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Context-Dependent Modulation of Cutaneous Reflexes During Walking

by

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Abstract

Cutaneous reflexes have previously been shown to undergo task- and phase-dependent modulation during walking. The pattern of modulation of these reflexes suggests they may serve a functional role in assisting in the maintenance of balance. Therefore, cutaneous reflexes should also modulate in an environment of altered stability. This thesis focused on the context-dependent modulation of cutaneous reflexes during walking.

Subjects walked on a motorized treadmill, while cutaneous reflexes in the legs and arms were elicited at certain points in the step cycle. These reflexes were evoked by electrically stimulating the superficial peroneal (SP; innervates the dorsum of the foot), distal tibial (plantar surface of the heel), sural (lateral margin of heel), superficial radial (lateral dorsum of the hand and fingers), and median (palmar surface of the hand and fingers) nerves. Mechanical perturbations were delivered to either the torso or the foot dorsum during certain walking conditions to create an environment in which stability was unpredictable.

In the lower limbs, cutaneous reflexes evoked from the foot were greater in amplitude during conditions with a higher level of postural threat, and suppressed when walking in the most stable condition. During walking in an environment where context-specific perturbations were delivered to the dorsum of the foot, reflexes evoked with SP nerve stimulation normally associated with the stumble corrective response were altered in a functionally relevant manner.

In the upper limbs, interlimb cutaneous reflexes evoked from the foot were shown to modulate according to the level of stability and arm task during walking.

With the arms crossed, reflex amplitudes were greatest during conditions with a higher threat to stability. With the arms free, reflex amplitudes were similar between conditions. Engaging the hands in balance control resulted in facilitated cutaneous reflexes elicited from the hands during walking.

Together, the results suggest that cutaneous reflexes in the lower and upper limbs are modulated in a context-dependent manner. Reflex changes were not due to a generalized change in excitability, as they were observed in select muscles at certain points of the step cycle. These findings suggest a functional role for context-dependent modulation of cutaneous reflexes during locomotion.

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Chapter 1 - General Introduction

1.1 Introduction

Movements require online adaptations to meet the demands of the environment, as well as to correct for unexpected disturbances that may be encountered. Ongoing feedback regarding our movements is provided by sensory information, which is attained by the visual and vestibular systems, as well as receptors in our joints, muscles, and skin. This afferent feedback informs the nervous system of changes in limb position and muscle length, as well as the environment in which we move. During the early 20th century, Sherrington (1906) discussed the importance of proprioceptive and cutaneous feedback in regulating movements. In these influential studies, he suggested that simple reflexes were the building blocks on which complex movements are produced. Essentially, the stereotyped reflex effects observed by the activation of cutaneous and muscle afferents (e.g. knee extension in response to patellar tendon tap) could be combined to produce more intricate movements such as locomotion. However, Graham Brown (1911) later showed that rhythmic locomotor patterns could be elicited in the absence of descending or afferent input to the spinal cord. Despite this finding, the concept of stereotyped reflex responses persisted for many years until it was later rediscovered that movements such as locomotion, albeit at a basic level, can be produced in the absence of afferent feedback in cats (Wetzel et al. 1976; Wetzel and Stuart 1976; Grillner and Zangger 1984; Giuliani and Smith 1987). Observations such as these have therefore led to the suggestion that the rhythmic pattern of locomotion is generated by spinal networks of neurons residing in the spinal cord (central pattern generators (CPG)).

Afferent feedback plays an important role in modifying the motor output from the CPG to produce an efficient locomotor pattern. During walking, adjustments are frequently required in response to disturbances such as uneven terrain or obstacles. Given the dynamic nature of locomotion, in which the limbs are constantly changing their biomechanical configuration, immediate afferent feedback is essential in providing real-time information to the CPG. In turn, this allows the CPG to generate a modifiable locomotor output that accounts for the current surrounding environment. In particular, information provided by joint and muscle proprioceptors and exteroceptors in the skin have been shown to regulate the timing and motor activity of stepping, as well as adjust the step cycle to unexpected perturbations.

Proprioceptive afferents have been shown to regulate the stepping pattern during locomotion. This can be observed in decerebrate and spinal cats, which are able to adapt their stepping in accordance to the speed of the treadmill on which they walk (Severin et al. 1967; Grillner and Rossignol 1978; Forssberg et al. 1980a; Forssberg et al. 1980b; Barbeau and Rossignol 1987). Studies have also shown that the fictive locomotor rhythm generated in decerebrate and spinalized cats can be entrained by movements of the hip joint (Andersson and Grillner 1983; Kriellaars et al. 1994). In chronic spinal cats, Grillner and Rossignol (1978) showed that flexion at the hip eliminated stepping movements in the same hindlimb during treadmill walking. Electrical stimulation of ankle extensor group I afferents has been shown to delay the onset of flexor burst locomotor activity and lengthen the duration of extensor burst activity, as well as reset the locomotor pattern (Conway et al. 1987; Pearson et al. 1992; Guertin et al. 1995; Whelan et al. 1995). Furthermore, flexor muscle afferents have been shown to shorten extensor burst duration and promote an earlier onset of flexor burst activity in the hindlimbs of decerebrate cats (Hiebert et al. 1996).

Proprioceptors have also been shown to contribute to the generation of extensor burst activity during the stance phase. Severin (1970) showed that inactivation of fusimotor drive to extensor muscle spindles reduced the level of extensor muscle activity by 50%. In addition, when cat hindlimb extensor muscles are unloaded during walking, thereby reducing afferent feedback, a decrease in extensor muscle activity is observed (Gorassini et al. 1994; Hiebert and Pearson 1999; Donelan and Pearson 2004). A similar result has also been observed in humans during locomotion (Harkema et al. 1997; Dietz and Colombo 1998; Dietz and Duysens 2000; Sinkjaer et al. 2000). As well, electrical stimulation of extensor group I afferents during fictive locomotion in decerebrate cats has been shown to increase the amplitude of extensor burst activity during extension (Guertin et al. 1995). Proprioceptors thus play an important role in reinforcing the ongoing motor activity during the step cycle.

Proprioceptive information is also important for producing complex corrections to unexpected perturbations during walking. Dietz et al. (1987) studied corrective responses to treadmill perturbations during human walking. They reported stretch reflexes mediated the observed compensatory responses in the ankle extensor muscle. It was suggested that group II muscle afferents were primarily responsible for these responses, since it was previously shown that ischemic nerve block of group I afferents did not alter these compensatory responses (Berger et al. 1984). Similarly, Sinkjaer et al. (2000) showed that a decrease in soleus activity to unloading of ankle extensor muscles during stance was not affected by an ischemic block of the leg. This block essentially removed Ia afferent feedback, as the short-latency stretch reflex was abolished. The results from these studies indicate an important role for group II afferents in generating corrective responses during walking.

As previously mentioned, exteroceptors located in the skin can also modify the motor activity during locomotion. Work done on spinalized (Forssberg et al. 1975; Forssberg et al. 1976) and decerebrate (Duysens and Pearson 1976) walking cats showed that cutaneous stimulation of the hindlimb during the flexion phase prolonged the duration of flexor burst activity. Interestingly, the same stimulation delivered during the extension phase resulted in an enhancement of ongoing extensor activity. A similar result was observed when the sural and tibial nerves, innervating different portions of the plantar surface of the distal hindlimb, were electrically stimulated during walking in decerebrate cats (Duysens 1977). It is therefore apparent that similar to proprioceptors, exteroceptors in the skin are also capable of modifying locomotor activity.

The predominant role for cutaneous information from the foot is to allow for the correct placement of the foot during the normal step cycle. Recent studies involving the removal of cutaneous afferents from the hindpaws has extended our knowledge regarding the importance of cutaneous afferents during locomotion (Bouyer and Rossignol 2003a; Bouyer and Rossignol 2003b). Bilateral removal of cutaneous input from the hindpaws in intact cats was shown to not adversely affect level treadmill walking (Bouyer and Rossignol 2003a). However, major deficits were observed when cats performed a precision task such as ladder walking. After cutaneous denervation of the hindpaw, cats were unable to properly place the hindpaws on the rungs of the ladder. The authors suggested that cutaneous information may be more relevant during more demanding tasks, in that it provides sensory cues to adjust locomotion. After spinalization, these cats were no longer able to correctly place the paw during level treadmill walking (Bouyer and Rossignol 2003b). The main deficit was a dragging of the paw on the treadmill during the onset of swing phase. Cats that were only spinalized and not deafferented were able to recover the ability to correctly place the foot during stance. Therefore, cutaneous input is important in the correct placement of the foot during locomotion.

In addition, cutaneous information is important for corrective adaptive responses to perturbations encountered during locomotion. Studies performed on spinal cats have shown that either mechanical perturbations or electrical stimulation delivered to the dorsum of the hindpaw during the swing phase of treadmill locomotion can evoke a coordinated reflex response (Forssberg et al. 1975; Forssberg et al. 1977). This response consisted of excitation in flexors and inhibition of extensors in the hindlimb, which led to flexion of the hindpaw and knee. In turn, this allowed the swing limb to step over an encountered perturbation and maintain stable locomotion. This functional "stumbling corrective response" has also been observed in intact cats (Forssberg 1979). Furthermore, when the same stimulation was applied during stance, excitatory cutaneous reflex responses were observed in extensor muscles, which would serve to provide additional weight-bearing support in the stance limb. Thus, cutaneous responses are dependent on the phase of the step cycle, which is useful given the ever-changing stability requirements during the locomotor cycle. Work from the laboratory of Prochazka and colleagues (Prochazka et al. 1978; Wand et al. 1980) reported similar results in intact walking cats. However, when the dorsum of the hindpaw was anesthetized, reflex responses normally observed in muscles involved in the "stumbling-corrective response" were abolished. This suggested that the responses originated from cutaneous afferents in the hindpaw. These findings have led to the suggestion that cutaneous reflexes may play a functional role in assisting in the maintenance of balance during locomotion (Zehr and Stein 1999).

The focus of this General Introduction will be on cutaneous reflexes and their suggested functional role in contributing to corrective responses. An overview of cutaneous reflexes will be presented first, followed by a discussion on the importance of cutaneous information in reactive balance control. This will lead to the suggested role of cutaneous reflexes in coordinating whole-body corrective responses, thereby creating the foundation of this thesis. Throughout this chapter, a strong emphasis will be placed on studies performed on humans. However, animal work will be raised where appropriate.

1.2 Cutaneous Reflexes

Cutaneous reflexes can be evoked in muscles by electrically stimulating nerves which contain Aβ, Aδ, and C axons of sensory mechanoreceptors located in the skin (Zehr and Stein 1999). In humans, this is done by delivering a train of electrical pulses to surface electrodes that are placed over the predicted path of the cutaneous nerve. The stimulus intensity is commonly set such that a strong perception of non-noxious paresthesia radiates throughout the innervation area of the stimulated nerve. Electrical stimulation of cutaneous nerves is primarily performed to investigate the influence of cutaneous afferents on muscle activity during static and dynamic tasks such as locomotion. Most studies that investigate cutaneous reflexes utilize electrical, as opposed to mechanical stimulation, due to the inherent difficulty in delivering reproducible mechanical stimuli at different phases of the step cycle.

The pathway for cutaneous reflexes is complex in nature. At the spinal level, cutaneous afferents synapse onto an undetermined number of interneurons, which in turn synapse onto their target motoneurones (Baldissera et al. 1981; Zehr 2006). In addition, the existence of parallel inhibitory and excitatory pathways has been suggested from cutaneous afferents to motoneurones (De Serres et al. 1995). Furthermore, transcortical pathways have been suggested to contribute to cutaneous reflexes, by acting along the chain of interneurons involved in the reflex pathway (Pijnappels et al. 1998; Christensen et al. 1999). As a result of the number of potential sites along the reflex pathway by which responses can be modulated, cutaneous reflexes are more variable compared to muscle afferent reflexes (i.e. H-reflex). For instance, cutaneous reflex responses are multiphasic, with an early latency (approximately < 70 ms), middle latency (~ 70-120 ms), and late latency components (> 120 ms) occurring after the delivery of electrical stimulation (Brooke et al. 1997). It is also common to observe differences across different latency components within a reflex response, such as an early latency inhibition followed by middle latency excitation. Adding to the complexity in reflex responses is the variation in stimulus intensity, as well as in responses between muscles, individuals, and studies.

Cutaneous reflexes have usually been studied in the muscles of the lower (Yang and Stein 1990; Burke et al. 1991; Aniss et al. 1992; Duysens et al. 1992; Duysens et al. 1993; Tax et al. 1995; Duysens et al. 1996; Van Wezel et al. 1997; Zehr et al. 1997; Zehr et al. 1998a; Zehr et al. 1998b) or upper limbs (Caccia et al. 1973; Jenner and Stephens 1982; Chen and Ashby 1993; Zehr and Chua 2000; Zehr and Kido 2001; Zehr and Haridas 2003), although they have also been reported in the muscles of the trunk and back (Alexander and Harrison 2003). These reflexes have been observed in the muscles of the legs with electrical stimulation of cutaneous nerves innervating the foot, and in the muscles of the arms with stimulation of cutaneous nerves innervating the hand. In addition, interlimb cutaneous reflexes, which are reflexes observed in muscles that are not located in the same limb as the stimulated cutaneous nerve, have also been reported (Haridas and Zehr, 2003).

Cutaneous reflexes are also able to change, or modulate both in amplitude and sign according to the task and phase of the movement. These properties of cutaneous reflexes are termed task- and phase-dependency respectively, and have been suggested to serve a functional role by assisting to adapt movements to the characteristics of the surrounding environment (Stein 1991). The following section of the General Introduction will first describe local cutaneous reflexes during static tasks, as well as their task- and phase-dependent modulation during rhythmic movements such as walking. Next, interlimb cutaneous reflexes will be discussed with respect to their task- and phase-dependent modulation, as well as their suggested importance in coordinating corrective responses.

1.2.1 'Local' effects of cutaneous nerve stimulation

As stated, the majority of studies on cutaneous reflexes have focused on the muscles of the leg with stimulation of cutaneous nerves innervating the foot. One such nerve that has been studied extensively is the largely cutaneous sural nerve. This nerve is normally stimulated near the lateral malleolus of the ankle, and it innervates the skin over the lateral aspect of the foot and heel. Stimulation of this nerve has been shown to evoke cutaneous reflex responses in the muscles of the ipsilateral (same side as nerve stimulation) leg. Kukulka (1994) reported complex reflex waveforms, with periods of facilitation and inhibition in triceps surae motor units at latencies between 30 to 120 ms (post-stimulus) while subjects lay prone. An early onset inhibition (~ 40 ms) and middle latency facilitation (~ 72 ms) of triceps surae motor unit firing were the most common responses observed across subjects. When laying supine, Aniss et al. (1992) reported an early latency inhibition in tibialis anterior and soleus (~ 50 ms), while facilitation occurred at a similar latency in peroneus longus, medial gastrocnemius, and lateral gastrocnemius. The authors also reported the responses lasting up to 200 ms, and concluded that sensory afferents in the foot have a polysynaptic connection with motor neurons innervating the muscles of the lower leg. Thus, local cutaneous reflex responses were similar in the muscles of the leg while lying in either prone or supine positions.

Burke et al. (1991) investigated cutaneous reflexes in leg muscles evoked with sural nerve stimulation while subjects maintained various postures. Inhibitory cutaneous reflex responses were observed within 100 ms in tibialis anterior, soleus, biceps femoris, and vastus lateralis. In addition, cutaneous reflexes in tibialis anterior were observed to change according to the task being performed. The early latency component of the reflex response was more evident as the balance demands of the task increased from being seated, to standing on a tilted platform, to standing on an unstable platform. This task-dependent modulation of cutaneous reflexes could not be explained by differences in ongoing muscle activity. The authors concluded that cutaneous reflexes in various muscles as well as within a single muscle are dependent upon the task being performed.

This task-dependent modulation is a trait commonly observed with cutaneous reflexes. In addition to sural nerve reflexes modulating according to various static postures, these cutaneous reflexes have also been observed to change between static and dynamic tasks. Komiyama et al. (2000) compared sural nerve reflexes between standing and walking, and reflexes were reported to be mainly suppressive and proportional to ongoing EMG activity during standing. This was in contrast to mainly facilitatory reflexes during walking, which were not correlated with background EMG. Further to this, Duysens et al. (1993) reported larger excitatory middle latency reflexes (latency of ~ 70-90 ms) in tibialis anterior and biceps femoris during treadmill running as compared to standing. It was suggested that the increase in facilitatory responses during running indicate the importance of cutaneous information during locomotion.

In addition to varying across different tasks, cutaneous reflex responses in the leg evoked from sural nerve stimulation have also been shown to modulate within a given task, such as during walking (Duysens et al. 1990; Duysens et al. 1992; Duysens et al. 1996; Zehr et al. 1998b), running (Duysens et al. 1993; Tax et al. 1995), and cycling (Mileva et al. 2004). Specifically, cutaneous reflex amplitudes in the muscles of the leg modulate both in size and sign according to the phase of the movement in which they are evoked. One of the first studies that reported phase-modulation of cutaneous reflexes during human walking was conducted by Duysens et al. (1990). Sural nerve stimulation evoked large reflex responses in tibialis anterior that were facilitatory during midswing. However, the same stimulation delivered at midstance elicited minimal reflex responses. It was also reported that the modulation observed in cutaneous reflex amplitudes was not correlated with the level of ongoing EMG activity. This phase-dependent modulation of cutaneous reflexes in humans was consistent with previous observations in the cat, where large reflex responses are evident in muscles with a low level of EMG activity during phases of the step cycle (Forssberg 1979; Duysens and Loeb 1980).

Since there was no correlation between cutaneous reflex amplitude and background EMG activity, Duysens et al. (1990) suggested a premotoneuronal gating for the modulation of cutaneous pathways in the leg, via interaction of afferent input and a CPG during walking. Proprioceptive information was considered unlikely to contribute to the modulation of cutaneous reflexes, as phase-modulation of these reflexes was also reported in fictive locomotion preparations (Andersson et al. 1978; Schomburg and Behrends 1978; LaBella et al. 1992). Further support for cutaneous reflex modulation being independent of proprioceptive feedback was given by Brooke et al. (1999), who examined the possibility of somatosensory receptors influencing the modulation of cutaneous reflexes in humans during movement. Reflexes were elicited from the foot during passive cycling movement of the leg. Through various experiments, they concluded that the activation of muscle, tendon, and joint receptors via passive movement of the leg did not significantly alter cutaneous reflexes. Thus, phase-modulation of cutaneous reflexes cannot simply be due to the activation of movement-related sensory receptors. This was in direct contrast to observed passive movement-related modulation of the monosynaptic H-reflex (Brooke et al. 1995; Misiaszek et al. 1995), which is mainly due to phasic, movement-activated discharge of proprioceptors (Cheng et al. 1995; Misiaszek et al. 1995).

Therefore, phase-dependent modulation of cutaneous reflexes is probably due to central mechanisms, such as networks of oscillatory interneurons.

As mentioned, phase-dependent modulation of cutaneous reflexes can also involve a change in the sign of the reflex during locomotion. With cutaneous nerve stimulation at the foot, middle latency reflex responses in tibialis anterior were observed to change from excitatory during swing phase to inhibitory during the transition from swing to stance (Duysens et al. 1990; Yang and Stein 1990; Duysens et al. 1992). Virtually no reflex response was observed in the same muscle during the stance phase. Phase-dependent cutaneous reflex modulation and reflex reversals were also observed in soleus and rectus femoris. Cutaneous reflex reversals during locomotion were originally reported in spinal cats (Forssberg et al. 1975), and have been attributed to parallel inhibitory and excitatory pathways to motoneurones (Duysens 1977; Andersson et al. 1978). Cutaneous reflex reversals observed in tibialis anterior during human locomotion may correspondingly be due to a shift in the weighting of parallel excitatory and inhibitory pathways from cutaneous afferents to the motor units of the muscle (De Serres et al. 1995).

Cutaneous reflexes have also been reported in the muscles of the leg with electrical stimulation of other cutaneous nerves innervating different portions of the foot during walking (Van Wezel et al. 1997; Zehr et al. 1997) and cycling (Brown and Kukulka 1993). Furthermore, these reflexes also exhibit properties observed with sural nerve stimulation. For instance, phase-dependent modulation of cutaneous reflexes elicited with distal tibial and superficial peroneal nerve stimulation has been reported during walking (Yang and Stein 1990; Zehr et al. 1997). In addition, reflexes elicited from stimulation of cutaneous nerves at the foot show similar features as well as nerve-specific responses. In tibialis anterior, inhibitory middle latency cutaneous reflexes are observed near the end of swing phase irrespective of the stimulated nerve (Duysens et al. 1990; Yang and Stein 1990; De Serres et al. 1995; Van Wezel et al. 1997; Zehr et al. 1997; Zehr et al. 1998b). Conversely at end stance, sural nerve responses were observed to be excitatory, while reflex responses elicited with superficial peroneal and distal tibial nerve stimulation were essentially absent. The changes in cutaneous reflex responses during locomotion may reflect a functional modulation, possibly serving to assist in appropriate compensatory responses to preserve stability (Zehr and Stein 1999).

The features of cutaneous reflex responses observed in the muscles of the leg with stimulation at the foot have also been reported in the muscles of the arm with stimulation of cutaneous nerves innervating the hand. Phase-dependent modulation of local cutaneous reflexes in the muscles of the arm was observed during arm cycling (Zehr and Chua 2000; Zehr and Kido 2001) and the natural arm swing of walking (Zehr and Haridas 2003). In addition, these studies reported cutaneous reflexes in most muscles of the arm were scaled to the level of background EMG activity during static contraction but not during movement (task-dependency), similar to observations in lower limb muscles during leg cycling (Zehr et al. 2001b) and walking (Duysens et al. 1990). Furthermore, nerve specificity was also observed with local cutaneous reflex responses in the muscles of the upper limbs (Zehr and Kido 2001), similar to previous observations in the lower limb (Van Wezel et al. 1997). Therefore, cutaneous reflexes in the upper limbs during movements such as arm cycling and walking display similar characteristics to that observed in the lower limbs during leg cycling and walking.

To summarize, cutaneous reflexes have been observed in the muscles of the lower limb with electrical stimulation of nerves at the foot, and in upper limb muscles with stimulation of cutaneous nerves innervating the hand. These reflexes can be modulated according to the task being performed. During tasks in which the limbs move in a rhythmic manner, cutaneous reflexes undergo modulation according to the different phases of the movement. This may serve a functional role, as phase-modulation ensures evoked reflex responses are appropriate for the different phases of a movement (Zehr and Duysens 2004). Given that task- and phase-modulation of cutaneous reflexes are observed in the muscles of the leg and arm, cutaneous reflexes may conceivably coordinate movements between the arms and legs. That is, electrical stimulation of cutaneous nerves may also evoke reflex responses in muscles that are remote from the site of stimulation. These interlimb reflexes, along with their properties, are the focus of the next section.

1.2.2 Interlimb cutaneous reflexes

In humans, cutaneous reflexes have been observed in the muscles of the contralateral leg with stimulation at the foot during various static tasks (Burke et al. 1991). The amplitude of these crossed[*] responses were on average 25-50% lower in amplitude compared to ipsilateral cutaneous reflexes. Interlimb cutaneous reflexes have also been observed in the muscles of the arm by electrical stimulation at the foot (Kearney and Chan 1979). They were observed in the proximal arm muscles at a latency of ~ 90 ms, which was analogous to reflexes found in muscles of the ipsilateral leg. The authors suggested the similar latencies in reflex responses in the upper and lower limb muscles may be due to propriospinal pathways mediating the responses from lower to higher segments of the spinal cord.

Interlimb cutaneous reflexes have also been observed in the muscles of the legs with stimulation at the arm. Using ulnar, median, and superficial radial nerve stimulation, Meinck and Piesiur-Strehlow (1981) showed interlimb cutaneous reflex responses in the lower limbs, consisting of an initial early latency inhibition (~ 60 ms) of ongoing tonic EMG activity followed by a middle latency facilitation (~ 80 ms). It was suggested that the responses observed in the muscles of the legs are mediated by propriospinal pathways within the spinal cord, with input originating from afferents in the arm. Similarly, Sarica and Ertekin (1985) verified the existence of reflex pathways from the upper to lower limbs by reporting descending lumbosacral cord potentials in response to median nerve stimulation, which led them to conclude that these responses originated from a fast-conducting descending propriospinal pathway from the stimulated arm,

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[*] *For clarity in this chapter, the term 'crossed' will from now refer to responses between <u>either</u> the lower or upper limbs. This differentiates these responses from those observed between the arms and legs, which will be termed 'interlimb'.*

similar to that proposed by Kearney and Chan (1979) for responses evoked at the foot.

A more comprehensive study of interlimb cutaneous reflexes was performed by Zehr et al. (2001a), who studied these responses in all limbs from stimulating cutaneous nerves at the foot and hand during static contractions. Electrical stimulation of the superficial peroneal and superficial radial nerves evoked crossed and interlimb reflexes in muscles of both the ipsilateral and contralateral arms and legs, which suggested the existence of strong cutaneous reflex connections between the cervical and lumbar segments of the spinal cord.

The existence of crossed and interlimb cutaneous reflexes has led to the suggestion that these responses could serve as a means by which coordination between the limbs can be achieved during posture and locomotion (Sarica and Ertekin 1985; Zehr et al. 2001a). Coordination between all of the limbs is important during movements such as walking, as the coordination of the arms and legs must be regulated to achieve efficient, rhythmic locomotion. As well, proper coordination between the limbs allows for dynamic stability to be preserved in response to encountering an unexpected perturbation. However, for crossed and interlimb cutaneous reflexes to serve a functional role during movement, they should display both task- and phase-dependent modulation similar to local cutaneous reflex responses (Zehr and Stein 1999).

Crossed cutaneous reflex responses between the lower limbs have been observed to undergo modulation during locomotion. Stimulation of cutaneous nerves innervating the foot evoked middle latency responses in the contralateral leg during locomotion, which shared several similarities to cutaneous reflexes in the ipsilateral leg (Tax et al. 1995; Van Wezel et al. 1997; Haridas and Zehr 2003). First, crossed reflexes in the muscles of the contralateral leg occurred at a similar latency (~ 80 ms), and exhibited phase-modulation across the step cycle (Tax et al. 1995). In addition, a reversal in the reflex sign was noted in contralateral tibialis anterior, in which suppression occurred at contralateral end swing. This suppression was similar to that observed in ipsilateral tibialis anterior at ipsilateral end swing (Duysens et al. 1990), which suggested that modulation of cutaneous reflexes in the contralateral limb are dependent on the phase of the corresponding leg, and not that of the stimulated leg (Duysens and Tax 1994). Crossed cutaneous reflexes were also not related to the ongoing level of muscle activity, which suggests a premotoneuronal source of modulation. Responses in the contralateral leg were also reported to be task-dependent, as crossed cutaneous reflexes were observed to be correlated to background EMG activity during static contractions, and not during locomotion (Haridas and Zehr 2003). Furthermore, as observed in the ipsilateral leg, crossed cutaneous reflexes were shown to be specific to the nerve that was stimulated (Van Wezel et al. 1997). Therefore, crossed cutaneous reflexes in the lower limbs exhibit task- and phase-dependency, which is similar to local cutaneous reflexes observed in the ipsilateral leg.

Crossed cutaneous reflex responses have also been observed in the upper limbs, and they share similarities to crossed responses occurring in the lower limbs during locomotion. During arm cycling and locomotion, coordinated patterns of phase-dependent reflex modulation were observed between ipsilateral and contralateral proximal arm muscles with electrical stimulation of cutaneous nerves innervating the hand (Zehr and Kido 2001; Zehr and Haridas 2003). Responses were also task-dependent, as crossed cutaneous reflexes evoked during positioned-matched static contraction were always excitatory as compared to larger amplitude or inhibitory responses observed during movement. Finally, it has also been recently reported that cutaneous reflex phase-modulation is mainly dependent on the movement of the arm in which the reflex is recorded (Carroll et al. 2005), similar to observations in the lower limbs (Duysens and Tax 1994).

Similar to responses observed either across the lower *or* upper limbs (i.e. crossed), cutaneous reflexes have also been reported between the legs *and* arms (i.e. interlimb). Haridas and Zehr (2003) reported interlimb cutaneous reflexes that were modulated to the phase of the step cycle. Stimulation of the superficial peroneal nerve at the foot evoked inhibitory reflexes during stance and essentially no reflex responses during swing in ipsilateral posterior deltoid. The corresponding muscle on the contralateral side displayed excitatory reflexes during swing. With superficial radial nerve stimulation at the wrist, interlimb cutaneous reflexes in both the ipsilateral and contralateral tibialis anterior were inhibited during ipsilateral late swing and the contralateral stance-swing transition respectively, similar to reflexes evoked with superficial peroneal nerve stimulation. However in contralateral medial gastrocnemius, reflexes evoked from stimulation at the wrist were inhibitory during swing, which was in direct contrast to the facilitatory reflexes observed at the same portion of the step cycle with stimulation at the foot. In addition, interlimb cutaneous reflexes were found to be task-dependent, as they were associated with ongoing muscle activity only during static contractions, and not during locomotion. The results indicate that interlimb cutaneous reflexes evoked from the hand and foot are modulated in a similar manner to local and crossed reflex responses.

Crossed and interlimb reflex pathways have been suggested to play a role in transferring important exteroceptive information from the hand and foot to muscles coordinating the movements of the arms and legs during locomotion (Zehr et al. 2001a). Findings from crossed and interlimb cutaneous reflex studies have shown not only the existence of widespread cutaneous reflexes throughout the muscles of the upper and lower limbs, but also that these responses share many properties to cutaneous reflexes evoked in the ipsilateral limb. Importantly, crossed and interlimb cutaneous reflex responses have been observed to undergo task- and phase-modulation, as well as coordination between the limbs. As mentioned by Zehr and Stein (1999), these properties suggested a functional relevance for cutaneous reflexes. Specifically, cutaneous reflexes may assist in coordinating corrective responses within and between the limbs, which assist in maintaining stability in the presence of a perturbation during walking. However, to understand the possible role that these cutaneous reflexes may play assisting in balance control, knowledge of the importance of cutaneous information to eliciting corrective responses that counteract destabilizing forces must first be discussed. This is the focus of the next section.

1.3 Cutaneous information in balance control

As discussed in the previous section, cutaneous reflexes have been suggested to assist in coordinating corrective responses across the body. These reflex responses are evoked from electrically stimulating cutaneous nerves, many of which innervate various portions of the foot and hand. Cutaneous information from these parts of the body is important, as suggested by the high density of somatosensory receptors and the large area of the cortex dedicated to processing attained sensory information. Specifically, exteroceptors in the sole of the foot and palmar surface of the hand provide information regarding support surfaces and touched objects in our environment. Interestingly, cutaneous information from these areas has been shown to contribute to balance control. This section of the General Introduction will focus on the role of cutaneous sensation from the foot and hand on balance control during standing and walking.

