankle extensor activity in humans (see previous

sections and Grey et al. 2004). Another parameter in humans may be the length of the ankle extensor muscles signalled by feedback from secondary muscle spindles (Grey et al. 2001, 2002). At present there is no evidence that feedback from secondary spindle endings has any influence on ankle extensor activity in walking cats. Differences in the relative importance of secondary muscle spindles may constitute a genuine difference in the walking systems of humans and cats, and could possibly be related to different kinematics of ankle movement. On a horizontal surface, the ankle extensor muscles of cats are briefly lengthened at the beginning of stance, and then shorten continuously for the remainder of the stance phase. This pattern of length change results in very little increase in secondary spindle activity at the beginning of stance (Prochazka and Gorassini 1998). In humans, however, there is lengthening of the fascicules in ankle extensors during most of the stance phase (Fukunaga et al. 2001), yielding a condition appropriate for the activation of secondary spindle endings and for a potential source of reinforcing activity in ankle extensors.

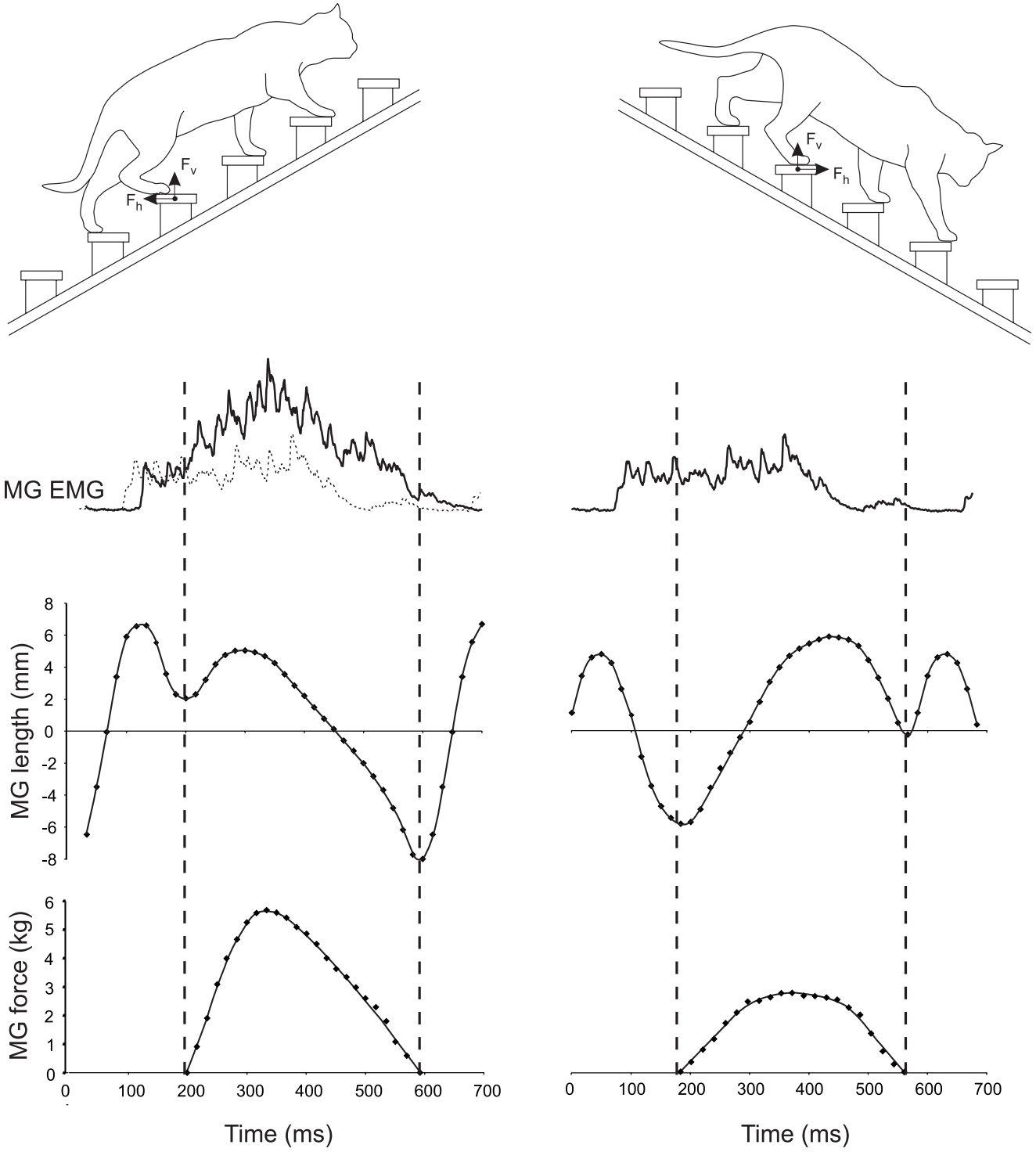
Two important issues arise from the finding that sensory feedback contributes to extensor activity during walking, neither of which has received any serious attention to date. The first is the extent to which differences in the magnitude of extensor activity that occur in different behavioural situations can be attributed to modifications in sensory signals contributing to motoneuronal activation, and the second is whether the enhancement of extensor activity is determined primarily by feedback for a specific group of receptors or from numerous groups of receptors distributed throughout the leg. A good example of the first of these issues is illustrated in Fig. 3. When cats walk up and down a series of steps, there are significant differences in the magnitude of burst activity in the MG muscle, which are appropriate to each condition (high when walking up and low when walking down). Estimates of the force and length of the MG muscle from ground-reaction forces and kinematics, respectively, show that these parameters are quite different in the 2 situations. Because force, length, and velocity signals can contribute to the activation of MG motoneurons, one obvious question is whether the difference in MG activation when walking up and down stairs can be attributed simply to differences in the pattern of feedback signals from the MG muscle. If not, to what extent do the differences reflect changes in central drive to the motoneurons? In addition to modifications in central drive and the pattern of activation of different groups of receptors, another possibility is that alteration in the gains of transmission in spinal pathways that mediate the reinforcing action of sensory feedback onto MG motoneurons may be involved. Currently, we simple do not know which of these mechanisms, either by itself or in combination with others, is responsible for modulating the magnitude of MG activity. Resolving this issue, even for this relatively simple case, is not easy. Obviously, more experimental data would be helpful, such as a comparison of the patterns of activity in different groups of afferents between the 2 situations. But with current technology, many important parameters cannot be determined experimentally in intact walking animals; the strength of transmission in spinal pathways is one of the most obvious.