1.3.1 The role of cutaneous information in balance control during standing

Cutaneous information from the foot sole contributes to the ongoing regulation of postural control during quiet stance. This is evidenced by studies that involve reducing cutaneous sensation from the sole of the foot. With cooling or anesthesia of the foot sole, many studies have reported an increase in postural sway during standing (Asai et al. 1990; Magnusson et al. 1990a; Magnusson et al. 1990b; Thoumie and Do 1996; Meyer et al. 2004b; McKeon and Hertel 2007). In addition, anesthesia of the foot sole has been shown to influence corrective responses to postural perturbations, such as greater use of multiple steps (Perry et al. 2000) and greater reliance on the muscles of the hip to produce compensatory torques (Horak et al. 1990; Meyer et al. 2004a) during unpredictable support surface translations. Furthermore, it has also been shown that muscle activity involved in a compensatory stepping reaction to an induced forward fall is decreased with plantar anesthesia (Do et al. 1990). Together, these findings implicate an important role for cutaneous information from the foot sole in postural control.

Adding to the notion that cutaneous information from the sole of the foot is important for balance control is the findings from studies that increase cutaneous sensation to the plantar surface during standing. Using low amplitude, high frequency mechanical vibration of the foot sole, Kavounoudias et al. (1998) induced postural sway that was directionally specific to the portion of the foot that was stimulated. For example, vibratory stimulation underneath the right heel produced a compensatory postural response directed forward and to the left. They attributed cutaneous afferents responsible for this observation, as proprioceptors in the leg could not explain the specific directions of the induced responses, and there were no reports of kinesthetic illusion to the long periods of vibration. Similarly, Maurer et al. (2001) reported mechanical stimulation of the plantar sole at frequencies similar to that of natural postural sway (0.1-0.4 Hz) induced body sway that was associated with cutaneous stimuli. Cutaneous information from the foot soles has also been shown to enhance postural control. Studies done by Collins and colleagues (Collins et al. 2003; Priplata et al. 2003;

Priplata et al. 2006) have observed decreased postural sway when subsensory mechanical noise was applied to the soles of the feet via vibrating insoles during quiet standing. Noise may enhance the detection of pressure changes on the foot soles during normal body sway, which in turn leads to an improvement in postural control (Priplata et al. 2006). Facilitation of cutaneous sensation from the perimeter of the plantar foot surface was also shown to lead to more efficient corrective reactions during unpredictable support surface perturbations, such as a decrease in the number of steps taken and movements of the arms (Maki et al. 1999). Therefore, cutaneous information from the plantar surface of the foot is important in the regulation of balance control during standing.

In addition to cutaneous information from the sole of the foot, tactile information from the arms and hands is also involved with balance control. For instance, lightly touching a stable surface (< 1 N force) while standing lead to a reduction in postural sway (Holden et al. 1994; Jeka and Lackner 1994; Jeka and Lackner 1995; Clapp and Wing 1999). Contact forces were strictly monitored, such that they were insufficient for mechanical support of the body. Small changes in contact force may provide information regarding the direction of postural sway, which leads to the activation of appropriate postural muscles to counteract body sway (Jeka and Lackner 1995). This decrease in sway with light touch has also been observed in patients with vestibular deficits and loss of vision (Jeka et al. 1996; Jeka 1997). Similar findings by Rogers et al. (2001) have also showed that passive tactile cues decrease the amount of body sway during standing. The results from these studies suggest an important role for cutaneous information from the hands in balance control during standing.

1.3.2 The role of cutaneous information in balance control during walking

In addition to standing, cutaneous feedback from the foot has also been shown to be important during locomotion. Through anesthesia of the plantar surface, previous studies have reported alterations in the normal kinematic pattern during walking. Starting from a resting stance position, Perry et al. (2001) observed increased variability in foot placement of the first step as well as a longer subsequent step during gait. Over a compliant surface, plantar anesthesia was also associated with a significant decrease in gait velocity in normal healthy subjects (McDonnell and Warden-Flood 2000). Similarly, it was recently reported that reduction of plantar sensitivity in the hindpaw during rat locomotion led to changes in hindlimb kinematics (Varejao and Filipe 2007). The removal of plantar surface feedback with cutaneous denervation of the cat hindpaws has also associated with changes in hindpaw trajectory, knee flexion velocity, as well as an increase in knee and ankle flexor activity (Bouyer and Rossignol 2003a). These results suggest an important role for cutaneous feedback from the plantar surface during locomotion.

Although not as widely studied as cutaneous information from the sole of the foot, it has also been shown that tactile information from the hands contributes to postural stability during walking. Dickstein and Laufer (2004) have shown that light fingertip touch onto a stable external object reduced body sway during treadmill locomotion. The magnitude of contact force at the finger was not sufficient to provide a mechanical support. The authors suggested that light touch provided somatosensory information from an external reference, which in turn provided information regarding spatial orientation. It was also mentioned that touch cues could be used in rehabilitation settings to aid patients with balance deficits.

In summary, cutaneous information plays an important role in the ongoing regulation of balance control during standing and locomotion. Specifically, cutaneous feedback from the sole of the foot as well as from the hands has been shown to influence postural sway. The reduction of cutaneous sensation from the feet has also been associated with increased body sway, as well as different kinematic profiles during locomotion. Interestingly, corrective reactions have also been shown to be adversely affected by the reduction of cutaneous input to the feet during standing. However, the role for cutaneous information for mediating corrective responses during walking is presently unclear. In order for corrective responses to be effective in maintaining balance in response to perturbations during walking, afferent information regarding our changing environment has to be rapidly translated into functional mechanical responses. Voluntary responses, originating from higher cortical centres are unlikely to be involved as they are too slow (~ 200 ms) to generate a functional corrective response to prevent a fall (Patla 2003). Rapid corrective responses in the muscles of the upper and lower limbs could therefore be regulated through spinal reflexes, such as proprioceptive and cutaneous reflex pathways. While it is possible that muscle afferents contribute to these responses, pathways from cutaneous afferents very likely play a major role in mediating corrective responses. The possibility that cutaneous reflexes may be important for regulating corrective responses in the muscles of the limbs during walking is the focus of the next section.

1.4 Does cutaneous information contribute to corrective responses?

As mentioned previously, cutaneous reflexes have been suggested to serve a functional role, assisting in the maintenance of balance during locomotion (Zehr and Stein 1999). Specifically, these reflexes are thought to be involved in the coordination between the limbs. This coordination is essential for evoking effective corrective responses that maintain stability in the presence of a perturbation. This section focuses on studies that investigate cutaneous reflex function during walking.

1.4.1 Functional responses to cutaneous nerve stimulation during walking?

An interesting study on coordination between the upper and lower limbs during walking was performed by Dietz et al. (2001). While walking on a split-belt motorized treadmill, the right treadmill belt underwent random rapid accelerations and decelerations, thereby perturbing the right leg. Mechanical displacements of the right leg evoked patterned EMG responses in the muscles of the left leg, as well as in the muscles of both arms. The authors also electrically stimulated the right distal tibial nerve during unperturbed walking at a stimulus intensity known to evoke cutaneous reflexes. Reflex responses in the muscles of both arms were observed to be similar to responses elicited with mechanical perturbations. In addition, neither mechanical perturbation nor cutaneous nerve stimulation elicited reflex responses in the arms when subjects were standing or seated. The results supported the notion of a flexible neuronal coupling between the muscles of the upper and lower limbs that is present according to the task being performed.

Despite observing interlimb cutaneous reflex responses during walking, these responses were not investigated over the step cycle. Rather, responses were elicited only at two points in the step cycle (midstance, end stance), thus no phase-dependent reflex modulation was reported. To serve a functional role during walking, cutaneous reflexes should display phase-dependent modulation across the step cycle. Additionally, a change in kinematics should also be observed with stimulation of cutaneous nerves. Zehr et al. (1997) and Van Wezel et al. (1997) showed kinematic responses at the ankle and knee, along with cutaneous reflexes in the muscles of the leg with stimulation of the foot dorsum. Superficial peroneal nerve stimulation evoked inhibition in tibialis anterior during the early swing phase, which correlated with an increase in plantar flexion. An increase in knee flexion was also observed by Zehr et al. (1997) during early swing. These responses at the ankle and knee would allow the foot to drag over an encountered obstacle during swing, thereby allowing the forward continuation of the foot. The authors concluded this response was indicative of a stumbling corrective response, which was first described in the cat by Forssberg (1979). Zehr et al. (1997) also observed an increase in dorsiflexion at the stance-swing transition, and an increase in plantar flexion at late swing with tibial nerve stimulation. This response evoked with stimulation of the plantar surface of the foot was suggested to represent a withdrawal response (stance-swing transition) and a placing reaction (late swing).

Electrical stimulation of the sural nerve at the foot was also shown to elicit kinematic changes at the hip, knee, and ankle during the step cycle (Zehr et al. 1998b). During swing phase, an increase in dorsiflexion and flexion was observed at the ankle and knee respectively. This was correlated with cutaneous reflex facilitation in tibialis anterior and vastus lateralis. Additionally, increased flexion at the hip and knee, along with increased dorsiflexion, were observed at late stance. The kinematic response at swing was thought to allow for obstacle clearance, and at late swing the increase in flexion could potentially allow for the single-support limb accommodation to uneven surfaces.

Further to these local cutaneous reflex responses, Haridas and Zehr (2003) have shown interlimb cutaneous reflexes are also able to modify lower limb kinematics. Superficial radial nerve stimulation at the wrist was shown to elicit an increase in dorsiflexion at the stance-swing transition in both the ipsilateral and contralateral ankle. At this point of the step cycle, the hand is forward from the torso, and the innervation area of the superficial radial nerve would be in contact with an obstacle during walking. The response observed at the ankle would assist in stopping locomotion, thus preventing collision with an obstacle in the environment. Thus, cutaneous nerve stimulation can evoke widespread functional, kinematic changes that are phase-dependent.

1.4.2 Context-dependency of cutaneous reflexes?

As discussed above, the ability of cutaneous reflexes to be modulated according to both the task and phase of the movement being performed has led to the suggestion that these reflexes may play a role assisting in the regulation of corrective responses. In turn, this would contribute to the maintenance of balance during walking. Subsequently, cutaneous reflexes should also be able to adapt appropriately to the context of the task being performed (e.g. task-related stability demands). With respect to cutaneous reflexes, the influence of context has not been investigated. However, context-dependency of the monosynaptic H-reflex has been studied by Llewellyn et al. (1990), in which the soleus H-reflex during treadmill walking was compared to balance beam walking. The authors found that the amplitude of the H-reflex decreased on average 40% during balance beam walking. This finding supports the idea that a change in environment (with regard to balance) contributes to reflex regulation.

If cutaneous reflexes are important for assisting in the maintenance of balance during walking, then similar to observations with H-reflex amplitudes, cutaneous reflexes should also undergo change during locomotion according to the context of the specific task. Specifically, when walking in an environment in which stability is challenged, reflexes should be modulated in a context-dependent manner. The main purpose of this thesis is to investigate the influence of walking in environments in which the demands on stability are varied on the modulation of cutaneous reflexes in the lower and upper limbs. In Chapter 2, the influence of walking in a generalized instability context (i.e. increased threat to stability) on reflexes in the muscles of the lower limbs, evoked from electrically stimulating cutaneous nerves innervating different portions of the foot, will be investigated. In Chapter 3, interlimb cutaneous reflexes in the muscles of the arms evoked by stimulating nerves innervating the foot will be investigated during walking with an increased threat to stability. The influence of walking in a specific instability context on cutaneous reflexes in the legs evoked by electrically stimulating a nerve innervating an area of the foot correlated to the targeted instability context will be investigated in Chapter 4. The last experiment detailed in Chapter 5 will investigate the influence of engaging the arms in balance control on cutaneous reflexes in the arms evoked from the hand during walking. Finally, Chapter 6 of this thesis will discuss the general results from these experiments their relevance, experimental limitations, as well as provide future directions for this area of research.

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Chapter 2 - Postural uncertainty leads to dynamic control of cutaneous reflexes from the foot during human walking[*]

2.1 Introduction

Cutaneous reflexes have been shown to exhibit both task-dependent and phase-dependent modulation (for review, see Zehr and Stein 1999). For instance, electrical stimulation of cutaneous nerves in the foot has been shown to evoke reflexes in the muscles of the leg that differed according to the task performed (Komiyama et al. 2000). The authors showed that during standing, the net reflexes evoked were largely inhibitory, whereas during walking, facilitatory net reflexes were observed. Additionally, cutaneous reflexes in the muscles of the legs have been shown to change both in sign and amplitude during walking according to the position of the stimulated leg within the step cycle (Duysens et al. 1992; Van Wezel et al. 1997; Zehr et al. 1997; Zehr et al. 1998). Therefore, these reflexes act in a functional manner by helping to maintain balance while encountering a perturbation during walking (Van Wezel et al. 1997; Zehr and Stein 1999).

Electrical stimulation of the cutaneous superficial peroneal nerve (innervates the dorsum of the foot) has been shown to elicit a "stumbling corrective response" in the leg during treadmill walking in cats (Forssberg 1979) and in humans (Zehr et al. 1997). In the human, this stumbling corrective response consists of an increase in knee flexion and a decrease in ankle

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[*] *A version of this chapter has been accepted for publication. Haridas et al. (2005) Brain Res 1062: 48-62.*

dorsiflexion during swing. This response would allow for the smooth forward progression of locomotion by allowing the swing leg to drag over an obstacle. In addition, the effects of distal tibial nerve (innervates the plantar surface of the heel) stimulation during walking have been investigated (Yang and Stein 1990; Van Wezel et al. 1997; Zehr et al. 1997). These studies have also suggested that cutaneous reflexes serve to assist balance during walking. Zehr et al. (1997) showed that the effects of cutaneous reflexes from the tibial nerve were predominant during late stance and late swing. The responses evoked by tibial nerve stimulation were suggested to be relevant to sensation of ground contact information and also have a functional role in stabilizing balance during walking.

Accordingly, if cutaneous reflexes do serve a role in the maintenance of balance during locomotion, they should be modulated during locomotion in an environment in which balance is challenged (e.g. walking on an unstable surface). To date, there are no studies that have specifically investigated cutaneous reflexes during locomotion in such an environment. Burke et al. (1991) demonstrated that cutaneous reflexes evoked in leg muscles were more prominent when standing in unstable conditions. Llewellyn et al. (1990) compared the soleus H-reflex during walking on a treadmill and balance beam. The authors found that the amplitude of the H-reflex decreased on average 40% during balance beam walking. This finding supports the idea that a change in environment (with regard to balance) contributes to reflex regulation. Similarly, the amplitude of cutaneous reflexes would be expected to be modified during locomotion in an unstable environment. This type of environment would be defined as one in which balance is threatened in a predictable or unpredictable manner.

Recently, we have developed a method to disturb balance during treadmill walking (Misiaszek 2003). This method involves applying random forward and backward pulls on a padded belt secured around the hips of a subject. The force of the pulls is strong enough to cause instability, but not enough to result in a fall. Furthermore, having the arms crossed during walking produces a more demanding task in which balance is challenged. Crossing the arms in such a fashion restricts the use of the arms for balance recovery. We have shown that restricting the use of the arms in this way increases the amplitude of compensatory reactions in muscles of the leg during walking (Misiaszek and Krauss 2005). The implication is that restricting the use of the arms results in a shift in postural set, by placing a greater emphasis on reactions in the legs. Indeed, postural control is scaled to the level of postural threat in both quiet standing (Adkin et al. 2000; Carpenter et al. 2001) and walking (Brown et al. 2002).

In this study, we tested the hypothesis that the amplitude of cutaneous reflexes is altered when walking in an unstable environment. We speculated that any effect on reflex control should be largest for effects related to the greatest instability (e.g. stumbling and falling). Thus, we further hypothesized that any effect related to perceived stability should be larger for SP than for TIB nerve. Instability was created by delivering unexpected forward and backward perturbations, as well as having the arms crossed while walking on a motorized treadmill. Portions of these results have been reported in abstract form (Haridas et al. 2004).

2.2 Materials and methods

2.2.1 Subjects and protocol

Eleven subjects between the ages of 20 and 35, with no history of neurologic, orthopedic or metabolic impairment participated with informed, written consent in a protocol approved by the Human Research Ethics Board (Health Research) at the University of Alberta. In this study, we examined cutaneous reflexes evoked with electrical stimulation of two nerves, the superficial peroneal (SP) and distal tibial (TIB) nerves. Subjects visited the lab on two different occasions, once for each nerve stimulation protocol. All eleven subjects participated in the SP nerve stimulation protocol, and ten also participated in the TIB nerve stimulation protocol. The order of presentation of nerve stimulation was randomized across subjects.

Subjects were asked to walk on a motorized treadmill at a self-selected speed (typically between 0.8 and 1.2 m/s). Cutaneous reflexes were elicited during 5 walking conditions: (1) normally, with the arms free (Normal); (2) with the arms crossed across the chest (Arms Crossed); (3) with the arms free, but while receiving unpredictable anterior-posterior perturbations applied at the waist (AP); (4) with the arms crossed and receiving unpredictable anterior-posterior perturbations (Arms Crossed + AP); (5) while holding onto stable fixed handles (Handles). The order of presentation of the walking conditions was randomized across subjects. The purpose of the anterior-posterior perturbations during walking was to create an environment in which stability was unpredictable. Therefore, cutaneous reflexes were not elicited during such perturbations, but rather during periods of steady walking between the perturbations. Subjects were instructed that they were free to grab for safety rails located in front and to the sides (~45 cm from lateral edge of the arms, ~75 cm in front of the subject) if they felt the need to do so to prevent falling. The purpose for having the arms crossed was to produce instability during walking, by constraining the arms from assisting in balance recovery. In contrast, we asked the subjects to hold onto fixed handles during walking in order to create a task with increased stability. In previous studies, we have shown that holding onto handles in this way eliminates compensatory reactions evoked in the leg muscles by a perturbation (Misiaszek et al. 2000; Misiaszek and Krauss 2005). Subjects were informed before performing each walking condition as to whether perturbations would be elicited.

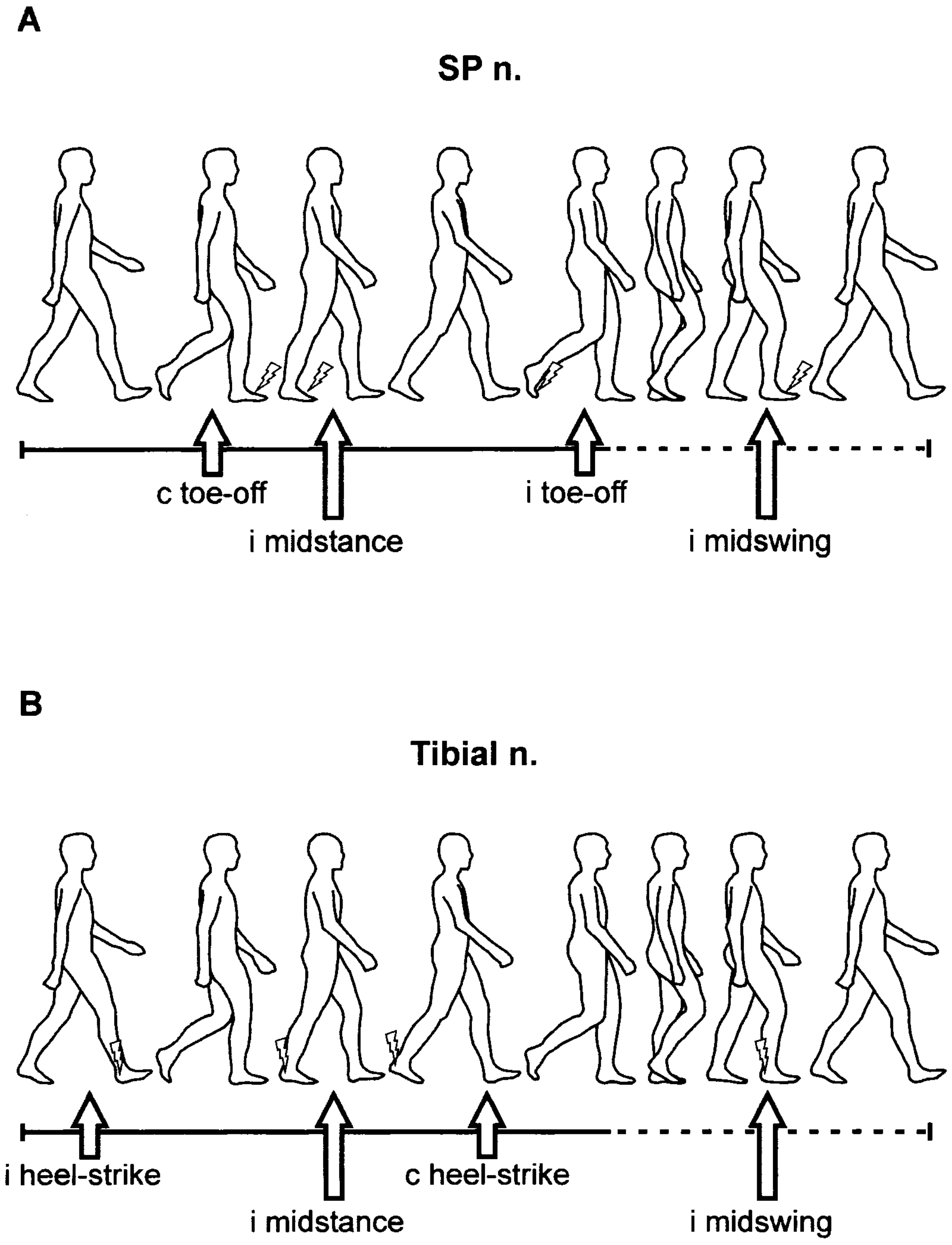
The perturbations were delivered by cables attached to a belt worn by the subject around the pelvis. From the belt, these cables ran in front and behind the subject, through a series of pulleys, to a drum to which a handle is attached. Pushing and pulling this handle caused anterior and posterior perturbations, respectively. A strain gauge placed on the lever arm of the handle was used to indicate when perturbations were applied. The magnitude of the perturbations was ~ 20% of the subjects' body weight. However, as the perturbations were used only to create an unpredictable environment, the magnitude was not specifically controlled. Perturbations were delivered randomly throughout the step cycle, with a frequency of approximately 3 per minute.

2.2.2 Nerve stimulation

Cutaneous reflexes were evoked by trains (5 x 1.0 ms pulses @ 300 Hz) of isolated constant current stimulation (Grass S88 stimulator with SIU5 and CCU1 isolation and constant current units, AstroMed Inc.) applied to the SP or TIB nerve of the right (ipsilateral) leg using flexible 1 cm disposable surface EMG electrodes (A10043-P, Vermed). Electrodes for the SP nerve were placed in a bipolar configuration on the anterior surface of the leg, near the crease of the ankle joint. The electrodes for TIB nerve stimulation were placed on the medial surface of the ankle, between the medial malleolus, and Achilles tendon. The intensity of stimulation was set as a multiple of radiating threshold (RT) for each subject, approximately 2-3 x RT (actual means (± SEM): 2.7 x RT ± 0.13 for SP, 2.05 x RT ± 0.09 for TIB), a value at which the stimulus is strong enough to evoke a reflex, yet is not perceived as painful by the subject (Duysens et al. 1990; Yang and Stein 1990; Zehr et al. 1997). Zehr et al. (1997) associated the RT value with the activation of fascicles in the cutaneous nerve under the stimulation electrodes. RT was estimated as the lowest stimulus intensity at which the subject first perceived a clear radiating cutaneous paresthesia into the innervation area of the nerve (SP: dorsum of foot; TIB: plantar surface of the heel). The appropriate innervation area was demonstrated to the subject by the experimenter and sensation in this area was confirmed by the subject. RT was checked between each walking trial to ensure that the stimulus properties remained similar throughout the experiment.

Electrical stimuli were delivered such that no more than one stimulus was delivered within a single step cycle. Typically, electrical stimuli were separated by 2-6 s. Electrical stimuli were delivered at four points throughout the step cycle for SP nerve (Figure 2.1A, contralateral toe-off, ipsilateral midstance, ipsilateral toe-off, and ipsilateral midswing). These four points of the step were chosen for the SP nerve stimulation paradigm as they represent critical points in the phase-dependent pattern of modulation observed during walking (Zehr et al. 1997; Haridas and Zehr 2003). For the TIB nerve stimulation paradigm, stimuli were delivered at ipsilateral heel-strike, ipsilateral midstance, contralateral heel-strike, and ipsilateral midswing (Figure 2.1B) (Van Wezel et al. 1997; Zehr et al. 1997). The timing of stimulus delivery was controlled manually by the experimenter to occur near the target points of the step cycle. Approximately 40 stimuli were delivered at each point in the cycle and then subsequently screened post hoc to select the stimuli which occurred within the appropriate time points. Manually targeting stimuli to occur at specific points in the step cycle reduced the total number of stimuli required and greatly reduced the time required of the subjects. This technique typically resulted in 15-30 stimuli being accepted for further analysis for each point in the step cycle for each walking condition (see below for the method used to screen the timing of the stimuli).

Figure 2.1: Schematic depicting the points in the step cycle that were isolated for stimulation for each nerve studied. (A) SP and (B) TIB. i: ipsilateral, c: contralateral (both with respect to side of stimulation).



2.2.3 Recording and data acquisition

After shaving, abrading, and cleaning the skin with alcohol, a pair of disposable surface electrodes (A10012, Vermed) were placed longitudinally parallel to the predicted path of the muscle fibers over the tibialis anterior (TA), soleus (SOL), medial gastrocnemius (MG), vastus lateralis (VL), and biceps femoris (BF) of the leg ipsilateral (i) to the stimulation, as well as TA and MG of the contralateral (c) leg. These muscles were selected for observation as it has been previously shown that cutaneous reflexes from the foot evoked in each express strong phase-dependent modulation during walking (Haridas and Zehr 2003). Ground electrodes were placed over electrically neutral tissue. Signals were pre-amplified and bandpass filtered at 30 Hz-3 kHz (P511 amplifiers (using 1/2 amplitude high and low pass filters), Grass Instruments, AstroMed Inc.).

Kinematic data were collected using electrogoniometers (Biometrics, Inc.) placed across both ankles, secured with two-sided tape. Foot contact information was obtained from custom-made force sensitive resistors placed in the soles of the subject's shoes.

EMG, kinematic, foot force sensor, stimulation, and perturbation force data were collected at a sampling rate of 1000 Hz and saved to disk using a custom-written LabView v.5 data acquisition routine and a National Instruments data acquisition card (PCI-MIO-16E-4, National Instruments, Austin, TX, USA). The EMG signals were then digitally full-wave rectified and subsequently low-pass filtered at 50 Hz (4th order dual-pass Butterworth filter). This filtering process provided a good linear envelope of the resulting responses. The kinematic signals were low-pass filtered at 50 Hz.

2.2.4 Data analysis

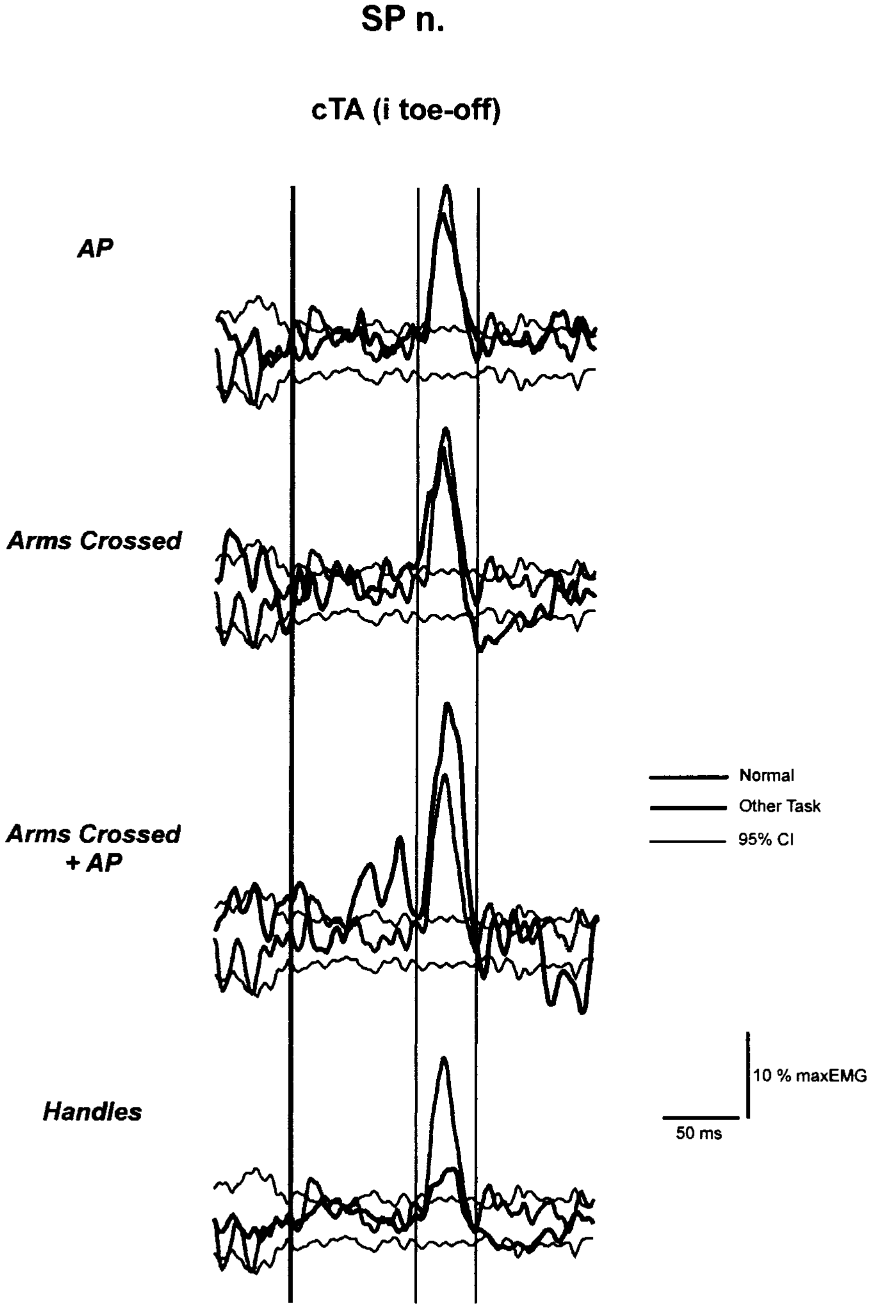
Data analysis for each subject began with the selection of 30 control step cycles for each walking trial (custom-written program, LabView v.5, National Instruments, Austin, TX, USA). Control steps were those for which no stimuli were applied and no perturbations occurred. Steps were not included if a perturbation occurred within the preceding two steps. For each of the control steps, an 1800 ms data trace was captured starting at heel-strike of the ipsilateral foot, and averaged to produce an average control trace.

Subsequently, the stimuli were selected and grouped into bins depending on the time at which they occurred in the step cycle. The four bins for each nerve stimulation protocol were defined as a time window of 10% of the average control step cycle duration, centered at the points in the step cycle described above (for example, if ipsilateral toe-off for a subject occurred at 56% of the step cycle then stimuli applied between 51% and 61% of the step cycle were included). Heel-strike represented 0% of the step cycle. Once the stimulus trials were sorted into bins, the data traces were aligned to stimulus delivery, and averaged together. The average non-stimulated EMG trace was subtracted from the stimulated average trace, yielding a subtracted evoked EMG trace for each subject.

Cutaneous reflexes were calculated from the subtracted traces for each muscle. An example of the traces produced by the subtraction process for cTA after SP stimulation is displayed in Figure 2.2. The early and middle latency components of the reflex were calculated for the time windows of 50-80 ms and 80-120 ms post-stimulus respectively. The cutaneous reflex amplitude was calculated as the average amplitude of the subtracted trace within these time windows. This is in contrast to other studies which typically identify reflex onset latencies in each subject individually and thereby average over slightly different time windows (e.g. Yang and Stein 1990; Van Wezel et al. 1997; Haridas and Zehr 2003). We chose to use the technique of averaging over a predetermined time window to ensure that comparable reflexes were compared across subjects. The time window chosen for the middle latency reflex was appropriate for this task as the middle latency reflexes from all subjects were captured within this window. Cutaneous reflex amplitudes for each subject were normalized to the maximum EMG amplitude occurring during the step cycle for each muscle, and expressed as a percentage.

Ongoing background EMG activity and the ankle angles of each leg were also calculated for each of the walking conditions. These were calculated from the undisturbed steps at the time when, on average, the reflexes for each bin would have been observed for that subject. In this way, the level of excitability in the motoneuron pools at the time the reflex arrives is estimated, rather than the EMG occurring prior to the stimulus onset. The background EMG and ankle angles were averaged for 40 ms during the control step data, starting 80 ms after the average occurrence of the stimulus onset taken from the stimulation trials for that bin.

Figure 2.2: Subtracted EMG traces of cTA after SP nerve stimulation for one representative subject following stimuli applied at ipsilateral (i) toe-off. Each set of traces depicts the evoked reflex during the Normal condition (thick grey line), one of the other walking conditions (thick black line), and the 95% confidence interval (CI, thin black lines). The thick vertical line indicates the point of stimulus onset. The thin vertical lines define the time window used for analysis of the middle latency reflex. AP: walking while being perturbed with anterior-posterior pulls, Arms Crossed: walking with the arms folded across the chest, Arms Crossed + AP: walking with the arms folded across the chest while being perturbed, Handles: walking while holding stable handles.



2.2.5 Statistics

Statistical analysis was performed using the averaged normalized values for each subject, from each part of the step cycle. For the statistical analysis, the absolute values of the reflexes were used. This was done rather than using the signed values, to account for our observation, which has been noted by others (Duysens et al. 1990; Yang and Stein 1990; Aniss et al. 1992; Tax et al. 1995; Van Wezel et al. 1997), that the sign of cutaneous reflexes (excitatory vs. inhibitory) is not always consistent between subjects. We noted that inter-subject variability was seemingly magnified in this study, where the overall effect of perceived postural threat modified reflexes was consistent within a subject, but in different directions between subjects. That is, a subject with an excitatory reflex may reveal a greater amount of excitation during one walking task, whereas a subject with an inhibitory reflex may reveal a greater amount of inhibition during the same walking task. Thus, in an analysis of the signed values, the consistent increase in response magnitude would be lost. As the purpose of this study was to determine if the amplitude of the reflex changed between tasks, we removed this potential between-subject confounder from the analysis by using the absolute values of reflex amplitude. For each nerve stimulation paradigm and for each muscle studied, a two-way repeated measures analysis of variance (ANOVA; bin [4] x condition [5]) was used to parse the sources of variance. Planned comparisons were then performed for the reflex amplitudes between each condition at each bin, utilizing experimental error as calculated by the ANOVA. Planned comparisons were also performed on the background EMG.

Ankle joint angles and step cycle durations were compared using repeated measures ANOVAs. Statistical significance was set at $p < 0.05$.

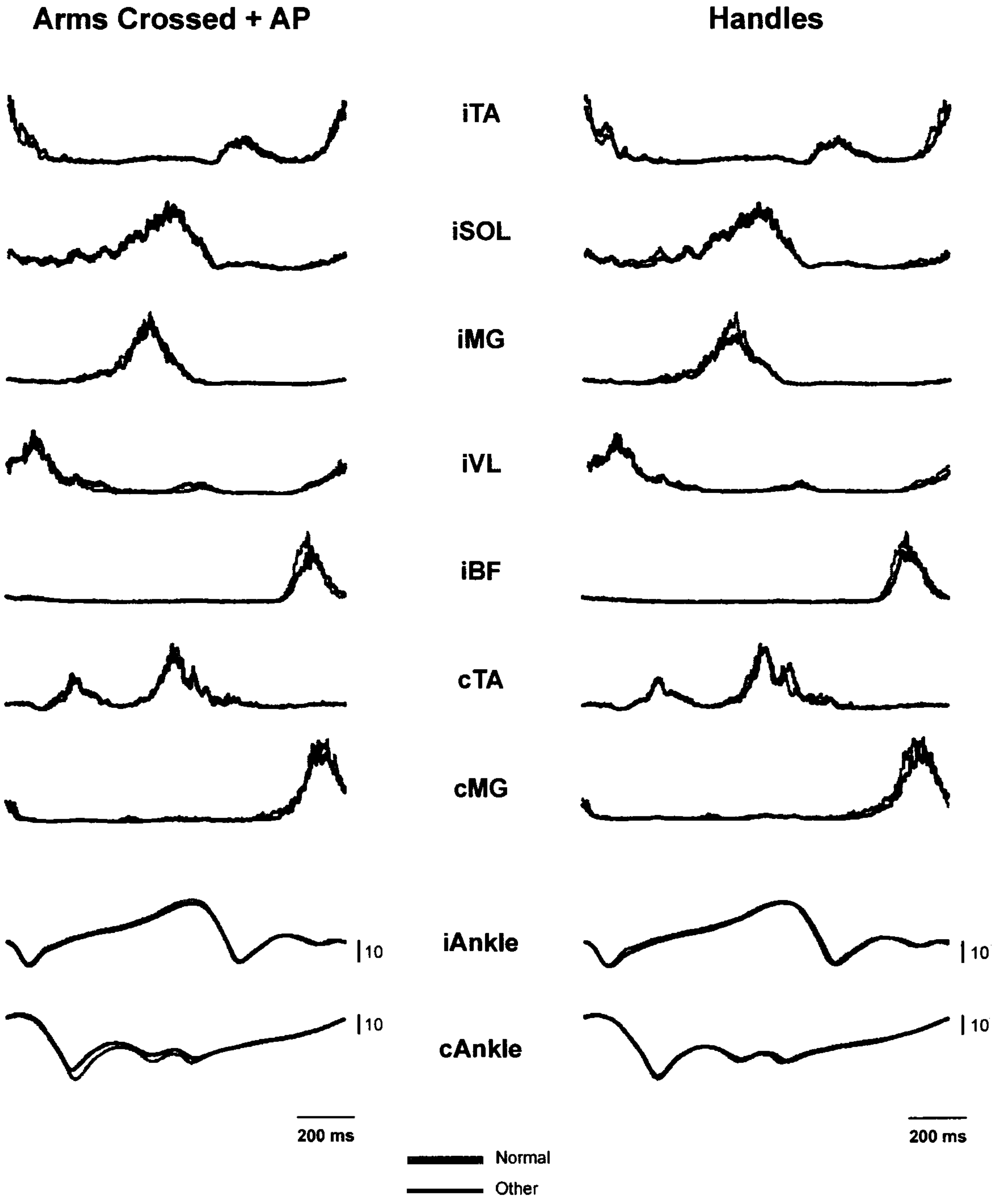
2.3 Results

There were no significant ($p > 0.05$) differences in early latency cutaneous reflex amplitudes across the five walking conditions for any of the phases of the step cycle for all recorded muscles with both SP and TIB nerve stimulation. Early latency cutaneous reflexes are relatively rare in humans (Baken et al. 2005). Therefore, we focused our analysis on the reflexes occurring within the middle latency time window.

2.3.1 EMG and kinematics

During this study, subjects were asked to walk under five conditions, including while holding handles, with the arms crossed, or while receiving unpredictable external perturbations. We compared the background EMG for each muscle and the ankle angle at each of the four points in the step cycle tested. In addition, we compared the step cycle duration and the proportions of the step cycle (stance and swing phases). In Figure 2.3, average control traces for one subject are displayed for the Arms Crossed + AP condition compared to Normal, and Handles compared to Normal. As can be seen from this example, the general walking pattern of the subject is largely the same under these various conditions. In particular, the ankle angles varied little between the walking conditions. This consistency in the walking pattern across tasks was seen in all of

Figure 2.3: Average EMG and ankle goniometer traces for control steps from one representative subject. The grey lines in each pair of traces represent the control steps obtained during the normal walking condition. The black lines represent the average control steps obtained from the arms crossed and receiving perturbations condition (left column), and the holding handles condition (right column). Each trace is the average of 30 control steps, starting at i heel-strike.



the subjects. Two-way repeated measures ANOVAs (bin [4] x condition [5]) were performed on the ankle angles. No main effects of walking condition were noted ($p > 0.05$). In addition, one-way repeated measures ANOVAs were performed on step cycle duration, stance phase duration, and swing phase duration for the group average data. No significant differences for any of these parameters across walking tasks were identified ($p > 0.05$).

Ongoing EMG levels were compared using the same analysis as the comparisons in reflex amplitudes. Thus, planned comparisons were performed on the EMG levels for each muscle between each walking condition at each point in the step. The average ongoing EMG activities recorded during the TIB nerve stimulation paradigm are shown in Figure 2.4, whereas those recorded during the SP nerve stimulation paradigm are shown in Figure 2.5. Differences in ongoing EMG were identified between some conditions in most of the muscles studied. In particular, the activity of iVL was elevated during early stance (i heel-strike of Figure 2.4 and c toe-off of Figure 2.5) in the Arms Crossed, AP, and Arms Crossed + AP conditions compared to both the Normal and Handles conditions. Activity in iTA also showed significant differences between conditions with a relatively consistent trend. At i heel-strike with the TIB nerve stimulation paradigm and at i toe-off with the SP nerve stimulation paradigm, the average activity tended to be highest during the Handles condition, and was found to be significantly different from all other conditions at these points except for the AP condition at i toe-off (Figure 2.5). This trend was repeated in cTA, where activity levels during the Handles condition were significantly increased compared to all

Figure 2.4: Group averaged data of the ongoing activity in each of the recorded muscles for each point in the step cycle analyzed for the TIB nerve stimulation protocol. The ongoing EMG activity was calculated from the unstimulated control steps for each walking condition. A 40 ms window at the point in the step cycle when the associated reflex would have occurred was used for the calculation. The ongoing EMG was normalized to the maximum EMG generated for that muscle across the step cycle. Each of the five conditions tested is indicated by a different symbol: open diamond - Normal; filled square - Arms Crossed; filled triangle - AP; open circle - Arms Crossed + AP; open triangle - Handles. Error bars represent one standard error. Asterisks indicate bins for which planned comparisons identified at least one difference between tasks (see text for details).

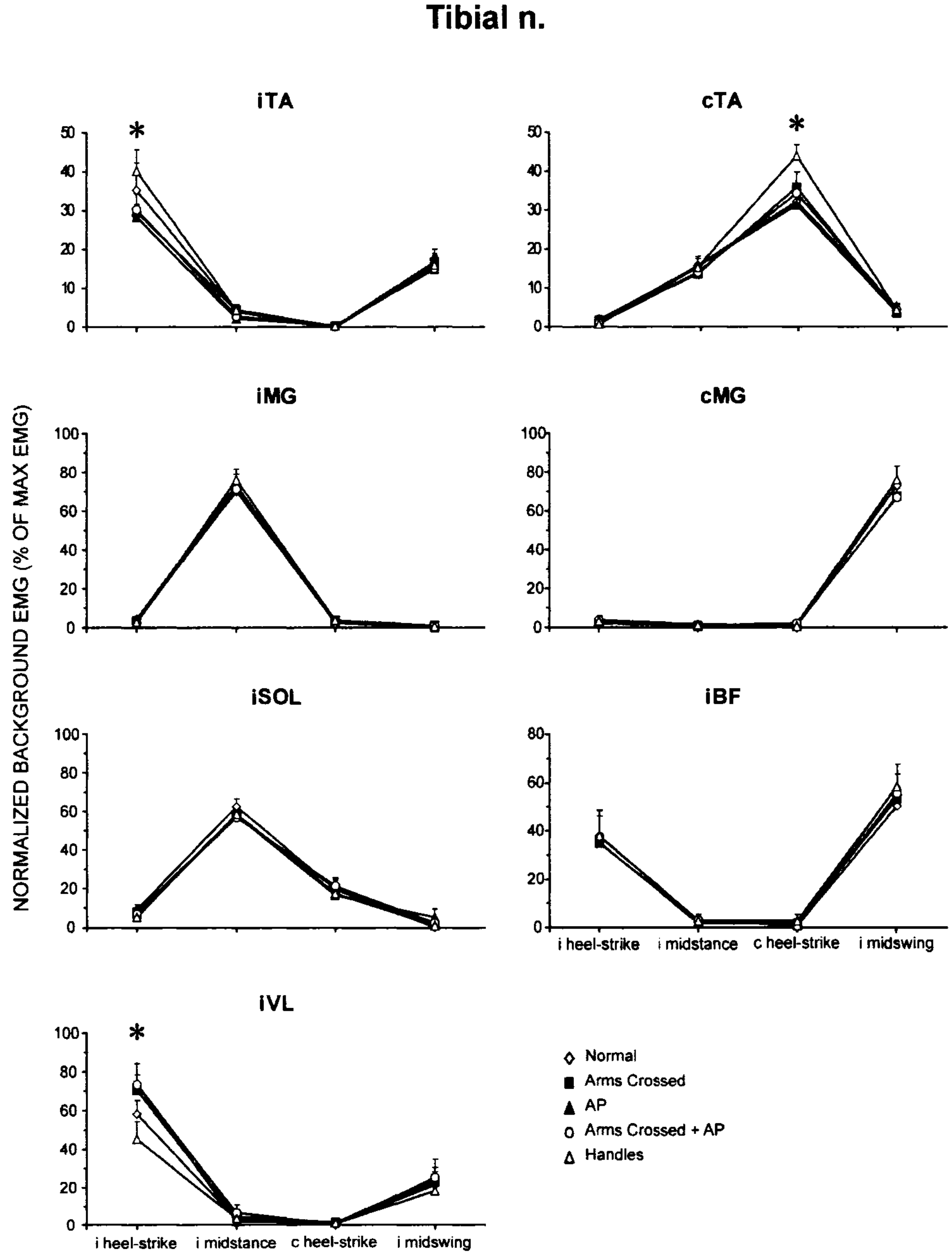
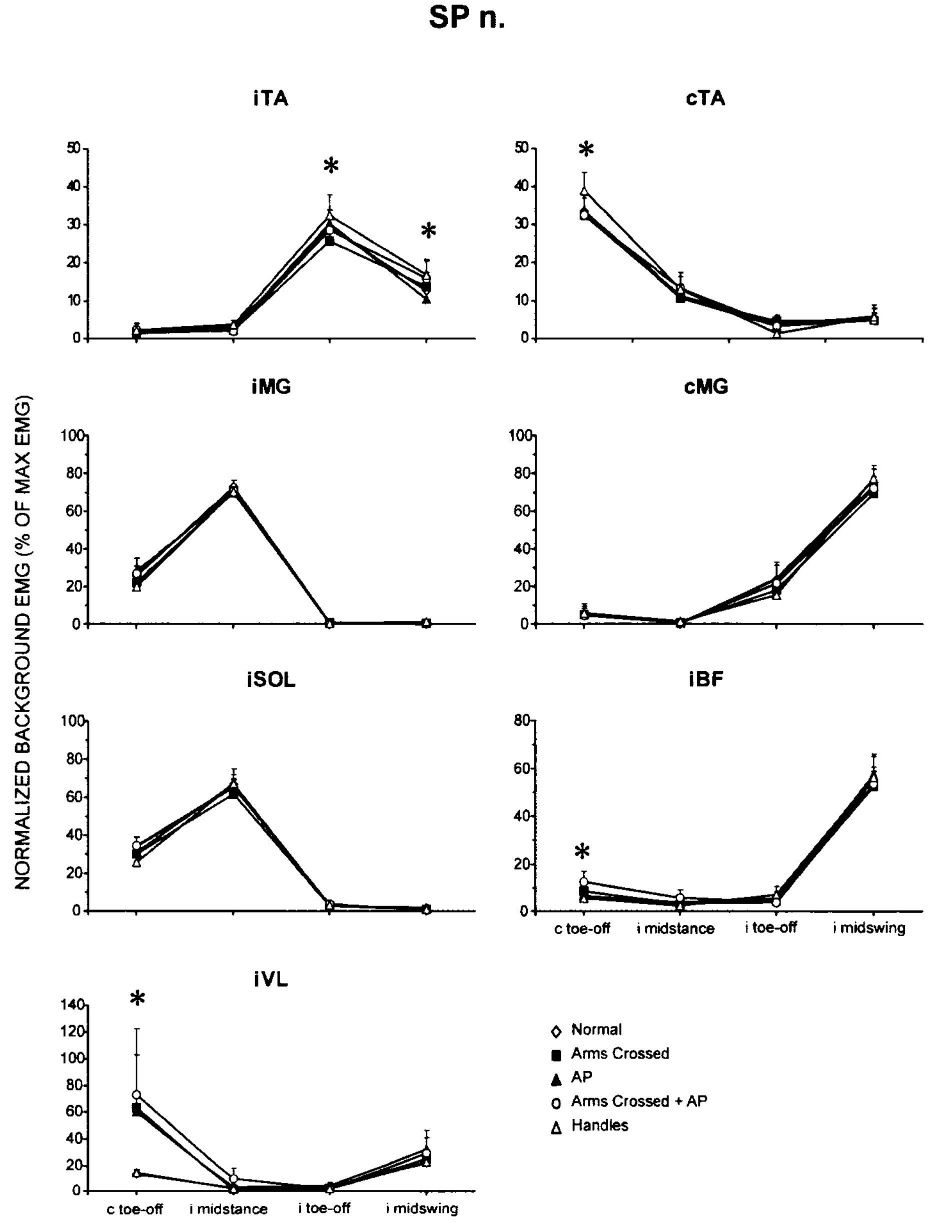


Figure 2.5: Group averaged data of the ongoing activity in each of the recorded muscles for each point in the step cycle analyzed for the SP nerve stimulation protocol. The ongoing EMG activity was calculated from the unstimulated control steps for each walking condition. A 40 ms window at the point in the step cycle when the associated reflex would have occurred was used for the calculation. The ongoing EMG was normalized to the maximum EMG generated for that muscle across the step cycle. The four points of the step cycle investigated are indicated along the abscissa. Each of the five conditions tested is indicated by a different symbol: open diamond - Normal; filled square - Arms Crossed; filled triangle - AP; open circle - Arms Crossed + AP; open triangle - Handles. Error bars represent one standard error. Asterisks indicate bins for which planned comparisons identified at least one difference between tasks (see text for details).

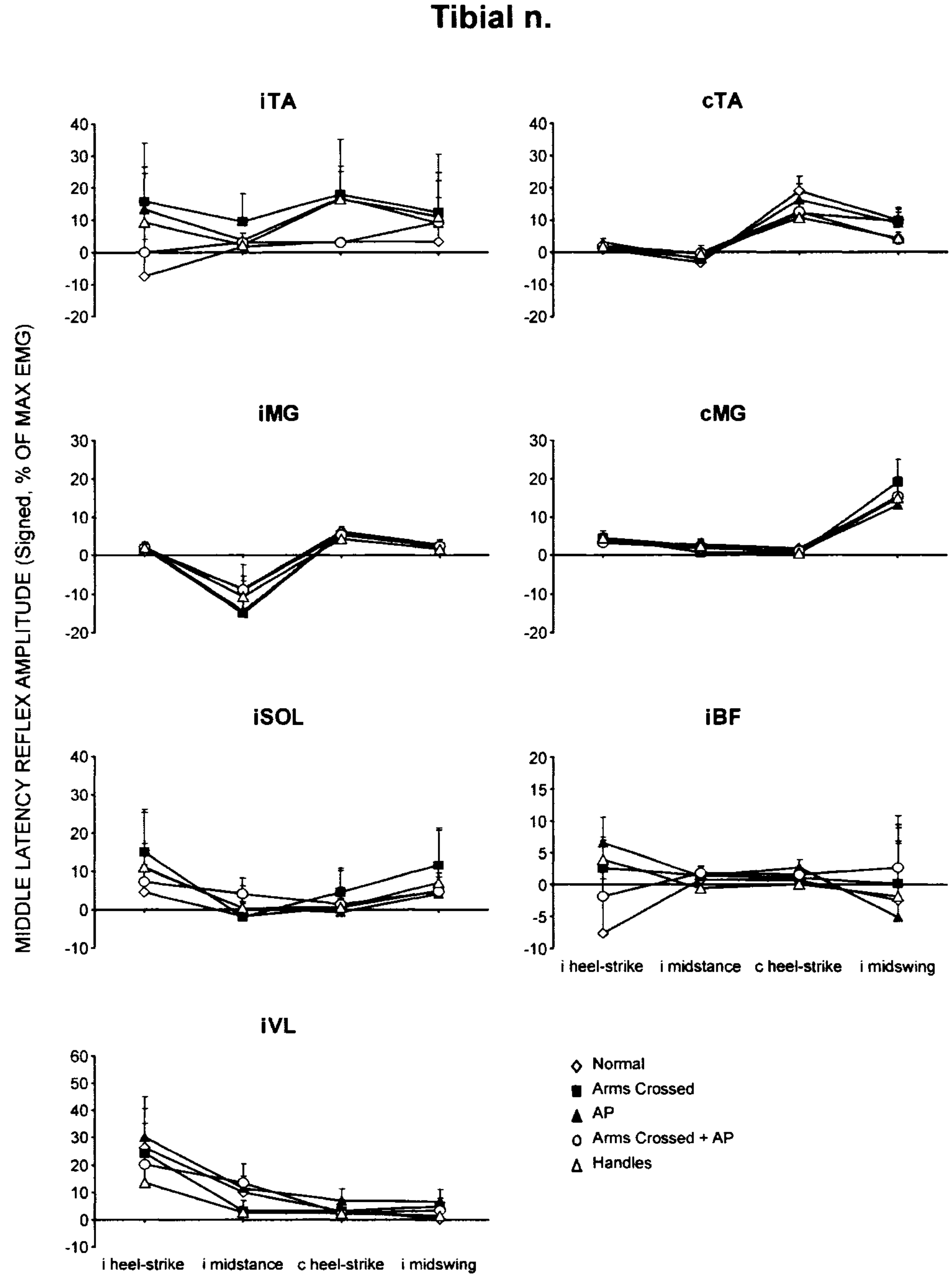


other conditions at both c toe-off (Figure 2.5) and c heel-strike (Figure 2.4). The only other marked difference in ongoing EMG activity that was observed between walking conditions was a significantly higher level of activity in iBF during the Arms Crossed + AP condition, compared with the Normal condition, at c toe-off during the SP nerve stimulation paradigm (Figure 2.5). No differences between conditions were identified in iMG, cMG, or iSOL. In general, walking in conditions of increased balance demand tended to result in an increase in the amplitude of VL activity. Whereas walking with increased stability (Handles) tended to lead to an increase in the activity level of TA.

2.3.2 TIB nerve cutaneous reflexes

The stimulation of the distal TIB nerve resulted in middle latency reflexes in each of the muscles tested. However, the appearance and sign of these reflexes was more variable across subjects than with SP nerve stimulation. In Figure 2.6, the data are presented with the sign of the reflexes for individual subjects retained so that these results can be compared with other studies and functional consequence can be discussed. In general, the reflexes evoked during the Normal condition displayed reflexes of comparable sign and with a comparable pattern of modulation over the step cycle to what has been reported previously (Yang and Stein 1990; Zehr et al. 1997). In most of the muscles tested, the pattern of modulation across the step cycle was retained during each of the walking conditions. However, the pattern of modulation appears to vary considerably from Normal during the other walking conditions in iTA and iBF. In

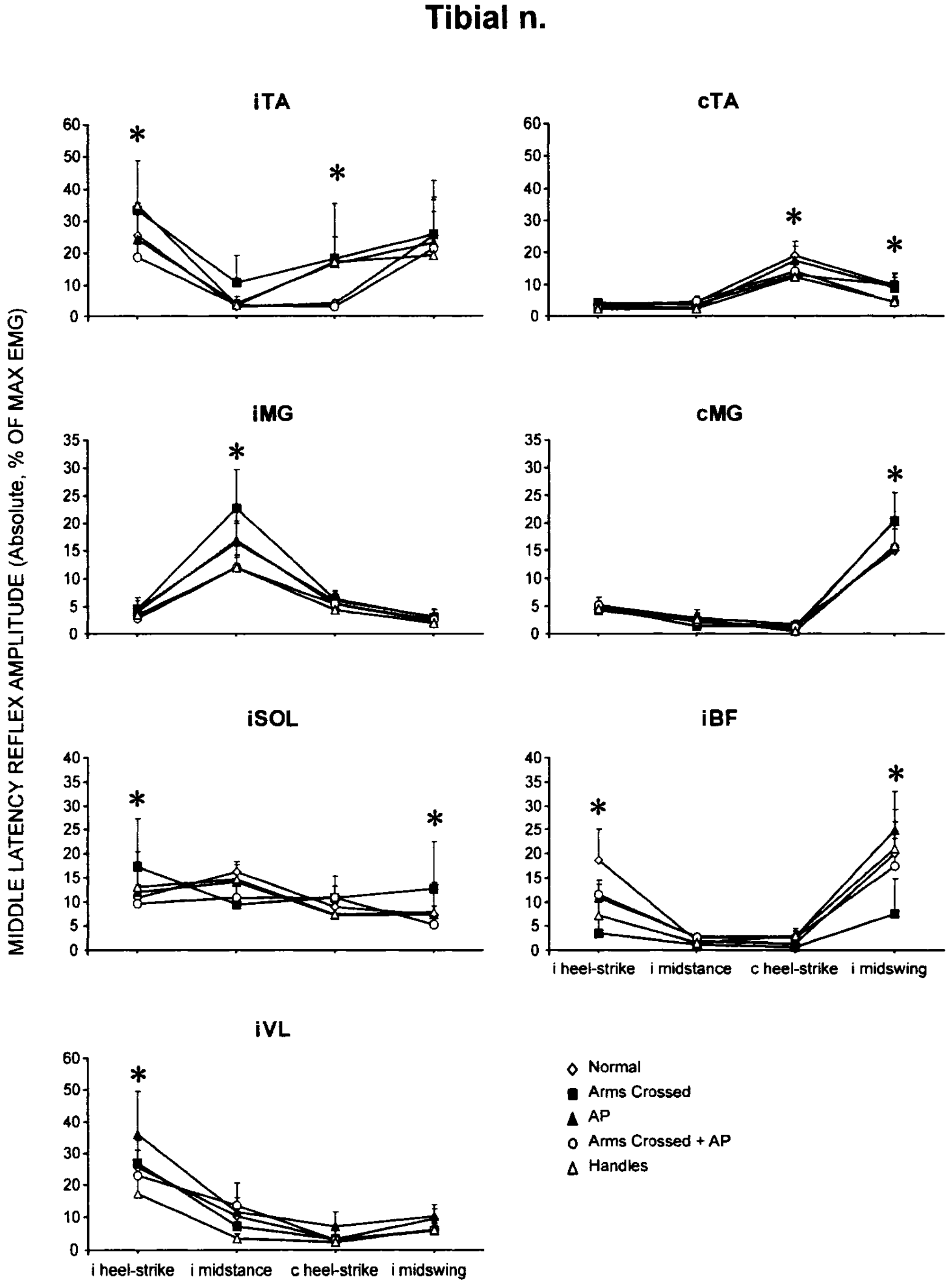
Figure 2.6: Group averaged data for middle latency cutaneous reflexes arising from TIB nerve stimulation with the *sign of the reflex retained.* Reflex amplitudes are normalized to the maximum EMG produced during normal, undisturbed walking for that muscle. The four points of the step cycle investigated are indicated along the abscissa. Each of the five conditions tested is indicated by a different symbol: open diamond - Normal walking; filled square - Walking with the arms crossed; filled triangle - Walking while being pulled forward and backward; open circle - Walking with the arms crossed and receiving forward and backward pulls; open triangle - Walking while holding stable fixed handles. Each point represents the mean with the standard error shown by the error bars.



both of these muscles, a sign reversal in the reflex evoked at i heel-strike appears to occur during some conditions. This was not a true reflex reversal as none of the data from individual subjects showed a sign reversal. Rather, as described in the Discussion, the sign of the reflex varied between subjects.

To assess the effect of walking condition on reflex amplitude, irrespective of sign, the absolute values of the reflex amplitude were used in the analysis. The group averaged data for the absolute values of the reflex amplitudes are displayed in Figure 2.7. Planned comparisons compared reflex amplitudes for each walking condition. The comparisons were performed separately for each point in the step cycle for reflexes evoked in each muscle. This identified differences in reflex amplitude between walking conditions in every muscle tested for at least one point in the step cycle. However, the nature of the differences in amplitudes between tasks was quite variable. For iTA, differences were noted at i heel-strike and c heel-strike. At i heel-strike reflexes evoked during Arms Crossed + AP were significantly ($p < 0.05$) decreased compared to Handles and Arms Crossed conditions. At c heel-strike the reflexes during Arms Crossed + AP and Normal conditions were of comparable amplitude, with the three other conditions showing significantly larger reflex amplitudes. Reflexes in cTA were significantly smaller during the Handles and Arms Crossed + AP conditions, compared with the Normal and AP conditions at c heel-strike, and all other conditions at i midswing. For iMG, walking with Arms Crossed resulted in reflexes significantly greater in amplitude than all other conditions at i midstance, and no differences were noted at other points in the step cycle. This compares with

Figure 2.7: Group averaged data for middle latency cutaneous reflexes taken as their *absolute values* arising from TIB nerve stimulation. Reflex amplitudes are normalized to the maximum EMG produced during normal, undisturbed walking for that muscle. The four points of the step cycle investigated are indicated along the abscissa. Each of the five conditions tested is indicated by a different symbol: open diamond - Normal; filled square - Arms Crossed; filled triangle - AP; open circle - Arms Crossed + AP; open triangle - Handles. Each point represents the mean with the standard error shown by the error bars. Asterisks indicate bins for which planned comparisons identified at least one difference between tasks (see text for details).



reflexes evoked in cMG in that reflexes during the Arms Crossed condition were significantly larger than during all other conditions but only at i midswing, which would be about c midstance. In iSOL, reflexes during the Arms Crossed condition tended to be larger than during other conditions at i heel-strike and i midswing, but were significantly greater than reflexes evoked during Arms Crossed + AP at both points. Differences in the reflex amplitudes between walking conditions for iBF varied tremendously between subjects. Consequently, few differences were identified by the analysis, despite the apparently large differences in mean amplitudes displayed. For iBF, reflexes evoked during all other conditions were significantly smaller than during the Normal condition at i heel-strike. At i midswing, the reflexes evoked during the Arms Crossed condition were significantly reduced compared only to the AP condition. In iVL, reflexes recorded at i heel-strike were significantly smaller in amplitude during the Handles condition compared only with those of the AP condition.