An alternative to the empirical approach favoured by most investigators is to use a theoretical approach to gain insight into the contribution of afferent feedback to ongoing muscle activity. Using mathematical models and computer simulations, it is possible to address questions that are difficult or impossible to address empirically. As an example, consider a question based on the topic of this review: In regulating ongoing muscle activity during walking, is it beneficial to prioritize feedback from a particular afferent pathway? Useful models for addressing this question range from very simple models of system components to necessarily complex models of the whole system. For example, Prochazka et al. (1997) approached this question using a simple model of reflex pathways that included idealized proprioceptors, motoneurons, and muscles (they concluded that force feedback is an effective mechanism for load compensation). An example of a slightly more realistic model concerned with the same question is provided by the work of Geyer et al. (2003). They used a forward solution of a 2-link biomechanical model to study the role of different afferent pathways in stabilizing hopping (they too concluded that force feedback is an effective mechanism). As complexity is added, models will likely involve simulations of 3 dimensional linked-segment whole-body models that incorporate existing information about the mechanical properties of the legs and body, the properties of muscles and sensory receptors, and the organization of reflex pathways in the spinal cord.

The complexity of the required model and modeling approach should depend on the question being addressed. For example, it may be possible to gain insight into the contribution of different afferent pathways using a model with a single muscle, whereas understanding heteronymous feedback may require a rigid-body model with multiple muscles. One drawback to studying more realistic models is that they are often so complex that it is difficult and time-consuming to explore the sensitivity of predictions to parameters and initial conditions. We favour a 2-pronged modeling approach that combines simple models with more realistic models (Full and Koditschek 1999). The utility of simple models is that they can be designed to capture the basic behaviour of interest with minimal complexity. This allows one to determine the robustness of predictions within a very large parameter space. More realistic models that more accurately reflect the underlying physiology can be constructed using insights gained from the simple models. This 2-pronged modeling approach is analogous to the empirical approach of studying both reduced preparations and intact animals.

Models typically yield many solutions to a given question. For example, a neuromechanical model of the cat hind limb will likely reproduce the kinematics of walking with many different weightings of afferent-feedback pathways. To choose among solutions, it is generally necessary to optimize some objective function. For example, if stability is to be maximized, then a particular feedback pathway may be of primary importance, but if economy is to be maximized, then a different pathway may be emphasized. Like the gain of feedback pathways, the results will likely be phase- and task-dependent. This should be viewed not only as a complication but also as a chance to develop alternative hypotheses to test empirically. The result may be that, as we learn more about the role of afferent pathways, we may also come to a

Fig. 3. Modulation of the magnitude of burst activity in the MG muscle when cats walk up and down a series of steps. The force (bottom graphs) and length (middle graphs) of the MG muscle in the two conditions were calculated from ground-reaction forces measured for one step, and from the kinematics of movements around the knee and ankle joints for the same step, respectively. The rectified/filtered EMG records (top traces) and the calculated force and length values are plotted for a single step, as the animal walked up (left) and down (right) the steps. The length of the muscle-tendon unit was measured relative to the length when the ankle and knee were at 90 degrees. Muscle lengthening and shortening is positive and negative, respectively. The two vertical dotted lines in each set of records indicate the beginning and end of the stance phase. The EMG record for walking down the steps has been superimposed on the EMG record for walking up the steps in the left set of records. Note the larger magnitude on the EMG when the animal walks up the steps, and the absence of any obvious relationship between muscle length and EMG magnitude.



greater understanding of the variables that are optimized under different walking conditions.

We believe that the most promising approach for gaining insight into the mechanisms underlying the modulation of motoneuronal activity in different behavioural situations is to combine empirical experiments with a more theoretical approach. Empiricism is paramount because it grounds our knowledge in biological reality. The strength of modeling lies in its deductive and inductive power. The union of these 2 approaches helps form and test quantitative hypotheses and then generalize the empirical results into a conceptual framework.

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