2.3.3 SP nerve cutaneous reflexes

Amplitudes of the middle latency reflexes from SP nerve stimulation were observed to differ across conditions for some muscles at specific points in the step cycle. The most pronounced differences observed across subjects were seen for the reflexes of muscles of the contralateral leg (with respect to the stimulation). Figure 2.2 shows the subtracted EMG traces for the cTA from all the walking conditions from one subject with SP nerve stimulation delivered at i toe-off (the contralateral leg is in early stance phase). For this subject, it can be seen that the amplitude of the excitatory middle latency cutaneous reflex in cTA was facilitated during walking with the arms crossed and while receiving unpredictable perturbations (Arms Crossed + AP), and suppressed during walking while holding stable handles (Handles), compared to the Normal condition (the thick grey lines in each graph).

The group averaged data are depicted in Figures 2.8 and 2.9. In Figure 2.8, the data are presented with the sign of the reflexes for individual subjects retained. Middle latency reflexes evoked with SP nerve stimulation were observed in all of the muscles studied. The amplitudes of the reflexes varied across the step cycle similar to what has been reported previously for reflexes evoked from SP nerve stimulation (Van Wezel et al. 1997; Haridas and Zehr 2003). In our analysis we did not specifically test for the phase-dependent modulation in reflex amplitude. However, the general pattern of reflex modulation was preserved across all of the walking conditions tested. For example, SP nerve stimulation resulted in inhibitory responses at the middle latency in iTA at i toe-off and i mid-swing, which was seen in each condition. In contrast, the responses in cTA were consistently excitatory at those same points in the step cycle.

The group averaged data for the reflex amplitude expressed in absolute values are depicted in Figure 2.9. Planned comparisons revealed task-specific modulation of the amplitude of the middle latency reflexes for at least one point in the step cycle for each muscle tested. Two pronounced patterns of task-specific adaptation emerged. First, the reflex amplitude was significantly greater during the Arms Crossed + AP condition than all other conditions in (a) cTA at i toe-off

Figure 2.8: Group averaged data for middle latency cutaneous reflexes arising from SP nerve stimulation with the *sign of the reflex retained.* Reflex amplitudes are normalized to the maximum EMG produced during normal, undisturbed walking for that muscle. The four points of the step cycle investigated are indicated along the abscissa. Each of the five conditions tested is indicated by a different symbol: open diamond - Normal walking; filled square - Walking with the arms crossed; filled triangle - Walking while being pulled forward and backward; open circle - Walking with the arms crossed and receiving forward and backward pulls; open triangle - Walking while holding stable fixed handles. Each point represents the mean with the standard error shown by the error bars.

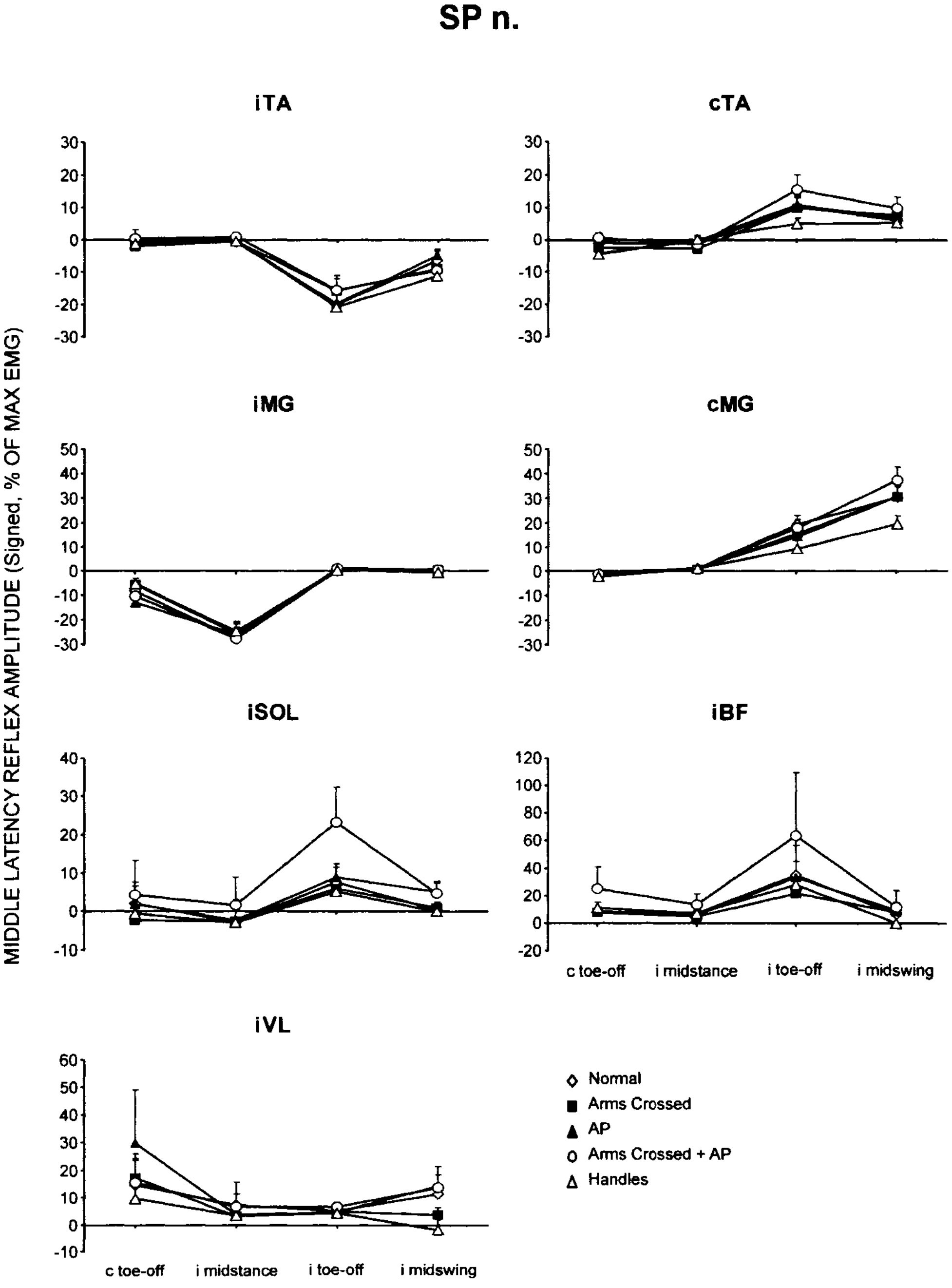
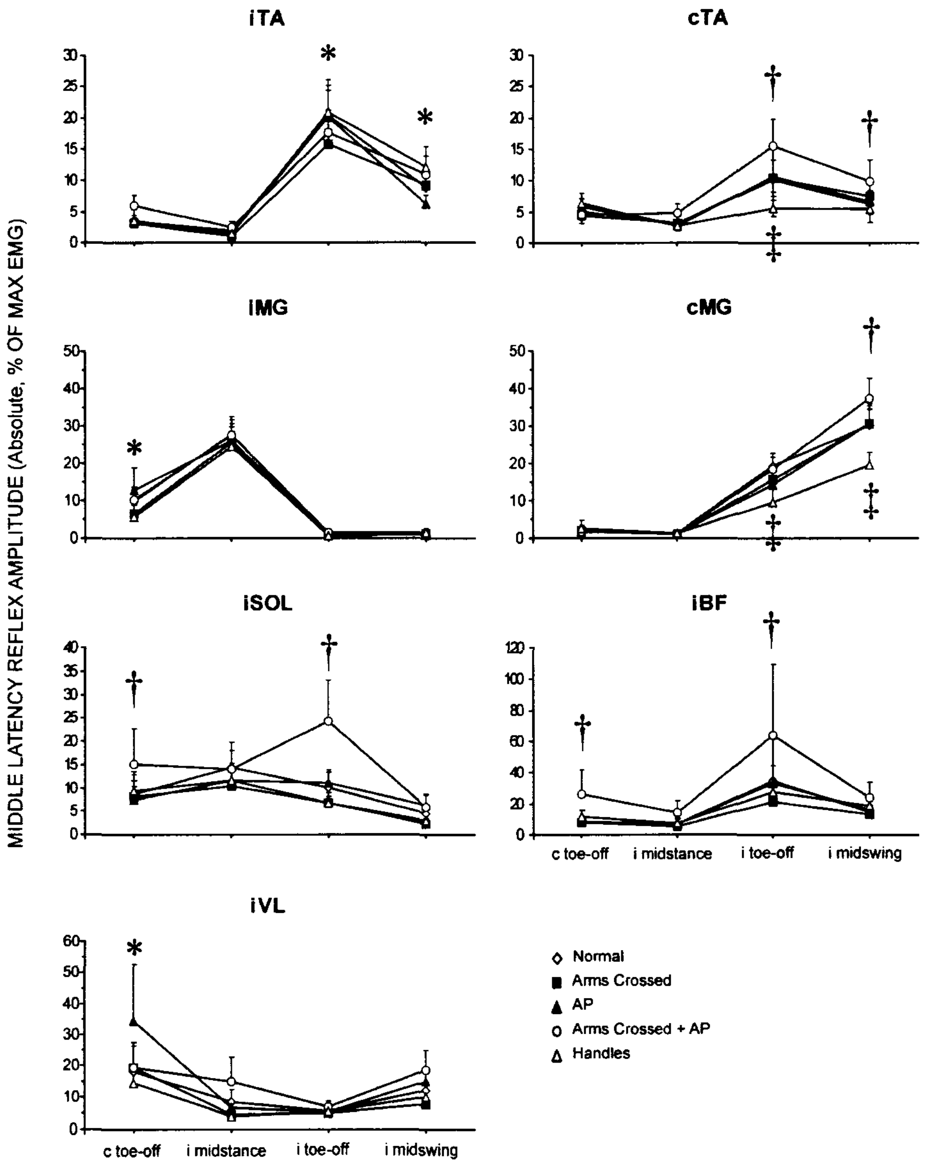


Figure 2.9: Group averaged data for middle latency cutaneous reflexes taken as their *absolute values* arising from SP nerve stimulation. Reflex amplitudes are normalized to the maximum EMG produced during normal, undisturbed walking for that muscle. The four points of the step cycle investigated are indicated along the abscissa. Each of the five conditions tested is indicated by a different symbol: open diamond - Normal; filled square - Arms Crossed; filled triangle - AP; open circle - Arms Crossed + AP; open triangle - Handles. Each point represents the mean with the standard error shown by the error bars. The † identify when the Arms Crossed + AP reflex amplitudes were significantly greater than all other conditions ($p < 0.05$). The ‡ identify when the Handles reflex amplitudes were significantly less than all other conditions ($p < 0.05$). Asterisks identify other points where at least one comparison was found to be significantly different.

SP n.



and i midswing; (b) cMG at i midswing; (c) iSOL at c toe-off and i toe-off; and (d) iBF at c toe-off and i toe-off. In addition, reflexes evoked during Arms Crossed + AP were elevated, but not significantly so, at several other points in the step cycle for these muscles. Second, the reflex amplitude was significantly decreased during the Handles condition, compared to all other conditions in (a) cTA at i toe-off; and (b) cMG at i toe-off and i midswing. The remaining differences identified by the planned comparisons were not consistent. For example, the planned comparisons identified reflexes in iVL evoked at c toe-off to be significantly greater during the AP condition, compared with all other conditions, whereas none of the other conditions were different from any others. In contrast, reflexes in iMG were significantly different between only the AP and Handles conditions. In iTA, the reflexes during the Arms Crossed condition were significantly smaller than during the Normal, Handles or AP conditions at i toe-off, but at i midswing, reflexes during the AP condition were smaller compared to only the Handles condition.

2.4 Discussion

In previous studies, cutaneous reflexes elicited from the electrical stimulation of nerves of the foot have been shown to modulate in amplitude in both a task-dependent and phase-dependent manner during locomotion (Yang and Stein 1990; Tax et al. 1995; Van Wezel et al. 1997). The pattern of reflex modulation that has been described previously has been argued to show the importance of these reflexes in maintaining stable locomotion. For example, electrical stimulation of the SP nerve has been suggested to evoke a pattern of reflex activity consistent with a stumbling corrective reaction if elicited during the swing phase of the step cycle (Zehr et al. 1997). In the present study, we examined the amplitude of cutaneous reflexes of both the ipsilateral and contralateral legs electrically evoked from two nerves innervating different parts of the foot during walking with varying degrees of stability. The main findings are (1) challenging the balance of the subjects during walking can lead to task-specific changes in reflex amplitudes, and (2) the influences are not related to a generalized change in reflex excitability; rather the changes observed are limited to specific reflex circuits at specific points in the step.

2.4.1 Methodological considerations

In our study a stimulus intensity of 2-3 times the radiating threshold was employed. Previously, this intensity of stimulation has been shown to elicit clear intra- and interlimb responses in several muscles (Haridas and Zehr 2003). However, it is a stronger stimulus than has been used by others to investigate cutaneous reflex modulation during walking (e.g. Duysens et al. 1990; Duysens et al. 1992; Tax et al. 1995; Van Wezel et al. 1997). Presently, both the SP and TIB nerve stimulation evoked middle latency reflexes during walking that were comparable to what has been reported previously (Yang and Stein 1990; Van Wezel et al. 1997; Haridas and Zehr 2003).

A fundamental difference in the analysis performed in this study compared with previous reports is the use of the absolute (unsigned) values to perform the statistical analysis. This was done because we noticed that on occasion reflexes evoked in some muscles were inhibitory in some subjects, excitatory in others, or were not expressed in yet others. Others have also described expression of reflexes that differed in sign between subjects (Duysens et al. 1990; Yang and Stein 1990; Aniss et al. 1992; Tax et al. 1995; Van Wezel et al. 1997). This phenomenon is best exemplified by the data at i heel-strike for iTA and iBF in Figure 2.6. The apparent sign reversal that is seen with some walking conditions is an aberration created by the grouped average effect of this phenomenon. A reversal in sign between task conditions would be an important finding; however, this in fact was not the case. Rather the sign of the evoked reflex at any point in the step for any individual subject remained the same across all walking conditions. The primary objective of this study was to characterize the change in reflex amplitude that may occur with changes in walking context. As none of the subjects displayed a sign reversal in the expressed reflex between walking conditions the absolute value of the reflex was calculated for each subject, thereby allowing us to identify the effect of walking condition on reflex amplitude per se. Note that the phase-dependent reflex reversals in some cutaneous reflexes that have been described previously were also noted in the present data. However, we were not primarily interested in the phase-dependent nature of the reflex per se. Instead, we ensured that no task-related reflex reversals occurred for any subject at any bin.

2.4.2 Context-dependent modulation of cutaneous reflexes?

The most robust new finding to arise from the present study is the task-dependent change in amplitude of the middle-latency reflexes with SP nerve stimulation. In 4 of 7 muscles recorded, reflexes evoked during the Arms Crossed + AP condition were significantly greater in amplitude than during other conditions. The muscles involved were both muscles of the contralateral leg (cTA and cMG), as well as iSOL and iBF. Thus, the important conclusion is that walking in a condition of highest threat to stability resulted in significantly increased middle latency reflex amplitudes in about half of the muscles studied. Additionally, this suggests that there was not a generalized increase in cutaneous reflex excitability during this task as about half of the muscles studied did not show this task-related increase in reflex amplitude. The most stable walking condition (Handles) resulted in significantly reduced reflex amplitudes in both cTA and cMG, and a trend of relatively lower amplitude reflexes in most of the other muscles tested. The implication is that the excitability of SP nerve elicited middle latency cutaneous reflexes in leg muscles is modulated with changing threat to stability during walking.

An important consideration is whether the differences in reflex amplitudes observed simply follow changes in the level of excitability of the target motoneuron pool, or if the modulation occurs via other factors. Walking under the various conditions did produce some changes in the ongoing EMG activity, notably in TA and VL. However, except for the changes in reflex amplitude noted in iTA, reflex amplitudes did not simply follow the background EMG. None of the marked changes noted in cTA, cMG, iSOL, or iBF are related to changes in ongoing levels of motor pool excitability between tasks. Therefore, these task-related adaptations in reflex amplitude must arise due to other factors associated with the changes in task.

Changes in amplitude were also noted between tasks for reflexes evoked with TIB nerve stimulation. However, these differences were not consistent with the hypothesized outcome. Moreover, the differences are not readily interpreted. For example, TIB nerve reflexes in cTA, iMG, cMG, iSOL, iBF, and iVL tended to adapt in the same direction for both the Arms Crossed + AP and Handles conditions, relative to Normal. The one consistent trend in the data was that the Arms Crossed condition tended to produce increased reflexes in the MG muscles, without any other task-related adaptations being observed. One possible reason for this seemingly random influence of the tasks on the reflex amplitudes is that the TIB nerve is a mixed nerve. Thus, stimulation at the intensities necessary to recruit cutaneous afferents will also activate muscle afferents (Yang and Stein 1990; Aniss et al. 1992; Van Wezel et al. 1997). Reflexes arising from muscle afferents have been shown to be regulated differentially from cutaneous reflexes (Zehr et al. 2001). Thus, the influence of the different tasks affects responses generated by each afferent group differentially such that the cumulative effect on motoneuron recruitment is a complicated interaction of the combined influences.

2.4.3 *Mechanism of adaptation*

This is the first study to characterize the influence of walking with an increased postural threat on the amplitude of cutaneous reflexes. Previously, Llewellyn et al. (1990) demonstrated that the amplitude of the soleus H-reflex, elicited with electrical stimulation of the tibial nerve, is suppressed during beam walking, compared to treadmill walking. By comparison, the cutaneous reflexes evoked in the present study were not suppressed during the walking task with the greatest postural threat. Rather, the main differences noted in the amplitude of cutaneous reflexes of the present study were facilitation of reflexes in specific muscles when postural threat was greatest. This indicates that the regulation of specific reflex pathways are modified according to the requirements of the task, rather than some generalized adaptation of reflexes by changing central states.

This sort of task and muscle-specific regulation of reflexes would suggest that a generalized increase or decrease in arousal does not account for the changes seen. In addition, changes in peripheral afferent discharge are unlikely to account for these changes as first, the walking patterns of the subjects was largely unaffected by the changes in task, and second, modulation of reflexes by the changing of afferent feedback tends to be seen across the movement cycle (Brooke et al. 1997). Moreover, the phase-dependent modulation of reflex amplitude was preserved across walking conditions (Figures 2.6 and 2.8), suggesting that any control of reflex pathways exerted by a central pattern generator for locomotion (for review, see Duysens et al. 2004; Zehr 2005) was not largely different. One potential mechanism to account for the very specific changes in reflex amplitude observed is from descending sources, in particular, the corticospinal tracts. Pijnappels et al. (1998) demonstrated that cortical facilitation of cutaneous reflexes can be observed during locomotion. Importantly, the amount of cortical facilitation exerted on the reflex pathways is phase-dependent. Thus, descending cortical influences are capable of producing specific phase-dependent changes in reflex output, such as those observed here.

An interesting observation is that when differences in the amplitude of SP nerve reflexes were noted between tasks, it was the most unstable task (Arms Crossed + AP) or the most stable task (Handles) that were identified. We had anticipated that intermediary changes in reflex amplitude would also be noted in the other conditions (Arms Crossed, or AP). This was not the case. One possible explanation for this lack of effect is that these other tasks did not induce a sufficient threat for there to be an adaptation in the reflexes tested.

2.4.4 Functional implications

The amplitude of cutaneous reflexes elicited in muscles bilaterally throughout the legs is modulated over the step cycle (Van Wezel et al. 1997; Zehr et al. 1997; Zehr et al. 1998; Haridas and Zehr 2003). This phase-dependent modulation of these reflexes occurs independently of the changing level of background activity (Van Wezel et al. 1997; Zehr et al. 1997). This has led to the suggestion that cutaneous reflexes are widely distributed, coordinated interlimb responses which are important for maintaining cadence and balance during the step cycle (Tax et al. 1995). In particular, it has been suggested that the responses evoked in the contralateral leg are important for the maintenance of stable locomotion, while the ipsilateral leg is engaged in the correction for the perturbation. The results of the SP nerve stimulation paradigm of the present study would be consistent with this hypothesis. Stimulation of the SP nerve leads to a coordinated interlimb response consistent with a stumbling corrective response (Zehr et al. 1997). In the present study, the responses evoked at i toe-off in iBF and iSOL were facilitated during the most unstable walking condition. The implication is that the increased facilitatory responses to SP nerve stimulation in iSOL and iBF observed at i toe-off in the present study ensure that the foot is able to clear an obstacle encountered at toe-off by increasing the net knee flexion and plantar flexion and permit the smooth transition from stance to swing. This is in agreement with a previous suggestion that the reflexes evoked with SP nerve stimulation produce a net plantar flexion response at the stance to-swing transition to facilitate clearance of an obstacle at that point in the step cycle (Zehr et al. 1997). In conjunction, the reflexes evoked in the cTA and cMG during the contralateral stance phase were also facilitated during the most unstable task. The implication is that the crossed reflexes to the stance limb, associated with the stumbling corrective response, are facilitated when walking in unstable conditions. This is similar to the results of Burke et al. (1991) who showed that cutaneous reflexes in the legs were increased when standing in unstable conditions. These authors also suggested that facilitation of cutaneous reflexes in the legs could serve to assist with stabilizing stance in an unstable environment. Presumably, this facilitation of excitatory reflexes in antagonist muscles of the contralateral ankle serves to assist in stabilizing the stance leg by increasing the stiffness at the ankle in an environment of balance uncertainty (Adkin et al. 2000; Misiaszek 2003; Misiaszek and Krauss 2005).

Rietdyk and Patla (1998) investigated context-dependent reflex control during two overground walking tasks in which the perceived threat to balance was manipulated. This was done by having subjects walk in unilimb (stance limb only source of support) and trilimb (stance leg plus two hands holding onto railings) conditions, and then tripping the subjects as they walked. The evoked responses were scaled to the level of threat to balance, with the more supportive walking condition (trilimb) showing suppressed reflexes in the stance limb. The authors suggested that the system modifies the reflex gain in order to optimize the recovery strategy output. Recently, we showed that having subjects walk with their arms folded across their chests increased the amplitude of early muscle activation in the legs following unpredictable pulls to the waist (Misiaszek and Krauss 2005). Increasing the postural threat in this way resulted in increased gain of the corrective responses in the legs. Conversely, the amplitude of corrective reactions in the leg muscles is decreased when subjects are asked to walk while holding stable handles (Misiaszek et al. 2000), suggesting suppression of corrective responses in the legs when postural threat is low. The findings of the present study are consistent with these more functional findings indicating that changing postural threat leads to a state-dependent adaptation in the expression of corrective reactions. This lends support to the hypothesis that cutaneous reflexes arising from the feet have a role in maintaining stability during walking. However, the present results also highlight that this is not achieved by a generalized increase or decrease in the excitability of the spinal circuitry. Rather, the adaptations are targeted to specific reflex circuits at specific points in the step cycle.

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Chapter 3 - Context-dependent modulation of interlimb cutaneous reflexes in arm muscles as a function of stability threat during walking[*]

3.1 Introduction

Electrical stimulation of cutaneous nerves in the foot during human locomotion has been shown to elicit reflexes which are modulated in amplitude depending on the task being performed (Duysens et al. 1993; Komiyama et al. 2000) as well as the phase of the step cycle in which the reflex is elicited (Duysens et al. 1990; Yang and Stein 1990; Duysens et al. 1992; Van Wezel et al. 1997; Zehr et al. 1997). Cutaneous reflex modulation may be important in assisting the maintenance of balance during walking (Zehr and Stein 1999). For instance, electrical stimulation of the superficial peroneal (SP; innervates the dorsum of the foot) nerve during the swing portion of the step cycle elicits reflex activity in the leg consistent with a "stumble corrective response", which would allow smooth forward progression of locomotion to continue (Van Wezel et al. 1997; Zehr et al. 1997). Recently, we showed that cutaneous reflexes in the leg are modulated in a task-dependent manner according to the level of postural threat. We discussed this modulation in terms of "context-dependency", in which the stability context plays a strong role in reflex modulation and also relates to the functional role of cutaneous reflexes (Haridas et al. 2005b). These results suggest cutaneous reflexes in the legs may assist in maintaining stability during walking.

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[*] *A version of this chapter has been accepted for publication. Haridas et al. (2006) J Neurophys 96: 3096-3103.*

A perturbation during walking may result in a corrective response that might include the use of the upper limbs to regain stability. For example, Marigold et al. (2002) demonstrated that an arm elevation strategy was typically incorporated in response to a slip during walking. Responses in the muscles of the arms have been shown to occur at latencies comparable to those in the legs following perturbations applied at the foot (Dietz et al. 2001; Marigold et al. 2003) or torso (Misiaszek 2003) during walking. The responses in the arms may contribute to whole-body responses in response to perturbations encountered during locomotion.

The neural mechanisms involved in coordinating these whole-body corrective responses are not well understood. One possible mechanism is via intersegmental reflex circuits, such as interlimb cutaneous reflexes. Interlimb cutaneous reflexes in the muscles of the upper limbs (evoked with stimulation at the foot) have been found after electrical stimulation of cutaneous nerves in the foot during locomotion. Dietz et al. (2001) reported responses in the muscles of the upper limbs to electrical stimulation of the distal tibial cutaneous nerve, which were more prominent during walking compared to static tasks such as sitting and standing. Haridas and Zehr (2003) found that interlimb cutaneous reflexes in the muscles of the upper limbs arising from SP nerve stimulation at the foot displayed significant phase-modulation and sign-reversal during treadmill locomotion. These results suggest the existence of functional and coordinated reflex pathways from the cutaneous nerves of the foot to the muscles of the arms during locomotion.

The task and phase specific adaptations in the amplitude of these reflexes suggest they may assist in regulating arm responses as part of a whole-body corrective response. If so, then these reflexes should be adapted to meet the specific postural demands of the task related to stability (e.g. "context-dependency"), similar to what we reported for cutaneous reflexes in the leg (Haridas et al. 2005b). Consequently, we hypothesize that interlimb cutaneous reflexes, elicited from stimulation of cutaneous nerves in the foot to muscles of the arm, will be facilitated when subjects walk in an environment with an increased postural threat. Portions of these results have been reported in abstract form (Haridas et al. 2005a).

3.2 Materials and Methods

3.2.1 Subjects and protocol

Twelve subjects between the ages of 20 and 35, with no history of neurologic, orthopedic or metabolic impairment participated with informed, written consent in a protocol approved by the Human Research Ethics Board (Health Research) at the University of Alberta. In this study we examined cutaneous reflexes evoked by electrical stimulation of a) the superficial peroneal (SP) nerve or b) the sural nerve. Subjects visited the lab on two different occasions, once for each nerve stimulation protocol. The order of presentation of nerve stimulation was randomized across subjects.

Subjects were asked to walk on a motorized treadmill at a self-selected speed (typically between 0.8 – 1.2 m/s). Cutaneous reflexes were elicited during

4 walking conditions: 1) with the arms free; 2) with the arms free, but while receiving unpredictable anterior-posterior perturbations applied at the waist (AP); 3) with the arms crossed across the chest (arms crossed); 4) with the arms crossed and receiving unpredictable anterior-posterior perturbations (arms crossed + AP). The order of presentation of the walking conditions was randomized across subjects. The purpose of the anterior-posterior perturbations during walking was to create an environment in which stability was unpredictably challenged. Therefore, cutaneous reflexes were not elicited during such perturbations, but rather during periods of steady walking between the perturbations. Subjects were instructed that they were free to grab for safety rails located in front and to the sides (~45 cm from lateral edge of the arms, ~75 cm in front of the subject) if they felt the need to do so to prevent falling. The purpose for having the arms crossed was to increase the threat of falling, by constraining the arms from assisting in balance recovery. Subjects reported feeling less stable when walking with their arms crossed or during conditions with anterior-posterior perturbations. We interpreted this to indicate that these manipulations achieved the objective of increasing the level of postural threat during walking. Subjects were informed before performing each walking condition as to whether perturbations would be elicited.

A detailed description of the device used for delivering the perturbations can be found elsewhere (Misiaszek and Krauss 2005). In brief, the perturbations were delivered by cables attached to a belt worn by the subject around the pelvis. From the belt, these cables ran in front and behind the subject to a drum to which a handle is attached. Pushing and pulling this handle caused anterior and posterior perturbations, respectively. A strain gauge placed on the lever arm of the handle was used to indicate when perturbations were applied. The magnitude of the perturbations was ~ 20% of the subjects' body weight. However, as the perturbations were used only to create an unpredictable environment, the magnitude was not specifically controlled. Perturbations were delivered randomly throughout the step cycle, with a frequency of approximately 3-5 per minute. This resulted in approximately 50 perturbations delivered for each perturbation walking trial that lasted between 10-15 min. The direction of perturbation (anterior vs. posterior) was also randomized.

3.2.2 Nerve stimulation

Cutaneous reflexes were evoked by trains (5 × 1.0 ms pulses @ 300 Hz) of isolated constant current stimulation (Grass S88 stimulator with SIU5 and CCU1 isolation and constant current units, AstroMed Inc.) applied to the SP or sural nerve of the right (ipsilateral; ipsi) leg using flexible 1 cm disposable surface electrodes (A10043-P, Vermed). Electrodes for the SP nerve were placed in a bipolar configuration on the anterior surface of the leg, near the crease of the ankle joint. The electrodes for sural nerve stimulation were placed on the lateral surface of the ankle, between the lateral malleolus and the Achilles tendon. The intensity of stimulation was set as a multiple of radiating threshold (RT) for each subject, approximately 3 × RT (actual means (± SEM): 2.8 × RT ± 0.12 for SP, 2.9 × RT ± 0.07 for sural), a value at which the stimulus is strong enough to evoke a reflex, yet is not perceived as painful by the subject. Radiating threshold was estimated as the lowest stimulus intensity at which the subject first perceived a clear radiating paresthesia into the innervation area of the nerve (SP: dorsum of foot; sural: lateral margin of the foot and plantar surface of the heel). This threshold value was checked between each walking trial to ensure that the stimulus properties remained similar throughout the experiment.

Stimuli were delivered such that no more than one stimulus was delivered within a single step cycle. Typically, stimuli were separated by approximately 2-6 s. Electrical stimuli were delivered at four points throughout the step cycle for SP nerve (contralateral (contra) toe-off, ipsi midstance, ipsi toe-off, and ipsi midswing) and sural nerve (ipsi heelstrike, ipsi midstance, ipsi toe-off, and ipsi midswing). These four points of the step cycle were chosen for the SP and sural nerve stimulation paradigms as they represent critical points in the phase-dependent pattern of modulation observed during walking (Zehr et al. 1997; Zehr et al. 1998; Haridas and Zehr 2003). The timing of stimulus delivery was controlled manually by the experimenter to occur near the target points of the step cycle. The experimenter was provided real-time feedback of the accuracy of the stimulus timing within the step cycle by viewing an oscilloscope display of the stimulus pulse along with the foot contact signals. Approximately 40 stimuli were delivered at each point in the cycle and then subsequently screened post hoc to select the stimuli occurring within the appropriate time points. This technique typically resulted in 15-30 stimuli being accepted for further analysis for each point in the step cycle for each walking condition (see below for the method used to screen the timing of the stimuli).

3.2.3 Recording and data acquisition

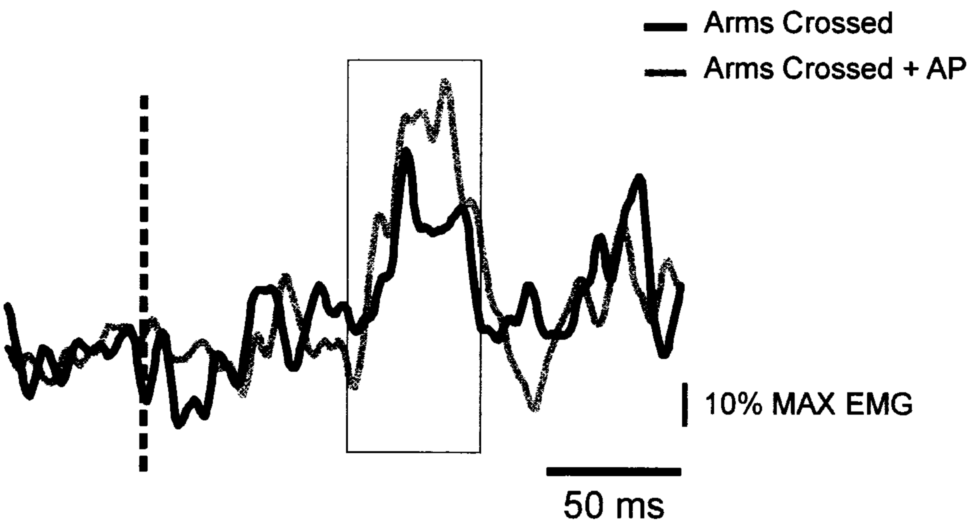
After shaving, abrading, and cleaning the skin with alcohol, disposable surface electrodes (A10012-60S, Vermed) were placed over the anterior deltoid (AD), posterior deltoid (PD), biceps brachii (BB), triceps brachii (TB), flexor carpi radialis (FCR), and extensor carpi radialis (ECR) of the arm ipsilateral (i) to the stimulation, as well as AD and PD of the contralateral (c) arm. Ground electrodes were placed over electrically neutral tissue. Signals were pre-amplified and bandpass filtered at 30 Hz - 3 kHz (P511 Grass Instruments, AstroMed Inc.). Kinematic data were collected using electrogoniometers (Biometrics, Inc.) placed across the ipsilateral ankle and elbow, secured with two-sided tape. Foot contact information was obtained from custom-made force sensitive resistors placed in the soles of the subject's shoes. EMG, kinematic, foot force sensor, stimulation, and perturbation force data were collected at a sampling rate of 1000 Hz and saved to disk using a custom-written LabView v.5 data acquisition routine and a National Instruments data acquisition card (PCI-MIO-16E-4, National Instruments, Austin, TX, USA). Post-hoc, the EMG signals were digitally full-wave rectified and then low-pass filtered at 50 Hz (4th order dual-pass Butterworth filter), while the kinematic signals were low-pass filtered at 50 Hz.

3.2.4 Data analysis

Data analysis for each subject began with the selection of 30 control step cycles for each walking trial (custom-written program, LabView v.5, National Instruments, Austin, TX, USA). Control steps were those for which no stimuli were applied and no perturbations occurred. Steps were also not included if a perturbation occurred within the preceding two steps. For each of the control steps, an 1800 ms data trace was captured starting at heelstrike of the ipsilateral foot, and averaged to produce an average control trace. Subsequently, reflex trials were selected and grouped into bins depending on the time at which the stimulus occurred within the step cycle. The four bins for each nerve stimulation protocol were defined as a time window spanning 10% of the average control step cycle duration, centered at that point in the step cycle (for example, if ipsilateral toe-off for a subject occurred at 56% of the step cycle, then stimuli applied between 51% and 61% of the step cycle were included). Ipsilateral heelstrike represented 0% of the step cycle. Once the stimulus trials were sorted into bins, the data traces were aligned to stimulus delivery, and averaged together. The average non-stimulated EMG trace was subtracted from the stimulated average trace, yielding a subtracted evoked EMG trace for each subject (Figure 3.1).

Cutaneous reflexes were calculated for the middle latency time window of 80-120 ms post-stimulus. The cutaneous reflex amplitude was calculated as the average amplitude of the subtracted trace within this time window. Cutaneous

Figure 3.1: Subtracted EMG traces for iPD after sural nerve stimulation for a single subject following electrical stimuli occurring at ipsilateral heelstrike. Both traces represent walking conditions in which the arms were crossed; arms crossed (thick black line), arms crossed + AP (thick grey line). The vertical dashed line indicates onset of stimulation. Rectangular box indicates the 80-120 ms post-stimulus) time window in which the middle latency reflex was analyzed. Arms crossed: walking with the arms folded across the chest, AP: walking with the arms folded across the chest while being perturbed.

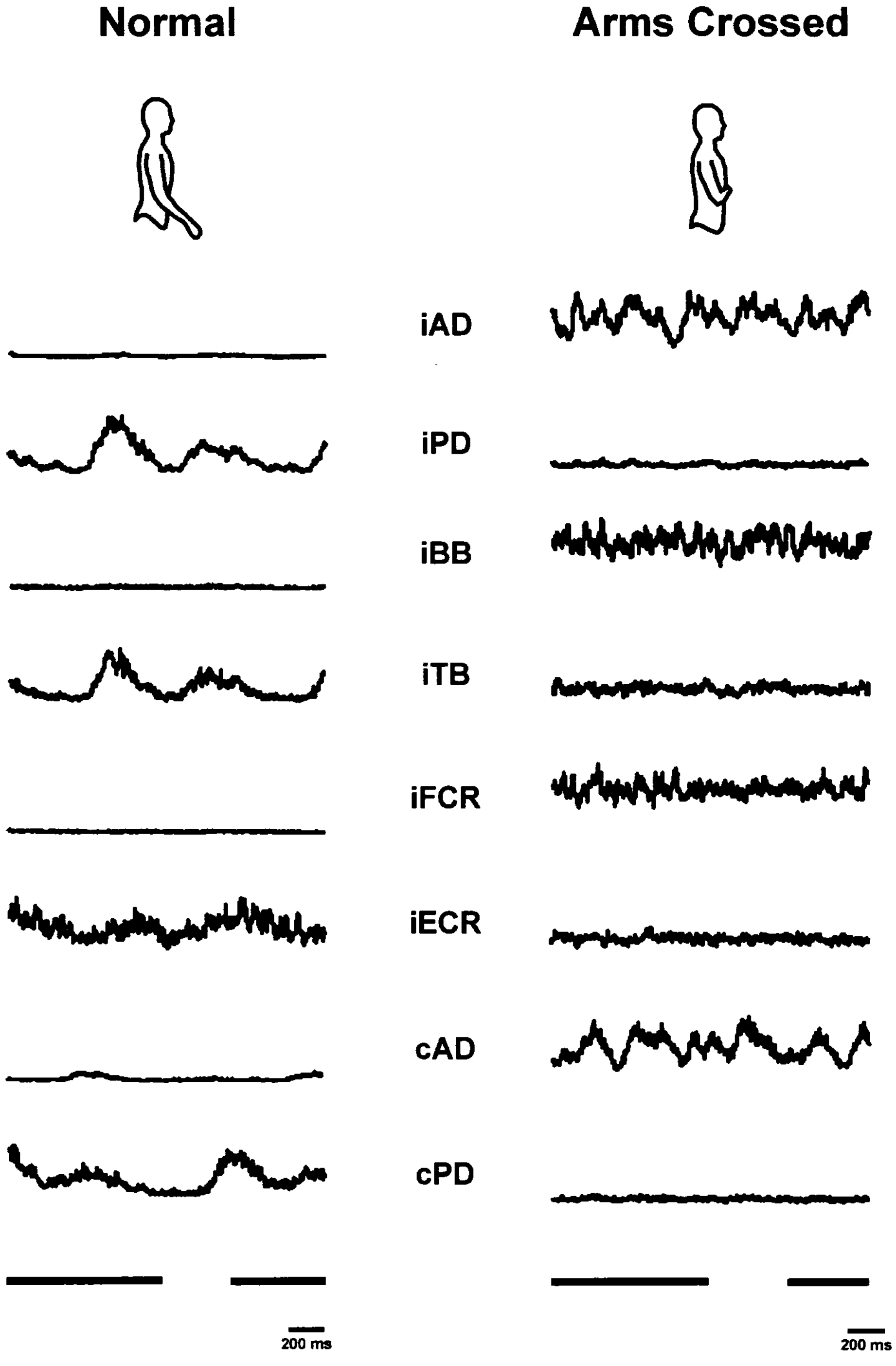


reflex amplitudes for each subject were normalized to the maximum EMG amplitude occurring during the step cycle for each muscle and expressed as a percentage. Ongoing background EMG activity and the ankle and elbow angles were also calculated for each of the walking conditions. These were calculated as the average full-wave rectified EMG amplitude or the joint angle occurring during each of the four bins of interest in the step cycle (see above).

3.2.5 Statistics

Since the arms are moving rhythmically in some conditions and restricted in other conditions, the pattern of muscle activation varied greatly between conditions. As a result, comparisons were made between tasks in which the arms were either allowed to swing in a natural manner (normal vs. AP), or were crossed in front of the subject (arms crossed vs. arms crossed + AP). This allowed for comparisons between tasks in which the background EMG of the arm muscles was similar (Figure 3.2). Statistical analysis was performed using the averaged normalized values for each subject, from each part of the step cycle. For each nerve stimulation paradigm and for each muscle studied, a two-way repeated measures analysis of variance (ANOVA; condition [2] x bin [4]) was used to isolate the sources of variance. Using the experimental error calculated by the ANOVA, planned comparisons were then performed for the reflex amplitudes between the two conditions of comparison at each bin. Similar analysis was performed on the background EMG as well as ankle and elbow joint

Figure 3.2: Average EMG for 30 control steps (starting at ipsi heelstrike) taken from a single subject. Left column displays EMG during the normal walking condition, and EMG during the arms crossed condition is shown in the right column. This subject displayed relatively tonic activity of the arm muscles during the arms crossed walking conditions, contrasting the more rhythmic activity observed during the normal walking conditions. EMG is scaled equally between the two walking conditions shown. Horizontal black line at the bottom of each column represents the stance phase of the step cycle.



angles. One-way repeated measures ANOVAs were also performed on step cycle durations for the group average data. Statistical significance was set at $p < 0.05$.

3.3 Results

In this study, we were interested in understanding the context-dependent modulation of interlimb reflexes. Interlimb cutaneous reflexes are usually not expressed if the muscle is not active; in particular, inhibitory reflexes cannot be observed without some level of activity. In our analysis, we only included data from a muscle for each subject if there was a clear response to the stimulation (see Materials and Methods) in at least one condition for at least one point in the step cycle. This led to data from a variable number of subjects being included in the statistical analysis for each muscle. In the figures showing the group averaged data, the numbers of subjects included in the analysis is detailed in the figure legend. The task-related differences reported below for the group averaged data were observed in all of the individual subjects included in the analysis.

3.3.1 Background EMG and kinematics

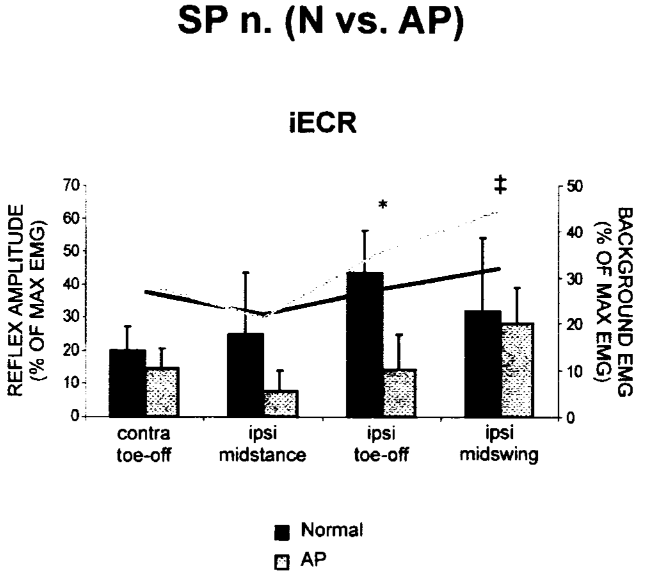
While walking on the motorized treadmill, subjects were asked either to swing their arms in a normal manner (normal and AP conditions), or to cross the arms in front (arms crossed and arms crossed + AP conditions). Shown in Figure 3.2 is single-subject average background EMG data during the step cycle for the normal (arms swinging; left column) and arms crossed (right column) walking conditions. The arms crossed conditions generally displayed relatively tonic EMG activity in some muscles, whereas in the arms free conditions some muscles displayed phasic modulation. Therefore, we compared the background EMG for each muscle between conditions in which the arms were being similarly used. Consequently, comparisons were only made between the two conditions for which the arms were free (normal versus AP conditions), or between the two conditions for which the arms were crossed (arms crossed versus arms crossed + AP conditions).

There was no main effect of walking condition ($p > 0.05$) on ipsilateral ankle and elbow angles between tasks of similar arm movement across all subjects. One-way repeated measures ANOVAs revealed no significant differences ($p > 0.05$) in step cycle durations between walking conditions.

3.3.2 Arms swinging rhythmically

When the arms were moving rhythmically (similar to normal walking), middle latency interlimb cutaneous reflex amplitude values did not show many significant differences between the normal and AP walking conditions. A similar pattern of modulation was observed for each walking condition across the step cycle. Shown in Figures 3.3 and 3.4 are the average middle latency interlimb cutaneous reflex amplitude values (and corresponding average background EMG values) for muscles in which significant differences between the normal and AP

Figure 3.3: Group averaged data for the middle latency interlimb cutaneous reflexes arising from SP nerve stimulation between conditions in which the arms were not restricted for the only muscle in which a significant difference was found. The four points of the step cycle investigated are shown on the abscissa. Average middle latency interlimb cutaneous reflex amplitude values are depicted as black (normal) and grey (AP) bars, with the standard error shown. Values for middle latency reflexes are shown on the left ordinate. Data from 7 subjects contributed to this figure. Average background EMG is represented by the black (normal) and grey (AP) lines, with its values along the right ordinate. Both reflex and background EMG values are normalized to the maximum EMG produced during normal, undisturbed walking. *: significant difference ($p < 0.05$) in middle latency interlimb cutaneous reflexes; ‡: significant difference ($p < 0.05$) in background EMG.

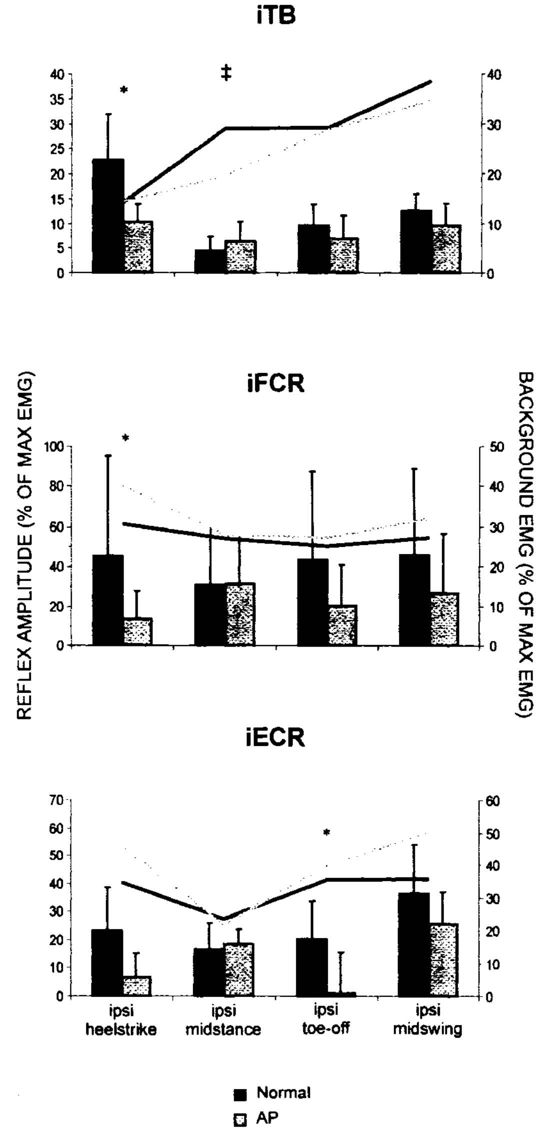


SP n. (N vs. AP)

iECR

Figure 3.4: Group averaged data for the middle latency interlimb cutaneous reflexes arising from sural nerve stimulation for muscles in which a significant difference was found between conditions in which the arms were not restricted. The four points of the step cycle investigated are shown on the abscissa. Average middle latency interlimb cutaneous reflex amplitude values are depicted as black (normal) and grey (AP) bars, with the standard error shown. Values for middle latency reflexes are shown on the left ordinate. These data were derived from 12, 11 and 9 subjects, for iTB, iFCR and iECR, respectively. Average background EMG is represented by the black (normal) and grey (AP) lines, with its values along the right ordinate. Both reflex and background EMG values are normalized to the maximum EMG produced during normal, undisturbed walking. *: significant difference ($p < 0.05$) in middle latency interlimb cutaneous reflexes; ‡: significant difference ($p < 0.05$) in background EMG.

Sural n. (N vs. AP)



walking conditions were found during the SP and sural nerve stimulation protocols respectively. The general trend observed was that the reflex amplitude during the AP walking condition was lower as compared to normal walking. A good example of this is seen in iECR with SP nerve stimulation (Figure 3.3). The only significant difference observed between the two walking conditions in this muscle was observed at ipsi toe-off, where the reflex amplitude was lower during the AP condition compared to the normal walking condition. In contrast, the background EMG activity for iECR was found to be significantly higher at ipsi midswing during the AP walking condition.

With the sural nerve stimulation paradigm, only three out of eight muscles recorded displayed significant differences in reflex amplitude values between walking conditions (Figure 3.4). Similar to SP nerve stimulation, the middle latency interlimb cutaneous reflex amplitude with sural nerve stimulation was significantly lower during the AP condition as compared to the normal walking condition in all three muscles, with iFCR and iTB displaying these differences at ipsi heelstrike, and at ipsi toe-off for iECR. The corresponding background EMG activity between the normal and AP walking conditions were comparable. The only significant difference in background EMG activity for all these muscles across the step cycle was observed in iTB at ipsi midstance, where the EMG activity was significantly lower during the AP walking condition compared to the normal condition.

3.3.3 Arms crossed

In contrast to the walking conditions in which the arms were moving rhythmically, there were more significant differences observed between walking conditions in which the arms were restricted from moving (arms crossed). The overall trend observed was higher middle latency interlimb cutaneous reflex amplitude values for the arms crossed + AP walking condition, the more unstable of the two walking conditions in which the arms were crossed. Figures 3.5 and 3.6 shows muscles that displayed significant differences in reflex amplitude values between the two arms crossed walking conditions with SP and sural nerve stimulation respectively. The average background EMG values are also displayed. During the SP nerve stimulation paradigm, significantly higher middle latency reflex amplitude values for the arms crossed + AP walking condition were observed in iAD at ipsi toe-off, iECR and cPD at contra toe-off, and iFCR at ipsi midswing (Figure 3.5). These differences in reflex amplitude were observed despite background EMG levels that were similar between the two conditions. The only significant difference in background EMG activity was observed for iFCR, with the EMG during the arms crossed + AP condition being higher at ipsi toe-off.

Similarly, the majority of muscles recorded displayed significant differences in reflex amplitude values between the two walking conditions during the sural nerve stimulation protocol (Figure 3.6). Significant differences were observed at ipsi midstance for iAD and iTB, and at ipsi toe-off for iFCR and iECR. Ipsilateral PD showed significant differences at two points of the step cycle, ipsi

Figure 3.5: Group averaged data for the middle latency interlimb cutaneous reflexes arising from SP nerve stimulation for muscles in which a significant difference was found between conditions involving the arms being crossed. The four points of the step cycle investigated are shown on the abscissa. Average middle latency interlimb cutaneous reflex amplitude values are depicted as black (arms crossed) and grey (arms crossed + AP) bars, with the standard error shown. Values for middle latency reflexes are shown on the left ordinate. These data were derived from 10, 6, 5 and 9 subjects, for iAD, cPD, iFCR and iECR, respectively. Average background EMG is represented by the black (arms crossed) and grey (arms crossed + AP) lines, with its values along the right ordinate. Both reflex and background EMG values are normalized to the maximum EMG produced during the arms crossed walking condition. *: significant difference ($p < 0.05$) in middle latency interlimb cutaneous reflexes; ‡: significant difference ($p < 0.05$) in background EMG.

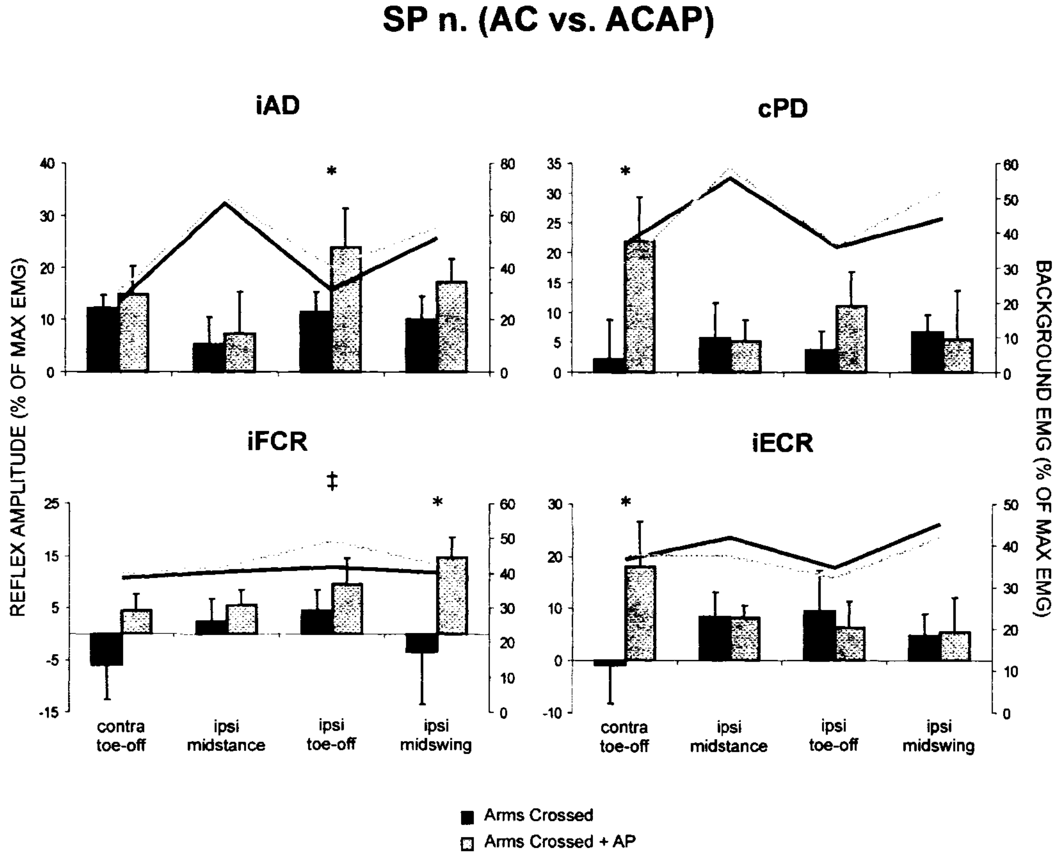
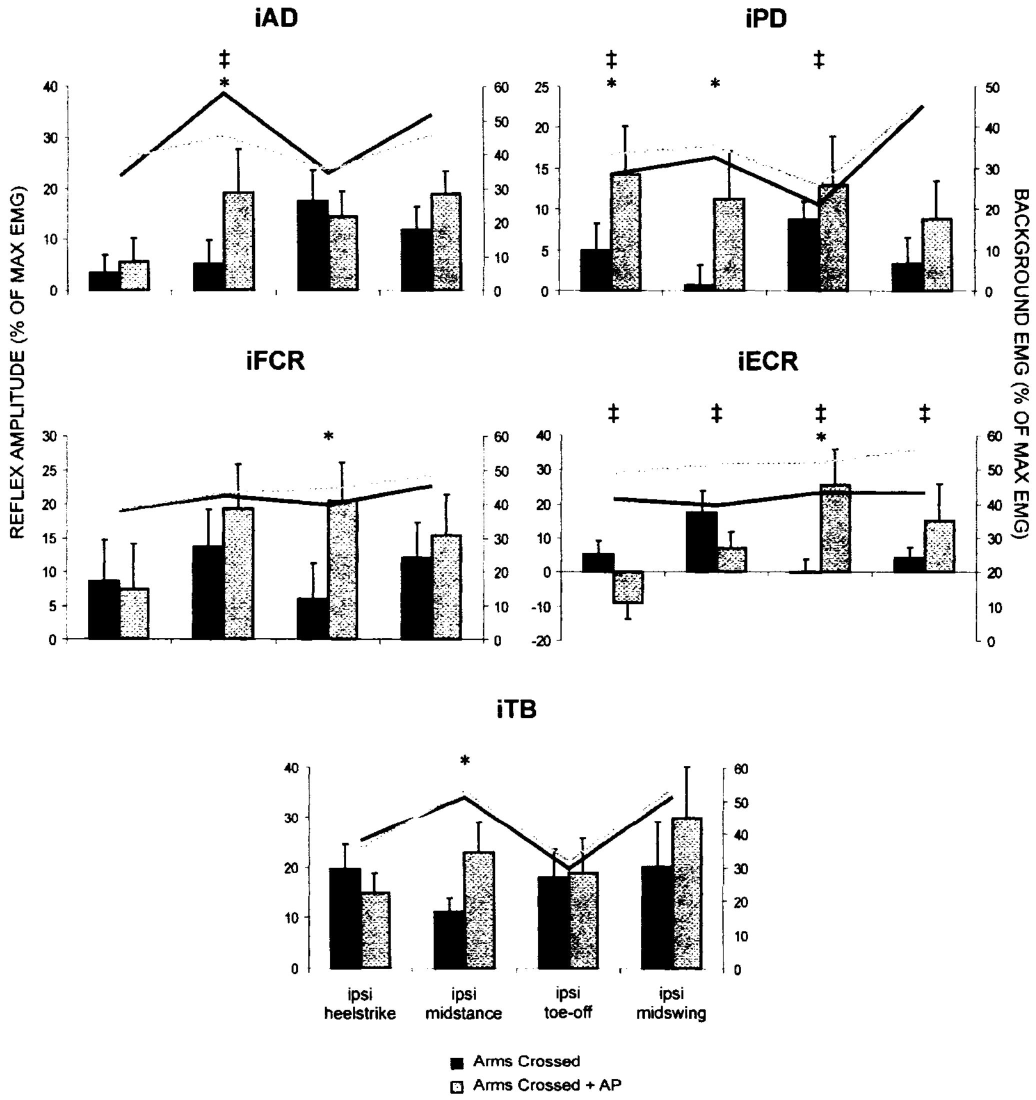


Figure 3.6: Group averaged data for the middle latency interlimb cutaneous reflexes arising from sural nerve stimulation for muscles in which a significant difference was found between conditions involving the arms being crossed. The four points of the step cycle investigated are shown on the abscissa. Average middle latency interlimb cutaneous reflex amplitude values are depicted as black (arms crossed) and grey (arms crossed + AP) bars, with the standard error shown. Values for middle latency reflexes are shown on the left ordinate. These data were derived from 9, 10, 9, 10 and 8 subjects, for iAD, iPD, iFCR, iECR and iTB, respectively. Average background EMG is represented by the black (arms crossed) and grey (arms crossed + AP) lines, with its values along the right ordinate. Both reflex and background EMG values are normalized to the maximum EMG produced during the arms crossed walking condition. *: significant difference ($p < 0.05$) in middle latency interlimb cutaneous reflexes; ‡: significant difference ($p < 0.05$) in background EMG.

Sural n. (AC vs. ACAP)



heelstrike and ipsi midstance. Despite these differences in reflex amplitudes, the EMG activity between the two arms crossed walking conditions was similar during sural nerve stimulation. The exception to this was observed in iECR, where significant differences in background EMG were seen at all points of interest in the step cycle. Significant differences were also observed at ipsi midstance for iAD, and iPD at ipsi heelstrike and ipsi toe-off.

In addition, a reversal in reflex sign was observed between walking conditions with both nerve stimulation paradigms in the muscles of the wrist. With SP nerve stimulation, reflex reversal was observed in iFCR at contra toe-off and ipsi midswing, and in iECR at contra toe-off (Figure 3.5). At each of these occurrences, inhibitory middle latency reflex amplitude values were observed during the arms crossed condition, in contrast to the facilitatory reflexes for the arms crossed + AP walking condition. Reflex reversal was also observed during the sural nerve stimulation paradigm, in which iECR displayed a facilitatory middle latency reflex amplitude value at ipsi heelstrike during the arms crossed walking condition, which became inhibitory during the arms crossed + AP condition (Figure 3.6). Of the four occurrences of reflex reversals observed between tasks for both nerve stimulation paradigms, two were found to be significantly different (SP nerve: iFCR at ipsi midswing; iECR at contra toe-off). These reflex reversals in the muscles of the wrist were not observed in walking conditions when the arms were not restricted. For these walking conditions (normal, AP), interlimb cutaneous reflexes evoked with SP and sural nerve stimulation were always excitatory.

3.4 Discussion

The arms have been shown to contribute in whole-body corrective responses to perturbations encountered during walking. Interlimb cutaneous reflexes could assist in coordinating these corrective responses, as they have been found in the arms with cutaneous nerve stimulation at the foot (Dietz et al. 2001; Haridas and Zehr 2003). If so, these reflexes should be regulated in a context-dependent manner, as a function of the level of threat to stability, as we observed with cutaneous reflexes (Haridas et al. 2005b). This study investigated the amplitude of interlimb cutaneous reflexes in the arms evoked from electrical stimulation of the SP and sural nerves in the foot during walking while varying the degree of stability. The main observations were i) that varying the level of stability during walking influenced the amplitude of interlimb cutaneous reflexes in the upper limbs, and ii) the differences observed between walking conditions were dependent upon the nerve being stimulated and the demands of the task.

3.4.1 Mechanisms of adaptation

To our knowledge, this study is the first to describe the modulation of interlimb cutaneous reflex amplitude in relation to walking in an environment in which postural stability is challenged (i.e. the general constraints and requirements of the task (walking) are unchanged, but the context within which the task is performed is altered). Recent work has described the influence of walking in such an environment on cutaneous reflexes in the legs (Haridas et al. 2005b). In the present study, the general finding was interlimb cutaneous reflexes evoked from the foot were facilitated when postural threat was greatest with the arms crossed. In contrast, when the arms were swinging freely, these reflexes were generally suppressed when postural threat was greatest. While walking with the arms crossed, the amplitude of interlimb cutaneous reflexes evoked with both SP and sural nerve stimulation were significantly greater when perturbations were also delivered. This finding was not observed in all muscles recorded, but rather isolated in muscles of the shoulder and wrist. When the arms were allowed to swing freely, the interlimb cutaneous reflexes observed in the muscles of the arms were relatively similar regardless of whether perturbations were delivered. This difference in the influence of postural threat on these reflexes in relation to the task of the arms (free vs. crossed) suggests that similar to previous findings with cutaneous reflexes (Haridas et al. 2005b), specific interlimb cutaneous reflex pathways are regulated appropriate to the task requirements and context, rather than some generalized reflex adaptation.

Differences in reflex amplitude between walking conditions could be due to differences in the ongoing EMG activity, which is representative of changes in motoneuronal pool excitability. The significant differences in interlimb cutaneous reflex amplitudes between tasks in which the arms were crossed were generally not associated with differences in the level of ongoing EMG activity. There were only three occurrences in which a significant difference between the two walking conditions in both background EMG and reflex amplitude value were observed. For one of these occurrences (Figure 3.6: sural nerve; iAD at ipsi midstance), the reflex was facilitated during the arms crossed + AP walking condition, despite significantly lower background EMG. For all other changes in interlimb cutaneous reflex amplitude values noted, the background EMG was similar between conditions. This also holds true for the occurrences of reflex reversals noted when the arms were crossed. For example with SP nerve stimulation, reflex reversals in the muscles of the wrist were observed at points in the step cycle where the corresponding background EMG activity was similar between walking conditions (Figure 3.5). Thus, the significantly higher interlimb cutaneous reflex amplitudes observed during walking conditions with the greatest postural threat are not simply due to an increase in ongoing muscle activity.

Reversal of cutaneous reflexes has previously been shown during locomotion in the cat (Forssberg et al. 1975; Duysens 1977) and human (Duysens et al. 1990; Yang and Stein 1990; Van Wezel et al. 1997). In these studies, there was a reversal in the sign of reflexes in the legs which was dependent on the phase of the step cycle. Cutaneous reflexes in the legs have also been shown to undergo reflex reversals between different tasks. Komiyama et al. (2000) reported that during standing, inhibitory cutaneous reflexes were predominant in contrast to mainly facilitatory reflexes observed during walking. To our knowledge, this is the first study to report reversal of interlimb cutaneous reflexes that are dependent upon the level of postural threat (i.e. context-dependency) during walking. Phase-dependent cutaneous reflex reversals occurring in the legs during cat locomotion has been attributed to parallel inhibitory and excitatory pathways to motoneurons (Duysens 1977; Andersson et al. 1978). Similarly, De Serres et al. (1995) suggested the cutaneous reflex reversal observed in tibialis anterior during human locomotion might be due to a shift in the weighting of parallel excitatory and inhibitory pathways from cutaneous afferents to the motor units of the muscle. A comparable mechanism is suggested for the context-dependent reflex reversal noted in the present study.

The results of the present study suggest specific regulation of interlimb cutaneous reflex pathways in a task-dependent manner as opposed to a generalized change in reflex excitability. Cutaneous reflexes in the muscles of the arms have been shown during rhythmic movements such as arm cycling (Zehr and Kido 2001) and human walking (Zehr and Haridas 2003). Zehr et al. (2004) suggested that these reflexes found in the muscles of the upper extremities are under the control of a central pattern generator (CPG). However, the similar pattern of phase-dependent interlimb cutaneous reflex modulation between walking conditions suggests it is unlikely that the differences in interlimb cutaneous reflex amplitude values observed between walking conditions are due to differential CPG control of reflex pathways. The specific regulation of interlimb cutaneous reflex pathways could be mediated by descending sources such as the corticospinal tract, as cutaneous reflexes in the muscles of the leg during walking have been shown to be facilitated with cortical stimulation (Pijnappels et al. 1998). The transmission of interlimb cutaneous reflexes may partially involve propriospinal projections connecting the upper and lower limbs (Zehr et al. 2001). In addition, the latency range (80 – 120 ms) in which these reflexes were observed allows for a supraspinal transmission of these responses (Nielsen et al. 1997; Christensen et al. 1999). Therefore, it is likely that supraspinal effects contribute to the task-related modulation of interlimb cutaneous reflexes observed in this study.

In the present study, interlimb cutaneous reflexes were elicited by delivering electrical stimulation to nerves in the foot to subjects while they walked under varying levels of postural threat. During the sural nerve stimulation protocol, more significant differences in reflex amplitude between tasks in which the arms were allowed to swing freely were observed as compared to SP nerve stimulation. This observation may serve as an example of nerve-specificity, which has been reported previously (Van Wezel et al. 1997; Zehr et al. 1997; Komiyama et al. 2000). The suggested nerve-specificity reported in this study may be explained by the innervation area of the nerves stimulated. The sural nerve innervation area includes a portion of the plantar surface of the heel. Sensory information from this region of the foot may contribute to regulation of foot placement (Kostov et al. 1999), which would be important when walking in an unstable environment and therefore be regulated in a context-dependent manner. In contrast, the innervation area of the SP nerve provides sensory information from the dorsum of the foot, which may not be of functional relevance in the current experimental context. More context-related perturbations (i.e. at the dorsum of the foot) may affect reflexes elicited with SP nerve stimulation to a greater extent than observed in the present study.

3.4.2 Evidence of a functional role for interlimb cutaneous reflexes?

In contrast to the walking conditions in which the arms were swinging freely, there were markedly more significant differences between the arms crossed and arms crossed + AP walking conditions. This was observed for both SP and sural nerve stimulation. One possibility for the difference noted may be the different number of muscles that are active for each arm position. As shown in Figure 3.2, more muscles are active when the arms are crossed, in contrast to when the arms are allowed to swing rhythmically. The greater number of muscles in the arms being activated would increase the probability of interlimb cutaneous reflexes being elicited, as cutaneous reflexes generally require activity in the muscles to be expressed. Consequently, there is a greater likelihood of observing task-dependent differences in reflex amplitudes.

Interlimb cutaneous reflex amplitudes were generally facilitated for the arms crossed + AP walking condition as compared to the arms crossed condition (Figures 3.5 and 3.6), and these differences were observed primarily in the muscles of the shoulder girdle and wrist. In contrast, there was a general suppression of interlimb cutaneous reflexes while the arms were swinging rhythmically, where during the AP walking condition these reflexes were suppressed compared to normal walking (Figures 3.3 and 3.4), observed primarily in the muscles of the wrist. This trend in reflex amplitude due to the task of the arms may be indicative of a functional role for the interlimb cutaneous reflexes observed. When the arms are allowed to swing rhythmically, they are available to contribute towards any needed corrective responses in response to a perturbation. Furthermore, since the arms are allowed to move freely, there are multiple strategies in which they may be used to participate in a corrective response. The diversity of options available to execute a corrective response (e.g. reaching for safety rails around the treadmill) may lead to increased variability, which may contribute to the lack of significant differences observed between the normal and AP walking conditions. This may be particularly true for the muscles of the shoulder girdle, which may be more relevant for executing a gross movement of the arm related to regaining stability. This variability with the arms swinging freely is similar to findings by Misiaszek (2003), who noted inconsistent responses in the muscles of the arms between subjects in response to perturbations received during walking.

In contrast, having the arms crossed in front of the body limits their contribution to assisting in any corrective responses. To use the crossed arms for maintaining stability during walking, all subjects would have to first uncross them regardless of the next course of action. This standardization of arm utilization, at least initially, may account for the more consistent results across subjects and the changes noted. It follows that the higher interlimb cutaneous reflex amplitudes observed bilaterally in the muscles of the arms during the arms crossed + AP condition may serve to assist in a coordinated corrective response, such as to uncross the arms to allow a reaching movement towards the safety rails positioned around the treadmill. The significantly higher reflex value in iTB during sural nerve stimulation could also contribute in an uncrossing and reaching response. In addition, the higher interlimb reflex values in the muscles of the wrist could facilitate in a guided reaching response towards a stable support.

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Chapter 4 - Adaptation of cutaneous stumble correction when tripping is part of the locomotor environment*

4.1 Introduction

Spinal reflexes during human locomotion have been widely studied, and have been shown to change in amplitude during walking (reviewed in Zehr and Stein 1999). Specifically, reflexes in the muscles of the legs evoked from electrical stimulation of cutaneous nerves in the foot are modulated according to the phase of the step cycle (Yang and Stein 1990; Duysens et al. 1992; Van Wezel et al. 1997; Zehr et al. 1997) as well as the task being performed (Duysens et al. 1993; Komiyama et al. 2000). Both Zehr et al. (1997) and Van Wezel et al. (1997) observed cutaneous reflexes in the muscles of the leg with electrical stimulation of the superficial peroneal (SP; innervating the dorsum of the foot) nerve during walking. During swing phase, SP nerve stimulation elicited a suppression of ankle flexor activity as well as excitation of the proximal muscles of the leg. These responses in the muscles were associated with a reduction in dorsiflexion and an increase in knee flexion. The authors suggested the evoked response was representative of a “stumbling corrective response”, comparable to that first reported in the cat by Forssberg (1979). It was argued that this response served a functional role, by allowing the swing limb to smoothly progress forward when encountering an obstacle during locomotion.

Therefore, cutaneous reflexes may serve to assist in maintaining stability during walking. If so, these reflexes should be altered when walking in an

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** A version of this chapter has been submitted to J Neurophys for publication (July 17, 2007)* environment in which stability is challenged. A recent study in our laboratory showed that cutaneous reflexes evoked by electrical stimulation of the SP nerve were modulated to the context of the behaviour being performed, primarily in the muscles of the non-stimulated (contralateral) leg (Haridas et al. 2005). Interestingly, cutaneous reflexes in the ipsilateral leg were less affected by varying the level of generalized postural threat induced by whole-body perturbations applied at the waist.

If the observed responses by Zehr et al. (1997) are indicative of a generalized role for stumble correction during walking as suggested above, then the context-dependent modulation that was observed in the muscles of the contralateral leg in Haridas et al. (2005) should have also been observed in the muscles of the ipsilateral leg. Mechanical perturbations were delivered at the torso to create a general unpredictable environment in which stability was challenged (Haridas et al. 2005). These perturbations may have had little relevance for cutaneous feedback arising from the innervation area of the SP nerve, which is argued to be important for correcting swing leg trajectory to avoid stumbling (see Zehr and Stein 1999). It follows that mechanical perturbations delivered to the dorsum of the foot, which would affect ipsilateral swing limb motion during walking, would more closely emulate a perturbation for which the cutaneous feedback arising from SP nerve stimulation is specifically tuned. The utilization of pertinent mechanical perturbations to the cutaneous nerve being stimulated may result in specific modulation of cutaneous reflexes in the legs during walking. Therefore, we hypothesized that cutaneous reflexes evoked by electrical stimulation of the SP nerve will be modulated when subjects walk in an environment in which mechanical perturbations were delivered to the cutaneous field innervated by the SP nerve, thereby creating a threat of a trip. Portions of these results have been reported in abstract form (Haridas et al. 2006).

4.2 Materials and Methods

4.2.1 Subjects and protocol

Ten subjects (6 males and 4 females; age range of 22 and 33), with no history of neurologic, orthopedic or metabolic impairment participated in this study. All procedures conformed to the Declaration of Helsinki for experiments on humans, and were approved by the Human Research Ethics Board at the University of Alberta. All subjects provided informed, written consent.

Subjects were asked to walk on a motorized treadmill at a self-selected speed (typically between 0.8 and 1.2 m/s). Cutaneous reflexes were elicited during 4 walking conditions: (1) normal; with the arms free (N); (2) normal while receiving mechanical perturbations to the dorsum of the ipsilateral foot (NP); (3) with the arms crossed across the chest (AC); (4) with the arms crossed while receiving mechanical perturbations at the dorsum of the foot (ACP). The order of presentation of the walking conditions was randomized across subjects. Cutaneous reflexes were not elicited simultaneously with the mechanical perturbations (see below), but rather during periods of steady walking between perturbations. Safety rails were located around the treadmill (~45 cm from lateral edge of the arms, ~75 cm in front of the subject), and subjects were instructed to grab hold of the rails if they felt a fall was imminent. Subjects were informed before performing each walking condition whether perturbations would be elicited.

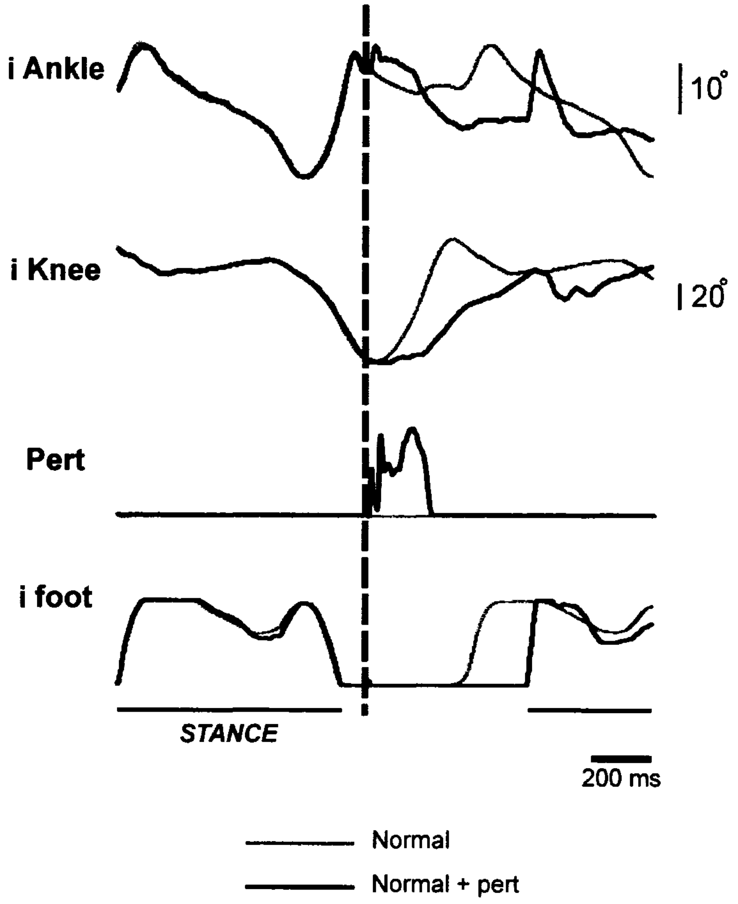
Mechanical perturbations were manually applied by tapping a steel rod against the dorsum of the right foot. The dorsum of the foot was selected for the location of the perturbation as it is also the innervation area for the SP nerve (see below). A force sensor was attached to the steel rod to indicate when perturbations were applied. Perturbations were always delivered at early swing, as perturbations to the foot dorsum encountered naturally would likely occur at this point in the step cycle. Furthermore, the suggested functional role of the SP nerve in a “stumbling corrective response” has been noted during the swing phase (Van Wezel et al. 1997; Zehr et al. 1997). Perturbations were delivered in a random manner such that subjects were unable to predict which step cycle would be perturbed. This resulted in approximately 4-6 mechanical perturbations being delivered per minute. However, since perturbations were always delivered at the same point of the step cycle, subjects were able to anticipate the effect of encountering mechanical perturbations to the dorsum of the foot at early swing as the experiment progressed.

The researcher was positioned adjacent to the treadmill to the right and just behind the subject. Subjects were instructed to look forward during each walking condition. The subjects indicated that they were not able to observe the researcher or the rod delivering the perturbations to the dorsum of the foot. In addition, the researcher continually monitored each subject to ensure they maintained a forward gaze. The magnitude of the disturbance was not specifically controlled, as the purpose was to create an unpredictable and unstable environment. Shown in Figure 4.1 is the effect of a single tap to the dorsum of the foot on the ankle and knee kinematics, as well as step cycle data for a single subject. Ankle and knee trajectories were altered as a result of receiving a perturbation, compared to the trajectories observed during control steps. In addition, the duration of the step cycle in which a mechanical perturbation was delivered was prolonged compared to the duration of the average control step cycle. Consequently, the mechanical perturbations were sufficient to cause a disturbance in the walking pattern of the subjects, requiring an active correction, and therefore posed a sufficient threat to stability for the purposes of this study.

4.2.2 Nerve stimulation

Cutaneous reflexes were evoked by trains (5 × 1.0 ms pulses @ 300 Hz) of isolated current stimulation (Grass S88 stimulator with SIU5 and CCU1 isolation and constant current units, AstroMed Inc.) applied to the SP nerve of the right (ipsilateral) foot using flexible 1 cm disposable Ag/AgCl surface EMG electrodes. The electrodes were placed in a bipolar configuration on the anterior surface of the foot, near the crease of the ankle joint. The intensity of the electrical stimulation was set at two times the radiating threshold (RT) as described elsewhere (Zehr et al. 1997). Stimuli at this intensity create a clear, radiating, non-noxious paresthesia in the innervation area of the nerve.

Figure 4.1: Ankle and knee kinematic data, as well as foot contact data taken from one representative subject. Data from a single step cycle in which a representative mechanical perturbation was delivered to the dorsum of the foot during normal walking (black) is compared to the average data of 30 control steps during normal walking (grey). Dashed vertical line indicates onset of mechanical perturbation.



Electrical stimuli were delivered approximately every 3-8 step cycles, and no more that one stimulus was delivered within a single step cycle. In addition, stimuli were delivered such that they did not occur at the same time as a mechanical perturbation. Stimuli were delivered at five points in the step cycle: heelstrike, midstance, toe-off, early swing, and midswing of the ipsilateral leg. The timing of stimulus delivery was controlled manually by the experimenter to occur near the targeted points of the step cycle. The experimenter was provided real-time feedback of the accuracy of the stimulus timing within the step cycle by viewing an oscilloscope display of the stimulus pulse along with the foot contact signals. Approximately 20 stimuli were delivered at each of the five points in the step cycle, and then subsequently screened offline to select the stimuli that occurred within the appropriate time points.

4.2.3 EMG

The sites on the skin that were used for recording EMG were first shaved, abraded, and cleaned using alcohol swabs. Disposable 1 cm Ag/AgCl surface electrodes (A10012, Vermed) were then placed longitudinally parallel to the predicted path of the muscle fibres in a bipolar configuration over the tibialis anterior (TA), soleus (SOL), medial gastrocnemius (MG), vastus lateralis (VL), and biceps femoris (BF) of the right leg ipsilateral (i) to the stimulation, as well as TA and MG of the left, contralateral (c) leg. Ground electrodes were placed over electrically neutral tissue. Signals were pre-amplified and bandpass filtered at 30

Hz – 3 kHz (P511 amplifiers (using ½ amplitude high and low pass filters), Grass Instruments, AstroMed Inc.).

4.2.4 Kinematics and step cycle detection

Kinematic data were collected using electrogoniometers (Biometrics, Inc.) placed across the ipsilateral ankle and knee, using two-sided tape. Custom-made force sensitive resistors placed in the sole of the subject's right shoe provided foot contact information (e.g. heelstrike, toe-off).

4.2.5 Data acquisition and analysis

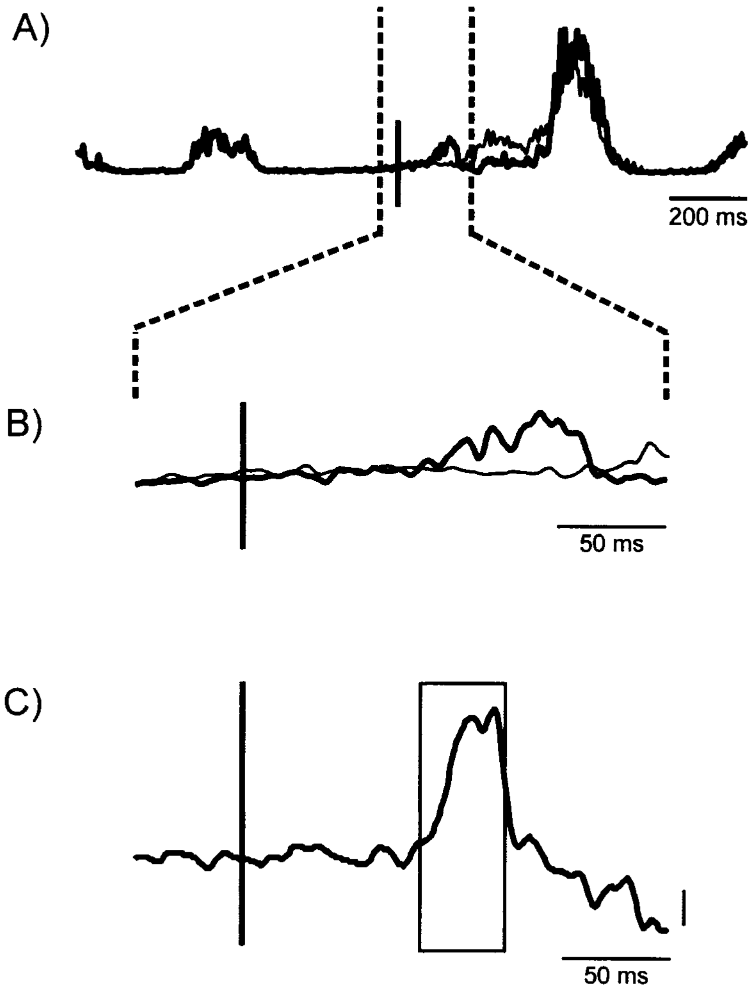
EMG, kinematic, foot contact, stimulation, and the onset of perturbation data were collected at a sampling rate of 1000 Hz and saved to disk using a custom-written LabView v.5 data acquisition program and a National Instruments data acquisition card (PCI-MIO-16E-4, National Instruments). The EMG signals were then digitally full-wave rectified and low-pass filtered at 50 Hz (4th order dual-pass Butterworth filter). Kinematic signals were low-pass filtered at 50 Hz.

Approximately 40 control step cycles for each walking condition were selected for each subject using a custom-written LabView v.5 program. Control steps were those in which no stimulus or perturbation occurred. In addition, control steps were not selected if a perturbation or stimulus was delivered within the preceding two steps. An 1800 ms data trace was captured for each control step starting at ipsilateral heelstrike, and an average control trace was calculated from all selected control steps.

After the control steps were selected, the stimuli were grouped into five bins according to their time of occurrence in the step cycle. Each bin, with the exception of one, was defined as a time window of 10% of the average step cycle duration. Every bin was centered at the five points of interest in the step cycle (for example, if midstance for a subject occurred at 31% of the step cycle, then stimuli applied between 26% and 36% of the step cycle were included). The time window for early swing was defined using a time window of 6%, which was centered at a value midway between toe-off and midswing. Since early swing occurs shortly after toe-off and before midswing, this smaller time window was used in order to prevent overlapping of the preceding and subsequent bins. Heelstrike represented 0% of the step cycle. This procedure resulted in approximately 17 stimuli in each bin being used for analysis (mean = 17.51; standard deviation = 3.07). Once the stimuli were sorted into bins, the corresponding data traces were aligned to the stimulus onset and averaged together. The average control EMG trace was then subtracted from the average stimulated data trace to produce a subtracted evoked EMG trace, which represented the pure reflex response for each subject. Figure 4.2 shows the process in which a subtracted EMG trace is produced, with the average control and stimulated data taken from cMG during the ACP walking condition for a single subject.

Cutaneous reflexes were calculated from the subtracted EMG traces for each muscle. The cutaneous reflex amplitude was calculated as the average value of the subtracted trace within the middle latency time period (80-120 ms

Figure 4.2: Process by which subtracted EMG traces were produced for analysis. Data are taken from a single subject for cMG during the ACP walking condition. Stimuli were delivered at toe-off; solid vertical lines represents occurrence of stimuli. A) Step cycle EMG activity for cMG during the ACP walking condition. Average stimulated step cycle data (thick black line) is shown superimposed onto average control step cycle data (thin black line). B) Expanded view of the data shown in A, focused about the occurrence of the stimuli. Note that the data are not aligned to stimulus delivery at this stage of processing. C) Subtracted EMG trace resulting from the subtraction of average control step cycle EMG data from the average stimulated step cycle EMG data (shown in B). Data are aligned to the onset of stimulus. The middle latency time window in which cutaneous reflexes were analyzed is shown by the rectangular box. Vertical scale line represents 10% of maximum EMG.



post-stimulus), similar to Haridas et al. (2005). Cutaneous reflex amplitude values for each subject were then normalized to the maximum background EMG value that occurred during the step cycle for each muscle and expressed as a percentage.

The ongoing background EMG activity and the angles for the ipsilateral ankle and knee were also calculated for each walking condition. These were calculated from the unstimulated steps at the time at which the reflexes for each bin would have been observed. Ongoing EMG and joint angles from the ankle and knee were averaged for 40 ms during the control step cycle data, starting 80 ms after the average occurrence of the stimulus onset taken from the stimulation trials for each bin.

Changes in ipsilateral ankle and knee joint angle were calculated similar to the cutaneous reflex data described above. The subtracted kinematic change was calculated over a time window of 120-200 ms post-stimulus (Zehr et al. 1997; Haridas and Zehr 2003), and then normalized to the maximum range of motion over the control step cycle for each subject.

4.2.6 Statistics

Statistical analysis was performed using the averaged normalized cutaneous reflex amplitudes for each subject, from each part of the step cycle. For each muscle studied, a two-way repeated measures analysis of variance (ANOVA; condition [4] × bin [5]) was used to parse the sources of variance. Planned comparisons were then performed for the reflex amplitudes between each condition at each bin, using the experimental error calculated by the ANOVA. Planned comparisons were also performed on the background EMG and kinematic changes in the ankle and knee to SP nerve stimulation. Ankle and knee joint angles over the average control steps as well as step cycle durations were compared using repeated measures ANOVAs. Statistical significance was set as $p < 0.05$.

4.3 Results

4.3.1 Background EMG and kinematics

Shown in Figure 4.3 are the average control traces for one subject for the NP and ACP conditions compared to the normal (N) condition. The general walking pattern was observed to be similar across conditions. In particular, the muscles crossing the ankle joint showed little difference in activity between conditions. The EMG activity between the N and NP walking conditions appears to be dissimilar for iBF near the swing phase, where the background activity is greater for the N condition. Higher EMG activity is also seen during the ACP condition as compared to the N walking condition in iVL around heelstrike.

The average ongoing EMG activity for all muscles across the step cycle for all walking conditions is plotted in Figure 4.4. Although the pattern of EMG activation was similar across all conditions for each muscle, planned comparisons revealed significant differences ($p < 0.05$) in background EMG activity between walking conditions at various points in the step cycle for some

Figure 4.3: Average EMG, ankle and knee goniometer, and foot contact data traces for 30 control steps (starting at ipsilateral heelstrike) taken from a single subject. The grey lines in each trace represent average data recorded during the normal walking condition. The black lines represent the average data during the normal walking while receiving mechanical perturbations at the dorsum of the foot (left column), and during the arms crossed while receiving mechanical perturbations at the dorsum of the foot walking condition (right column).

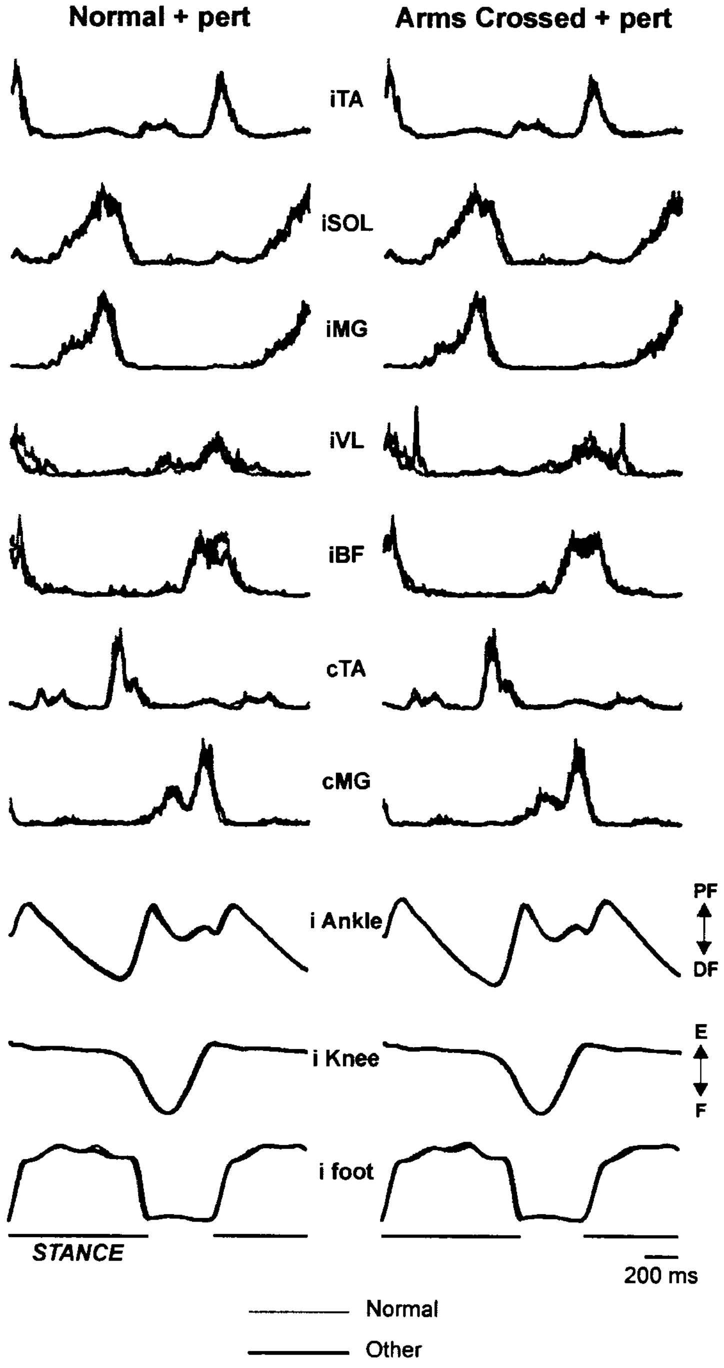
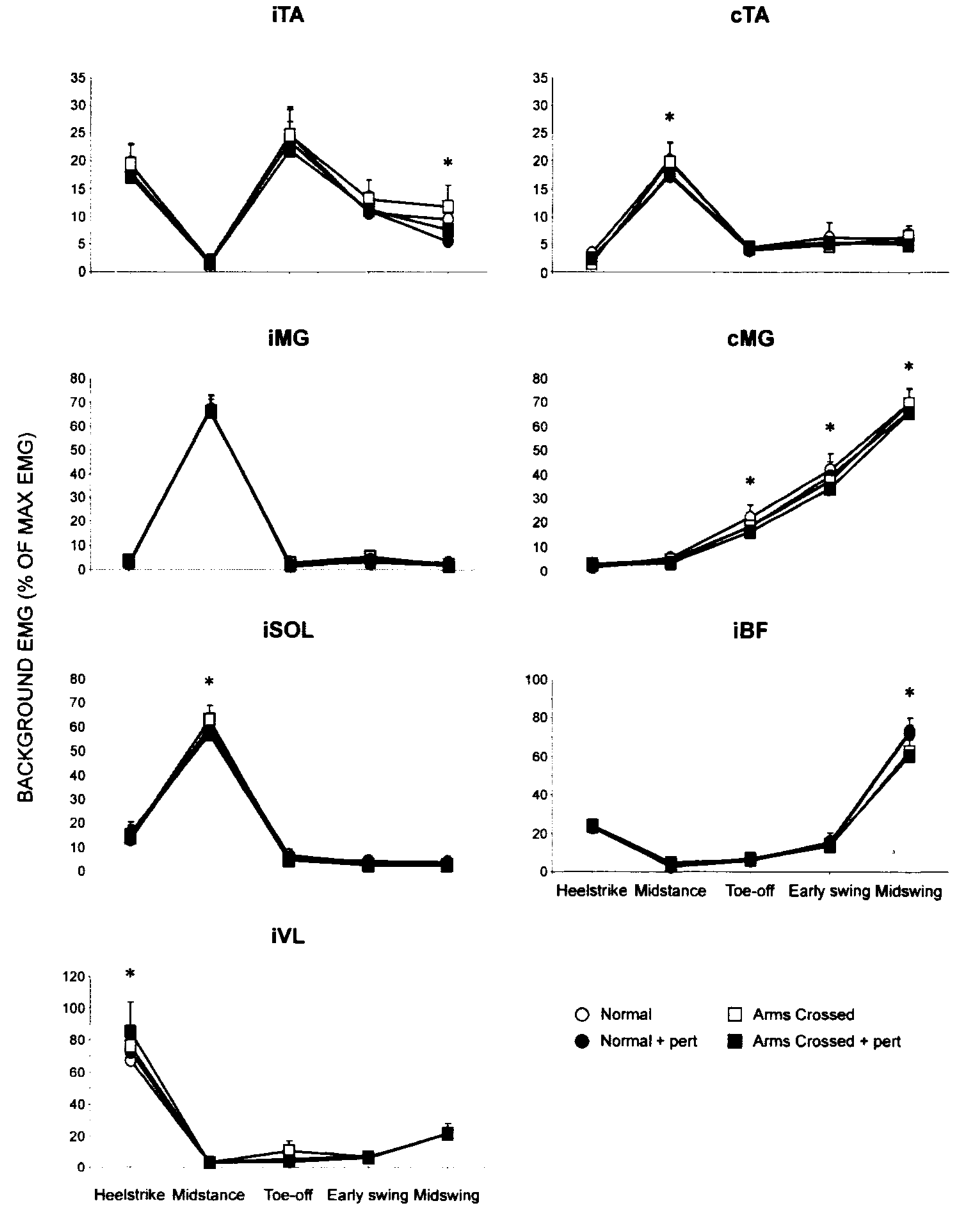


Figure 4.4: Group averaged data for the ongoing EMG activity in all recorded muscles for each point of the step cycle. Background EMG activity was calculated from the unstimulated control steps for each walking condition in which there was no mechanical perturbations delivered to the foot dorsum. A 40 ms time window at the point in the step cycle in which the corresponding reflex would have occurred was used for the calculation. The ongoing EMG activity was normalized to the maximum EMG observed for each muscle across the step cycle. The five points in the step cycle investigated are located on the abscissa. Each of the four walking conditions tested in represented by a different symbol: open circle – normal; filled circle – normal with mechanical perturbations; open square – arms crossed; filled square – arms crossed with mechanical perturbations. Error bars represent one standard error. Significant differences ($p < 0.05$) between walking conditions are indicated by *.



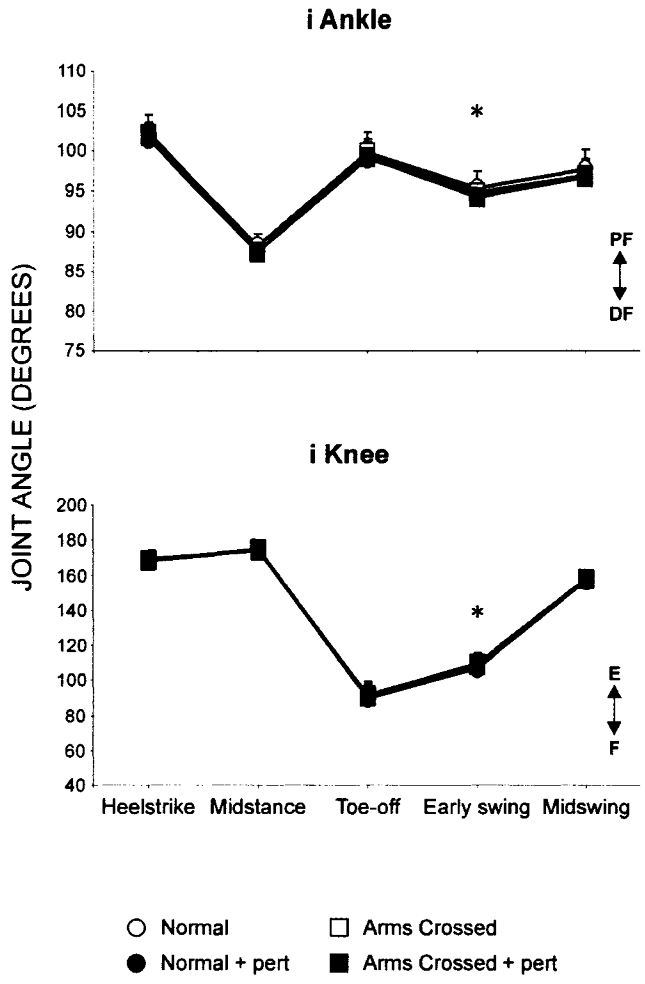
muscles. Ongoing EMG activity during the ACP condition was significantly higher than that for the N and NP walking conditions in iVL. For iBF, the arms crossed conditions had lower EMG activity at midswing versus the N and NP walking conditions. This trend was also observed in cMG at toe-off and early swing. Background EMG activity tended to be greater during conditions that did not have mechanical perturbations in iTA at midswing, cTA at midstance, and cMG at midswing. Significant differences in ongoing EMG activity were also observed in iSOL at midstance, with the greatest level of activity occurring during the AC walking condition.

As seen from the bottom portion of Figure 4.3, the ankle and knee angles for one subject were comparable between all walking conditions. The average ankle and knee angle data for all subjects for all walking conditions across the step cycle are displayed in Figure 4.5. The kinematic pattern for both the ankle and knee joint were similar for all walking conditions, however planned comparisons revealed significant differences ($p < 0.05$) for both joints at early swing. For the ankle, the joint angle for the N walking condition was significantly greater in plantar flexion than that for the ACP condition, and the knee angle for the AC condition was significantly greater in extension compared to the NP walking condition.

4.3.2 SP nerve cutaneous reflexes

Stimulation of the SP nerve evoked middle latency cutaneous reflexes in all muscles. The reflex amplitudes were modulated across the step cycle, similar

Figure 4.5: Group averaged ongoing kinematic data for the ankle and knee. Ongoing kinematic activity was calculated from the unstimulated control steps for each walking condition in which there were no mechanical perturbations delivered to the foot dorsum. A 40 ms time window at the point in the step cycle in which the corresponding reflex would have occurred was used for the calculation. The five points of the step cycle investigated are shown on the abscissa. Direction of dorsiflexion (DF) and plantar flexion (PF) for the ankle, as well as flexion (F) and extension (E) is indicated on graphs. Significant differences ($p < 0.05$) between walking conditions are indicated by *.



to previous findings with SP nerve stimulation (Van Wezel et al. 1997; Zehr et al. 1997; Haridas and Zehr 2003; Haridas et al. 2005). For instance, inhibitory cutaneous reflexes were observed at the stance-swing and swing-stance transition points of the step cycle in iTA during normal (N) walking, and excitatory reflexes were observed during swing in cMG.

The amplitudes of middle latency reflexes evoked from SP nerve stimulation differed across conditions for some muscles. Figure 4.6 shows the subtracted EMG traces taken from a single subject for iTA and cMG during the AC and ACP walking conditions with SP nerve stimulation delivered at toe-off. The amplitude of the inhibitory middle latency response in iTA was suppressed when walking in an environment in which a threat of tripping was present (ACP). Also, the excitatory response in cMG during the AC condition was facilitated when perturbations were present.

The group averaged data for the middle latency cutaneous reflex values across the step cycle for all walking conditions showed significant differences between walking conditions as revealed by planned comparisons (Figure 4.7). A clear enhancement of excitatory reflex amplitudes was observed in cMG from toe-off to midswing. Cutaneous reflexes elicited during the NP and ACP conditions were significantly higher in amplitude compared to the N and AC walking conditions. The reflex amplitude was also significantly higher during the ACP condition as compared to both the N and NP walking conditions in iBF and iVL at midswing. The reflex amplitude for the NP condition was also significantly higher than that for the AC condition for iBF at midswing.

Figure 4.6: Subtracted EMG traces for iTA and cMG after SP nerve stimulation for one representative subject following electrical stimuli occurring at toe-off. Each set of traces shows the evoked cutaneous reflex during the arms crossed walking condition (thick grey line) and arms crossed + perts walking condition (thick black line), and the 95% confidence interval around the average control steps (thin black lines). The dashed vertical line indicates the onset of stimulus. The middle latency time window in which cutaneous reflexes were analyzed is shown by the rectangular box. Solid black vertical line represents 10% of maximum EMG.

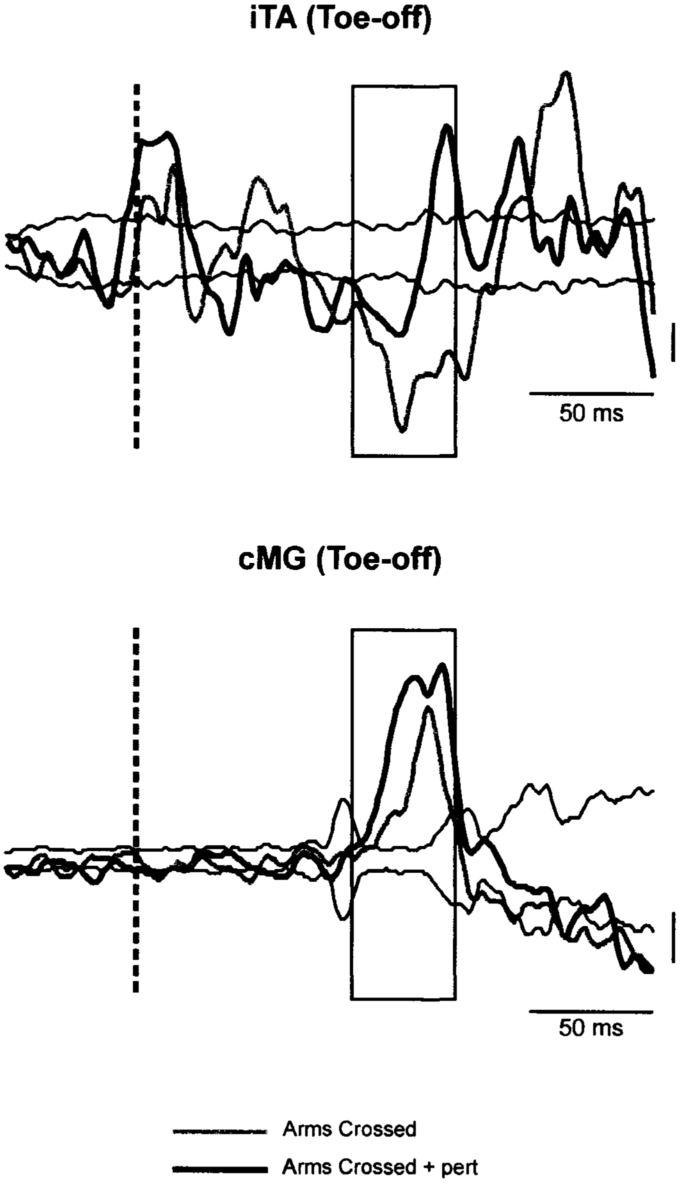
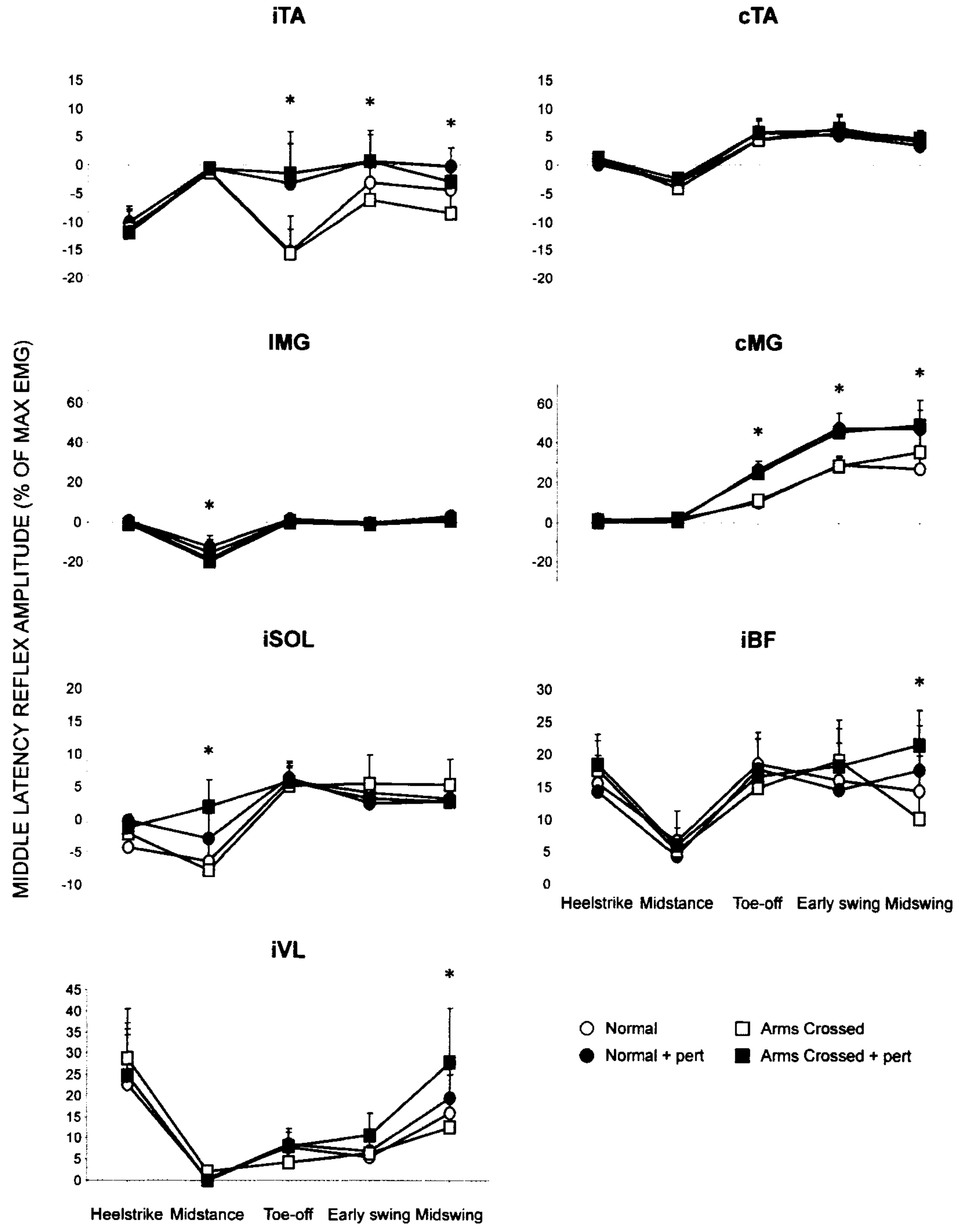


Figure 4.7: Group averaged data for middle latency cutaneous reflexes in all recorded muscles for each point of the step cycle. Reflex amplitudes are normalized to the maximum EMG observed for each muscle across the step cycle. The five points in the step cycle investigated are located on the abscissa. Each of the four walking conditions tested in represented by a different symbol: open circle – normal; filled circle – normal with mechanical perturbations; open square – arms crossed; filled square – arms crossed with mechanical perturbations. Error bars represent one standard error. Significant differences ($p < 0.05$) between walking conditions are indicated by *.

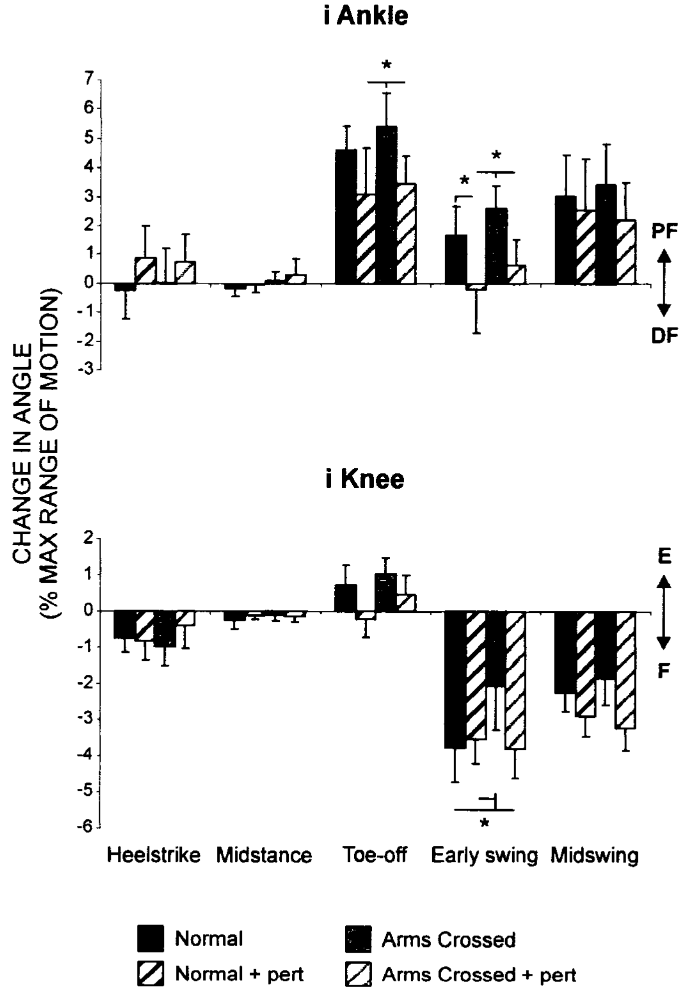


In iTA, significant differences were found in reflex amplitudes between walking conditions from toe-off to midswing. During the N and AC walking condition, SP nerve stimulation evoked relatively large cutaneous reflexes that were inhibitory. However during the NP and ACP conditions, these inhibitory reflexes were suppressed with the reflex amplitudes approaching zero. Similar findings were observed in iSOL at midstance, where the average reflex amplitude value for the ACP condition was significantly higher than all other walking conditions, and the reflex amplitude associated with the NP condition was significantly higher than that for the AC walking condition. Significant differences also existed between walking conditions for iMG at midstance, where the reflex value for the NP condition was significantly greater than that for both the AC and ACP walking conditions.

4.3.3 Kinematic effect of SP nerve stimulation

It has been previously shown that with SP nerve stimulation there is an increase in plantar flexion at the stance-swing transition and an increase in knee flexion during swing, which is indicative of a stumbling corrective response (Van Wezel et al. 1997; Zehr et al. 1997; Haridas and Zehr 2003). In this study, similar findings were observed. The effect of SP nerve stimulation on both ipsilateral ankle and knee kinematics are displayed in Figure 4.8. In the ipsilateral ankle (top), an overall trend of decreased stimulus-induced plantar flexion was observed during walking conditions in which mechanical perturbations were delivered compared to conditions with no perturbations from toe-off to midswing.

Figure 4.8: Group averaged kinematic changes for the ipsilateral ankle (top) and knee (bottom) with SP nerve stimulation. Values are presented as percentages of the maximum range of motion. The five points of the step cycle investigated are shown on the abscissa. Each of the four walking conditions is represented by a different bar: black – normal; white with slanted black lines – normal with mechanical perturbations; grey – arms crossed; white with slanted grey lines – arms crossed with mechanical perturbations. Error bars represent one standard error. Direction of dorsiflexion (DF) and plantar flexion (PF), as well as flexion (F) and extension (E) is indicated on graphs. Significant differences ($p < 0.05$) between walking conditions are indicated by horizontal lines over the vertical bars and *.



i Ankle

i Knee

Plantar flexion was significantly lower ($p < 0.05$) during the NP and ACP conditions compared to the AC walking condition at toe-off and early swing. A significant difference was also observed at early swing between the N and NP walking conditions, with plantar flexion being lower during the NP condition. For the ipsilateral knee (bottom), significant differences between walking conditions were observed at early swing, where the degree of flexion that was induced by SP nerve stimulation was lower during the AC walking condition compared to the N, NP, and ACP conditions.

4.4 Discussion

In a recent study from this laboratory, we showed that cutaneous reflexes evoked in the leg with SP nerve stimulation during walking were modulated according to the level of postural threat (Haridas et al. 2005). However, this finding was mainly isolated to the muscles of the contralateral leg, and it was thought that the lack of differences in ipsilateral cutaneous reflexes was due to the locus of the perturbations. In this study, we investigated the influence of context-specific perturbations (with respect to the innervation area of the SP nerve) on cutaneous reflexes in the muscles of the legs during walking. When walking under conditions in which mechanical perturbations were delivered to the dorsum of the foot, cutaneous reflex amplitude values were facilitated compared to walking during conditions with no mechanical perturbations. In addition, the findings suggest that not only are local cutaneous reflexes influenced by the presence of context-specific perturbations, but they are also gated according to the phase of the step cycle. Furthermore, inhibitory cutaneous reflexes were shown to be essentially abolished in iTA when walking in the presence of mechanical perturbations. This context-specific effect suggests cutaneous reflex responses in the lower limbs may be gated out or deleted when extraneous to the locomotor task.

4.4.1 Functional context-dependent gating of cutaneous reflexes

Numerous studies have reported the existence of a stumbling corrective response in both cats (Forssberg et al. 1975; Forssberg et al. 1977; Prochazka et al. 1978; Forssberg 1979; Buford and Smith 1993) and humans (Eng et al. 1994; Van Wezel et al. 1997; Zehr et al. 1997; Schillings et al. 2000; Lam et al. 2003), which serves to clear an encountered obstacle thus allowing for stability to be maintained during walking. In humans, inhibition of iTA during swing in response to electrical stimulation of the foot dorsum is a defining feature of a stumbling corrective response (Van Wezel et al. 1997; Zehr et al. 1997). In this study, the inhibitory reflexes observed in iTA from toe-off to midswing during walking conditions with no mechanical perturbations were suppressed such that the reflex amplitude values were closer to zero during walking conditions in which a threat of a trip existed. Increasing instability by crossing the arms did not result in reflex changes; only the threat of a trip was associated with the changes observed in cutaneous reflex amplitudes. This is in stark contrast to our previous findings in which a generalized threat to stability by perturbations delivered to the torso did not affect the reflexes of the ipsilateral leg (Haridas et al. 2005). We suggest that a novel cutaneous reflex response was evoked by changing the context of the task (i.e. locus of mechanical perturbations), and was not related to changes in sensory information or the phase of the step cycle.

This study is the first to report that cutaneous reflexes associated with the stumbling corrective response are capable of being attenuated according to the context of the task being performed. More important, however, is the observation that inhibitory reflexes in iTA were essentially abolished from toe-off to midswing. Suppression of inhibitory cutaneous reflexes in iTA during conditions in which mechanical perturbations were delivered to the dorsum of the foot would potentially act to maintain normal dorsiflexion. In so doing, the foot would be capable of displacing the object, rather than avoiding further contact. Conceivably within certain locomotor contexts, maintaining the forward progression of the swing limb is more beneficial despite encountering an obstacle. This may be particularly useful when walking in environments with easily displaced but densely placed objects, for example walking through brush or bramble, or deep snow. The facilitation of reflexes in cMG during walking conditions with an increased threat of tripping at the same points in the step cycle as described for iTA could assist in maintaining stability, by increasing contralateral extensor activity while the ipsilateral leg is overcoming an obstacle. We suggest that these coordinated bilateral adaptations in the responses of the lower legs during walking conditions with an increased threat of a trip serve as an example of cutaneous reflexes being adapted in a functional manner.

In the present study, we report that repeated exposure to perturbations to the dorsum of the foot modulates the cutaneous reflexes from the foot. Baken et al. (2006) recently reported that a pre-stimulus pulse delivered before a reflex-evoking pulse train led to reduced cutaneous reflex amplitudes. Taken together, these results suggest that prior knowledge of the arrival of sensory information leads to modulation of their influences, indicating that reflexes are adapted with contextual expectation. In turn, this can lead to reshaping of evoked responses (such as the stumble-corrective response) to generate different patterns of output appropriate for the context of the task. This particular context-dependent adaptation of reflexes in relation to the task being performed may be involved with the ongoing regulation of dynamic stability during walking.

4.4.2 Mechanisms of context-dependent reflex modulation

The context-dependent differences in cutaneous reflex amplitude were specific to certain muscles at specific points in the step cycle. This reflex modification can thus not be explained by a generalized change in the state of cutaneous reflex pathways. In addition, changing the context of the task led to adaptations in the profile of the background EMG over the step cycle, suggesting a change in the behavioural set (Prochazka 1989). However, the changes in cutaneous reflex amplitudes observed did not simply follow the changes in background EMG. Therefore, the differences in reflex amplitudes cannot be explained directly by differences in motoneuronal pool excitability, suggesting that changes in reflex amplitude must be related to factors associated with walking in the imposed conditions.

One possible mechanism for the context-dependent modulation observed involves supraspinal pathways projecting onto reflex pathways of the muscles of the legs. Pijnappels et al. (1998) reported the amount of cortical facilitation onto cutaneous reflex pathways varied according to the phase of the step cycle, suggesting that cortical input is able to generate the differential modulation observed. Similarly, Bretzner and Drew (2005) showed differential modulation of cutaneous reflexes according to the nerve and cortical site stimulated in intact cats at the onset of swing. Responses in some muscles were facilitated, whereas responses in other muscles were depressed, suggesting that cortical and cutaneous pathways have specific terminations to various interneuronal networks residing in the spinal cord. The convergence of cortical input onto interneurons of the reflex pathways could serve to modify the magnitude of reflex responses in relation to context. Corticospinal tract neurons in the cat have been shown to increase their firing rate when walking over a series of barriers as compared to level walking (Beloozerova and Sirota 1993). Bretzner and Drew (2005) suggest that this increased rate of firing could allow for greater modulation of cutaneous reflex excitability, and thus function as a mechanism to facilitate or inhibit reflexes that assist or interfere with stable locomotion. Taken together, descending cortical input is likely involved in the context-dependent modulation of cutaneous reflexes observed in this study.

4.5 References

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Chapter 5 - The influence of engaging the hands in balance control on cutaneous reflexes in the arms during walking

5.1 Introduction

Encountering a destabilizing perturbation during locomotion can evoke corrective responses that serve to recover balance. The majority of studies that have focused on balance have reported corrective responses in the muscles of the lower limbs (Berger et al. 1984; Dietz et al. 1987; Tang and Woollacott 1999). Additionally, responses in the muscles of the upper limbs have also been reported. Dietz et al. (2001) showed rapid responses in the muscles of the arms in response to rapid deceleration of a treadmill belt during walking. An arm elevation strategy was described by Marigold and Patla (2002) in response to an unexpected slip. In addition, perturbations applied to the torso during walking have also been shown to evoke responses in arm muscles by Misiaszek (2003). It is therefore apparent that the arms can be employed in an overall corrective response to perturbations during locomotion.

These corrective responses in the muscles of the arms can be utilized to increase stability. This can be achieved by a variety of methods, such as moving the arms to i) produce counterbalancing torques, ii) redistribute the centre of mass, and iii) reach/grasp for objects in the environment (e.g. grabbing onto a handrail). Grasping onto a stable support allows for additional stability by acting against a fixed support structure. Holding onto stable handles has also been shown to influence the organization of corrective responses to perturbations during standing and dynamic (walking) balance control. Cordo and Nashner

(1982) showed perturbations to standing subjects' balance evoked responses in arm and leg muscles. When standing subjects held onto fixed support handles, the responses evoked in the legs were attenuated while the responses in the arms became predominant. A similar finding has also been recently observed during walking by Misiaszek et al. (2000), who reported responses in the muscles of the leg evoked by forward and backward perturbations at the torso during walking to be suppressed while holding onto fixed handles. Conversely, the amplitude of corrective responses evoked in leg muscles was shown to increase when the arms were restricted from contributing to the correction of balance during walking (Misiaszek and Krauss 2005). Taken together, these results suggest the arms can serve an important role in balance control.

In addition to holding onto a stable support, light contact with a stable surface has also been shown to influence stability. Jeka (1997) showed that somatosensory information attained from stable surface contact reduced the inherent postural sway in standing subjects. A similar finding was reported by Rogers et al. (2001), who showed passive tactile cues reduce postural sway during standing. Furthermore, sensory input provided by light fingertip contact to a fixed support helped sustain body stability during treadmill walking (Dickstein and Laufer 2004). This suggests that tactile information from the hands and arms provides important sensory cues involved in regulating balance and balance strategies.

The mechanisms that govern the compensatory reactions in the arms during walking are not well understood. Since cutaneous information has been shown to be important in increasing stability, compensatory reactions in the arms may involve cutaneous reflexes. These reflexes have been evoked in the muscles of the arms during rhythmic arm movements such as arm cycling (Zehr and Chua 2000; Zehr and Kido 2001; Hundza and Zehr 2006) and walking (Zehr and Haridas 2003), and were modulated according to the phase of the step cycle as well as the task (static contraction, moving) being performed. In addition, cutaneous reflexes in the arms have been shown to be specific to the nerve being stimulated during arm cycling (Zehr and Kido 2001). These features of cutaneous reflexes in the arms (task-, phase-dependency, nerve specificity) have been previously described for cutaneous reflexes in the muscles of the legs with electrical stimulation of cutaneous nerves in the foot (Yang and Stein 1990; Van Wezel et al. 1997; Zehr et al. 1997; Zehr et al. 1998), and have led to the suggestion that cutaneous reflexes may serve to assist in maintaining stability during walking (Zehr and Stein 1999).

Given the putative importance of tactile information from the hands in regulating balance control, and the suggested role of arm actions in maintaining balance, we hypothesized that cutaneous reflexes evoked in the upper limbs will be influenced according to the manner in which the arms are engaged in balance control. We were interested in how cutaneous reflexes were modulated as a result of (i) varying the cutaneous input to the hand (by altering arm task), and (ii) varying the environment in which walking took place by adding perturbations.

5.2 Materials and Methods

5.2.1 Subjects and protocol

Ten subjects between the ages of 21 to 33, with no history of neurologic, orthopedic, or metabolic impairment participated with informed, written consent in a protocol approved by the Health Research Ethics Board at the University of Alberta. In this study, we examined cutaneous reflexes evoked with electrical stimulation of two nerves, the superficial radial (SR: innervates lateral dorsum of hand and fingers, from the thumb to the lateral half of the 3rd digit) and median (innervates palmar surface of hand and fingers, from the thumb to lateral half of the 3rd digit) nerves. Subjects visited the lab on two separate occasions, once for each nerve stimulation protocol. The order of presentation of nerve stimulation was randomized across subjects.

Subjects were asked to walk on a motorized treadmill at a self-selected speed (typically between 0.8 - 1.2 m/s). Cutaneous reflexes were evoked during 6 walking conditions: (1) normal with the arms free (N); (2) normal while receiving unpredictable anterior-posterior perturbations applied at the torso (NP); (3) holding onto moving handles (MH); (4) holding onto moving handles while receiving unpredictable anterior-posterior perturbations applied at the torso (MHP); (5) holding onto stable fixed handles (H); (6) holding onto stable fixed handles while receiving unpredictable anterior-posterior perturbations applied at the torso (HP). The order of walking conditions was randomized across subjects.

To investigate the influence of engaging the hands for balance control during walking on cutaneous reflexes, different arm tasks were incorporated into the study. Holding onto stable fixed handles engaged the hands such that postural threat was reduced during walking, compared to the normal condition in which the arms were allowed to swing freely (Krauss and Misiaszek 2007). The moving handles condition engaged the hands in an intermediate manner between the normal and stable fixed handles conditions. As subjects receive anterior-posterior perturbations, the handles are able to move, thus influencing postural threat in a different manner then when fixed into position. Handles were attached to a custom-built metal frame that was secured to the treadmill apparatus. Rails were built onto the frame, which allowed for the handles to move horizontally towards and away from the subject on a set of near friction-free rollers. For the stable fixed handles conditions, the handles were locked in place. The height of the handles was adjusted such that when held, the upper arms were perpendicular to the ground and the angles of both elbows were approximately 90 degrees.

Anterior-posterior perturbations were used to create an environment in which stability was unpredictable, and subjects reported feeling less stable during walking conditions in which these perturbations were delivered (Haridas et al. 2005). Cutaneous reflexes were evoked during periods of steady walking between perturbations. The perturbations were delivered by cables attached to a belt worn by the subject around the pelvis. From the belt, these cables ran in front and behind the subject to a drum to which a handle was attached. Pushing and pulling this handle caused anterior and posterior perturbations, respectively. A strain gauge located on the lever arm of the handle was used to indicate when perturbations were applied. A detailed description of this apparatus can be found elsewhere (Haridas et al. 2005; Misiaszek and Krauss 2005). The magnitude of the perturbations was approximately 20% of the subjects' body weight. However, because the perturbations were used only to create an unpredictable environment, the magnitude was not specifically controlled. Anterior-posterior perturbations were delivered throughout the step cycle, at a frequency of approximately 3-5 per minute. This resulted in approximately 50 perturbations delivered for each perturbation walking trial that lasted between 10-15 min. The direction of perturbation (anterior vs. posterior) was also randomized. Safety rails were placed in front (~75 cm) and to the sides (~45 cm from lateral edge of the arms) of the subject. Subjects were instructed that they were free to reach for these safety rails if they felt the need to do so to prevent a fall.

5.2.2 Nerve stimulation

Cutaneous reflexes were evoked by trains (5 × 1.0 ms pulses @ 300 Hz) of isolated constant current stimulation (Grass S88 stimulator with SIU5 and CCU1 isolation and constant current units, AstroMed Inc.) applied to the SR or median nerve of the right arm using flexible 1 cm disposable surface electrodes (A10043, Vermed). Electrodes for the SR nerve were placed on the dorsal surface of the wrist just proximal to the radial head and the crease of the wrist joint. The electrodes for median nerve stimulation were placed on the ventral surface of the wrist just proximal to the radial head. The intensity of stimulation was set at 2 × radiating threshold (RT) for each subject, which is strong enough to evoke a reflex, yet is not perceived as painful by the subject. This level of intensity has been used previously to evoke cutaneous reflexes in the muscles of the arms (Zehr and Chua 2000; Zehr and Kido 2001). Radiating threshold was estimated as the lowest stimulus intensity at which the subject first perceived a clear radiating paresthesia into the innervation area of the nerve. The stimulating intensity was checked between each walking trial to ensure that the stimulus properties remained similar throughout the experiment.

Electrical stimuli were delivered such that no more than one stimulus was delivered within a single step cycle. Stimuli were typically separated by 2-6 seconds, and were delivered at four points throughout the step cycle with respect to the ipsilateral leg (heelstrike, midstance, toe-off, midswing). The timing of stimulus delivery was controlled manually by the experimenter to occur near the target points of the step cycle. The experimenter was provided real-time feedback of the accuracy of the stimulus timing within the step cycle by viewing an oscilloscope display of the stimulus pulse, along with the foot contact signal. Approximately 20 stimuli were delivered at each point of interest in the step cycle, and then subsequently screened (see below) post-hoc to select the stimuli which occurred within the appropriate time points. This technique typically resulted in 14-20 stimuli being accepted for further analysis for each point in the step cycle for each walking condition.

5.2.3 Recording and data acquisition

After shaving, abrading, and cleaning the skin with alcohol, disposable surface electrodes (A10043, Vermed) were placed in a bipolar configuration over the anterior deltoid (AD), posterior deltoid (PD), biceps brachii (BB), triceps brachii (TB), flexor carpi radialis (FCR), and extensor carpi radialis (ECR). EMG recordings were made in both the right arm, ipsilateral (i) to the nerve stimulation, and left contralateral (c) arm. Ground electrodes were placed over electrically neutral tissue. Signals were pre-amplified and bandpass filtered at 30 Hz – 3 kHz (P511 amplifiers (using ½ amplitude high and low pass filters), Grass Instruments, AstroMed Inc.). Kinematic data were collected using electrogoniometers (Biometrics, Inc.) placed across the right elbow, secured with two-sided tape. Foot contact information was obtained using custom-made force sensitive resistors placed in the sole of the subject's right shoe. EMG, kinematic, foot force sensor, stimulation, and perturbation force data were collected at a sampling rate of 1000 Hz and saved to disk using a custom-written LabView v.5 data acquisition routine and a National Instruments data acquisition card (PCI-MIO-16E-4, National Instruments). Post-hoc, the EMG signals were digitally full-wave rectified and then low-pass filtered at 50 Hz (4th order dual-pass Butterworth filter), while the kinematic signals were low-pass filtered at 50 Hz.

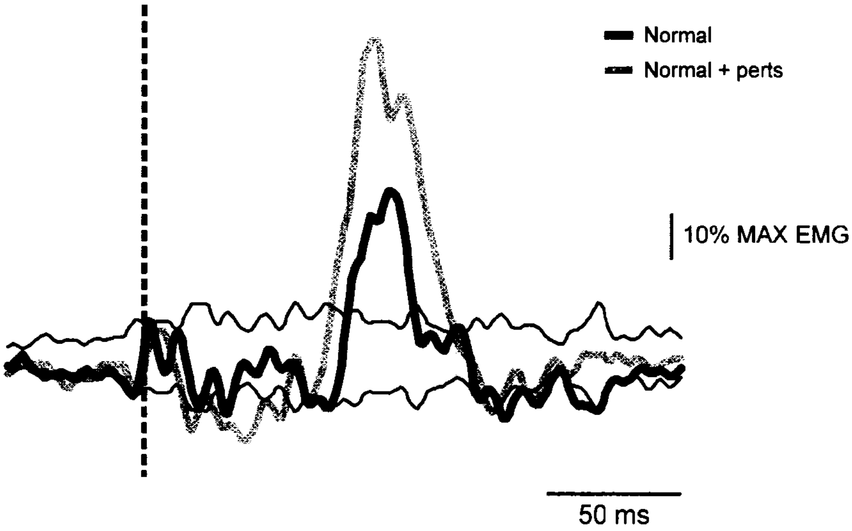
5.2.4 Data analysis

First, the selection of 30 control step cycles for each walking trial was performed using a custom-written software program (LabView v.5, National

Instruments). Control steps were those in which no stimuli or perturbations were delivered. Steps were not included if a perturbation or stimulus occurred within the preceding two steps. For each control step selected, an 1800 ms data trace was captured, starting at heelstrike. The data traces were then averaged to produce an average control trace. Next, stimuli were selected and grouped into bins depending on the time at which they occurred in the step cycle. The four points (bins) in the step cycle were defined as a time window of 10% of the average control step cycle duration. Each bin was centred at the occurrence of the specific point in the step cycle of interest (e.g. if midswing for a subject occurred at 82% of the step cycle, then stimuli applied between 77% and 87% of the step cycle were included). Heelstrike represented 0% of the step cycle. After the stimulus trials were sorted into bins, the corresponding data traces were aligned to the time of stimulus delivery and averaged. The average control EMG trace was subtracted from the average stimulated EMG trace, yielding a subtracted evoked EMG trace for each subject (Figure 5.1).

From these subtracted EMG traces, cutaneous reflex amplitude values were calculated for each muscle. For each walking condition, the middle latency component of the reflex was calculated as the average of the subtracted EMG within the time window of 80-120 ms post-stimulus for all subjects. Cutaneous reflex amplitudes for each subject were normalized to the maximum EMG amplitude occurring during the step cycle for each muscle and expressed as a percentage. The ongoing background EMG and kinematic activity were also calculated for all walking conditions. These were calculated as the average full-

Figure 5.1: Subtracted EMG traces for cPD after median nerve stimulation for a single subject following electrical stimuli occurring at midstance. Both traces represent walking conditions in which the arms were allowed to swing rhythmically; normal (thick black line), normal with perturbations (thick grey line). The vertical dashed line indicates onset of stimulation. Rectangular box indicates the 80-120 ms (post-stimulus) time window in which the middle latency reflex was analyzed.



wave rectified EMG amplitude or the absolute joint angle occurring during each of the four bins of interest in the step cycle.

5.2.5 Statistics

Separate statistical analysis was performed to determine the influence of hand engagement and perturbations on cutaneous reflexes. A two-way repeated measures analysis of variance (RM ANOVA; task [3] × bin [4]) was performed between the N, MH, and H walking conditions to determine the influence of engaging the hands with balance control on the amplitude of cutaneous reflexes. A separate two-way RM ANOVA (task [2] × bin [4]) was performed between tasks in which the hands were engaged in a similar manner to determine the influence of receiving perturbations on cutaneous reflex amplitudes during walking (i.e. N vs. NP; MH vs. MHP; H vs. HP). The experimental error calculated by the ANOVA was used to perform planned comparisons for the reflex amplitudes between the conditions of comparison at each bin. Similar analysis was performed on the background EMG as well as ipsilateral elbow joint angles. One-way RM ANOVAs were also performed on step cycle durations for group averaged data between conditions. Statistical significance was set at $p < 0.05$.

5.3 Results

5.3.1 Kinematics and step cycle duration

During treadmill walking, subjects were asked to swing their arms normally (N, NP), or engage the hands in balance control by holding onto a) moving handles (MH, MHP) or b) stable handles (H, HP). There was no main effect of walking condition ($p > 0.05$) on elbow angle between conditions in which the arms were performing similar tasks (e.g. N vs. NP; MH vs. MHP).

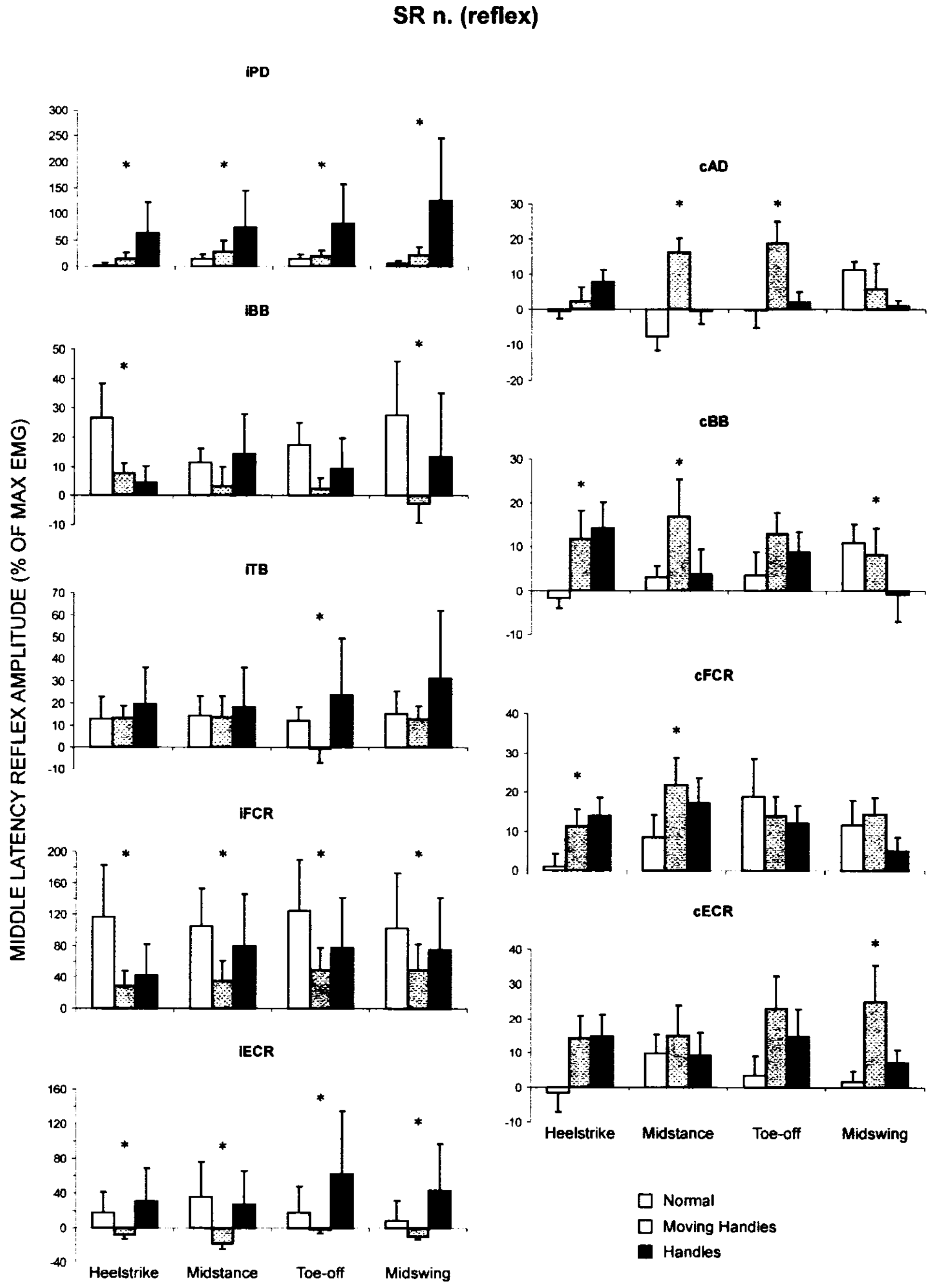
In addition, engaging the hands in different manners did not influence the duration of the step cycle, as one-way RM ANOVAs revealed no significant differences ($p > 0.05$) in step cycle durations between all walking conditions. Importantly, during walking with the arms freely moving, the average step cycle duration for N walking was similar to that for the NP walking condition. Furthermore, step cycle durations were similar between conditions in which the hands were engaged in balance, irrespective of the presence of perturbations. Thus, the tasks performed did not significantly affect walking patterns.

5.3.2 Influence of hand engagement on cutaneous reflex amplitudes

One of the comparisons of interest in this study was the potential influence of engaging the hands with balance control on cutaneous reflexes arising from the hands. Consequently, planned comparisons were made between the three walking conditions for which no perturbations were applied. These results are summarized in Figure 5.2 for the SR nerve and Figure 5.4 for the median nerve. In general, engaging the hands in balance control during walking led to a number of differences in cutaneous reflex amplitude and in many instances, reflex sign.

Muscles in which significant differences in average cutaneous reflex amplitude values were observed between the N, MH, and H walking conditions with SR nerve stimulation are shown in Figure 5.2. Engaging the hands in

Figure 5.2: Group averaged data for middle latency interlimb cutaneous reflexes arising from SR nerve stimulation for muscles in which a significant difference was found between conditions in which the arms were allowed to swing freely, and conditions in which handles were held. The four points of the step cycle investigated are shown on the abscissa. Average middle latency interlimb cutaneous reflex amplitude values are depicted as open (N), grey (MH), and black (H) bars, with the standard error shown. Reflex values are normalized to the maximum EMG produced during normal, undisturbed walking. *: significant difference ($p < 0.05$) in middle latency interlimb cutaneous reflexes.

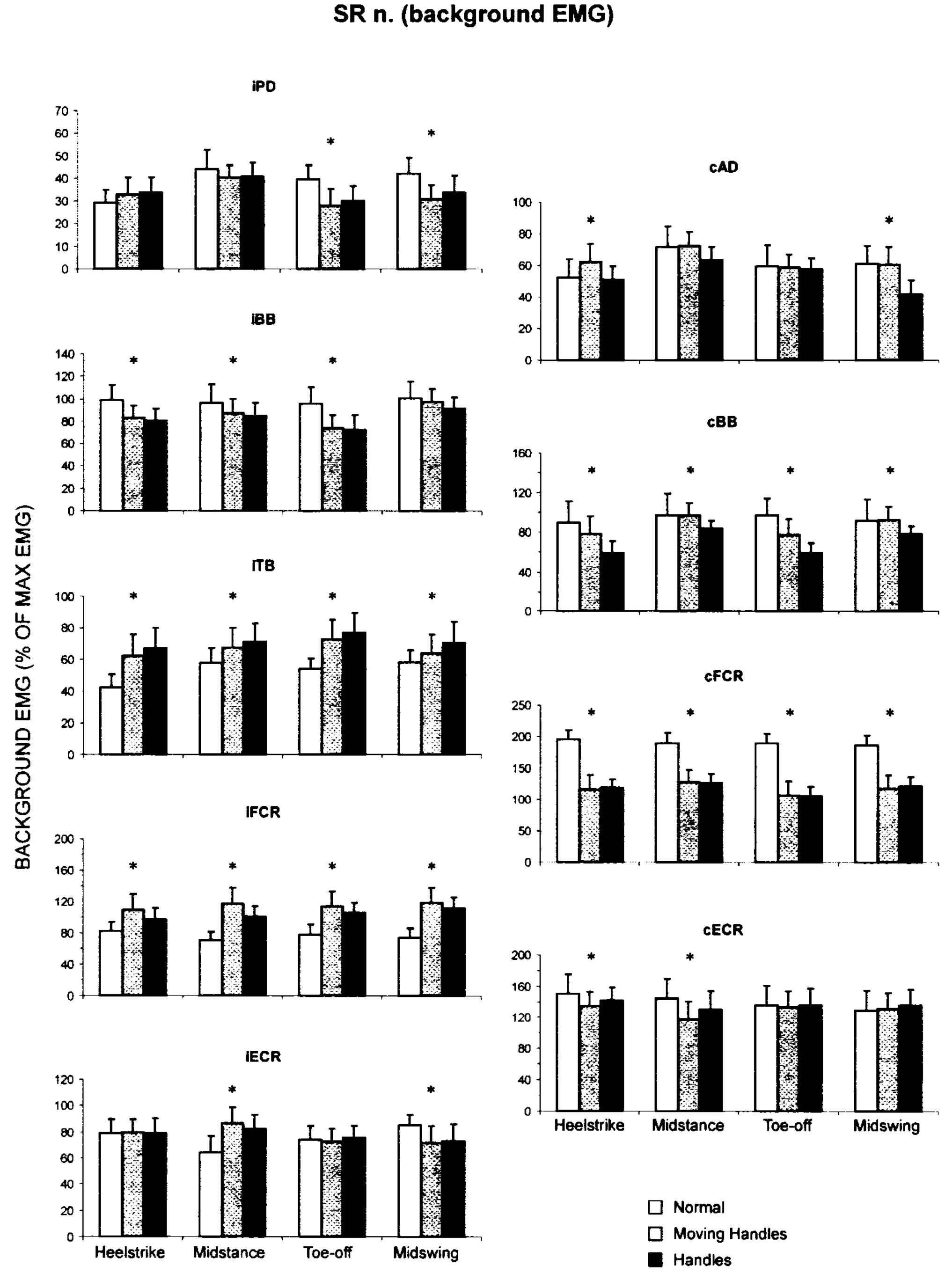


balance control (i.e. holding onto handles) led to widespread task-related changes, with nine out of twelve muscles displaying significant differences in reflex amplitudes between walking conditions. In some muscles, the cutaneous reflex amplitude increased when holding onto handles; in others, the reflex amplitude decreased. Cutaneous reflex amplitudes were larger when holding onto stable handles (H), compared to normal walking for iPD and iTB at all points of the step cycle, and for iECR at most points, except at midstance. For cBB and cFCR, larger reflex amplitudes were observed during the H walking condition at most points of the step cycle except at midswing and toe-off respectively. Interestingly, the reflex amplitude was generally larger at heelstrike during the H condition in all these muscles. Planned comparisons revealed significantly larger ($p < 0.05$) cutaneous reflex amplitudes during the H walking condition compared to normal walking for iPD at all points of the step cycle, iECR at toe-off and midswing, as well as cBB and cFCR at heelstrike. Furthermore, when the hands were engaged in balance control by holding onto moving handles (MH), larger cutaneous reflex amplitudes were observed for cECR at most points of the step cycle compared to normal walking, except at heelstrike. In line with this observation, planned comparisons revealed a significantly larger reflex amplitude value for the MH condition at midswing. In some instances, lower cutaneous reflex amplitudes were observed during conditions in which the hands were engaged in balance control compared to normal walking. For iFCR, the reflex amplitude was generally lower during the MH and H walking conditions at all points of the step cycle. This trend was also generally observed in iBB for most points in the step cycle, except at midstance. Significantly lower reflex amplitudes during the MH and H conditions, compared to normal, were observed for iBB at heelstrike and midswing, iFCR at all four points of the step cycle, iECR at midstance, and cBB at midswing.

Furthermore, a number of cutaneous reflex reversals between walking conditions were observed with SR nerve stimulation. Both positive and negative signed reflex amplitudes were noted in half of the muscles recorded. For iECR, facilitatory reflex amplitudes were observed during the N and H walking conditions, in contrast to inhibitory reflex amplitudes during the MH condition for all points in the step cycle. This observation was also noted for iBB at midswing. Reflex reversals were also observed in cAD at midstance and toe-off, cBB at heelstrike and midswing, and cECR at heelstrike.

The corresponding average background EMG values for all points in the step cycle during the SR nerve stimulation paradigm are shown in Figure 5.3 for the same muscles displayed in Figure 5.2. Generally, background EMG activity differed between conditions in which the arms were allowed to swing freely and those conditions in which handles were held. During the MH and H conditions, higher background activity was observed compared to normal walking for iTB and iFCR at all points of the step cycle. Lower background EMG activity during the MH and H walking conditions was observed for iBB, cBB, and cFCR at all points of the step cycle. In addition, differences were observed in ongoing EMG activity between the MH and H walking conditions. Ongoing EMG activity was generally greater during the MH condition for iFCR, cAD, and cBB for all points of

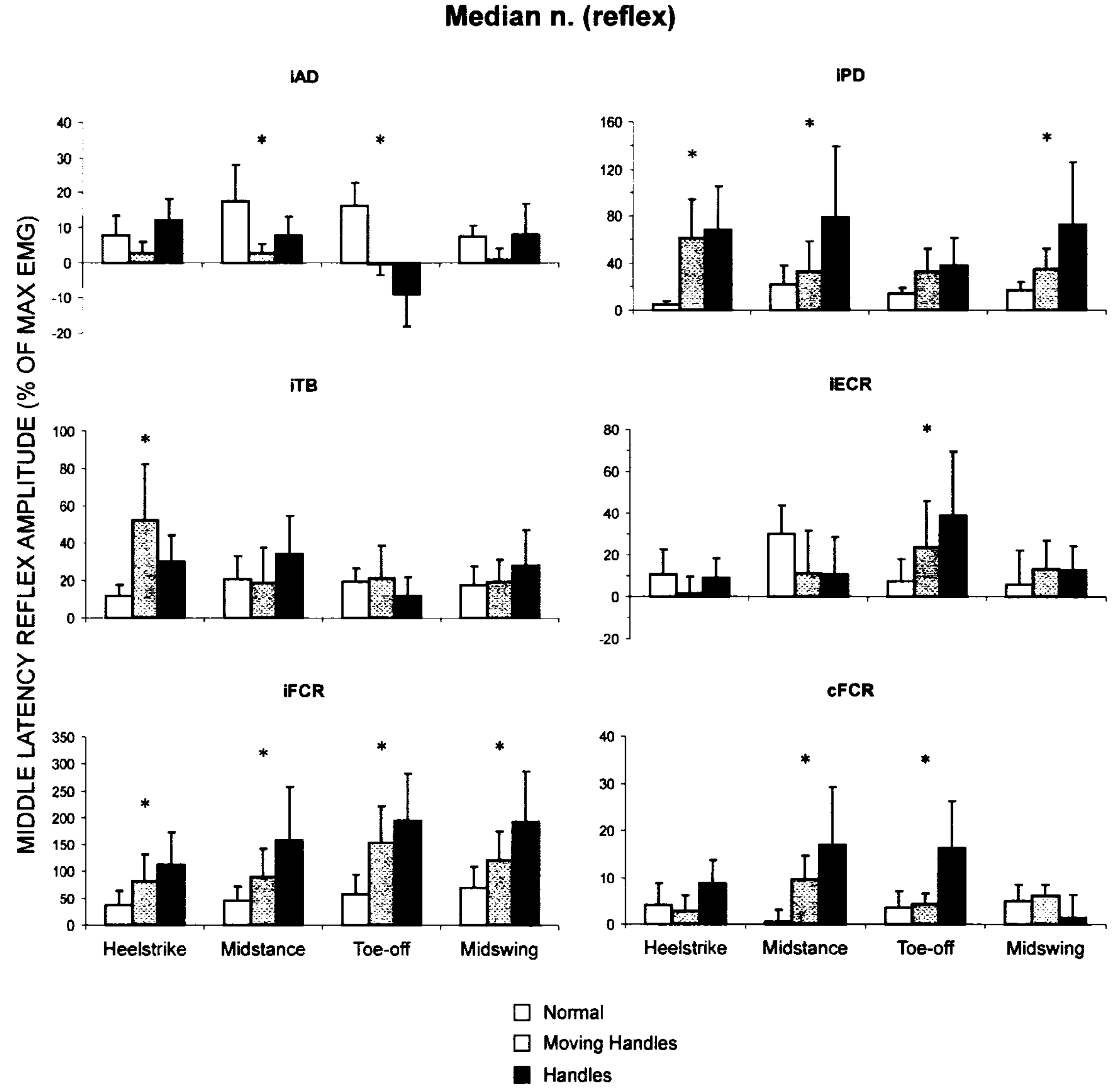
Figure 5.3: Group averaged data for background EMG activity during the SR nerve stimulation paradigm for muscles in which a significant difference was found in cutaneous reflex amplitude values between conditions in which the arms were allowed to swing freely and conditions in which handles were held. The four points of the step cycle investigated are shown on the abscissa. Average middle latency interlimb cutaneous reflex amplitude values are depicted as open (N), grey (MH), and black (H) bars, with the standard error shown. Reflex values are normalized to the maximum EMG produced during normal, undisturbed walking. *: significant difference ($p < 0.05$) in middle latency interlimb cutaneous reflexes.



the step cycle, compared to the H condition. Specific instances at which significant differences ($p < 0.05$) in background EMG activity were observed between conditions are indicated by asterisks in Figure 5.3.

Differences in reflex amplitude were also observed with median nerve stimulation, with half of recorded muscles displaying significant differences between walking conditions (Figure 5.4). Generally, stimulation of the median nerve resulted in larger cutaneous reflex amplitudes during conditions in which the handles were engaged in balance control compared to normal walking. This trend was observed in five of the six muscles that showed significant differences in reflex amplitude values between walking conditions. Cutaneous reflex amplitudes were generally larger during conditions in which the handles were held for iPD, iTB, iFCR, and cFCR across the step cycle. Planned comparisons revealed significantly larger reflex amplitudes during the H condition compared to normal walking for iPD at most points of the step cycle (except toe-off), iFCR at all points of the step cycle, iECR at toe-off, and cFCR at midstance and toe-off. For iTB, the reflex amplitude value during the MH condition was significantly higher than that for the H and normal walking conditions at heelstrike. Also, lower cutaneous reflex amplitude values were noted during handles holding conditions compared to normal walking for iAD, with significantly lower reflex amplitudes observed at midstance and toe-off. Compared to the many instances of reflex reversals with SR nerve stimulation, only one occurrence of a reversal in reflex sign was observed with median nerve stimulation, where a facilitatory cutaneous reflex during the normal walking condition became inhibitory during the MH and

Figure 5.4: Group averaged data for middle latency interlimb cutaneous reflexes arising from median nerve stimulation for muscles in which a significant difference was found between conditions in which the arms were allowed to swing freely, and conditions in which handles were held. The four points of the step cycle investigated are shown on the abscissa. Average middle latency interlimb cutaneous reflex amplitude values are depicted as open (N), grey (MH), and black (H) bars, with the standard error shown. Reflex values are normalized to the maximum EMG produced during normal, undisturbed walking. *: significant difference ($p < 0.05$) in middle latency interlimb cutaneous reflexes.



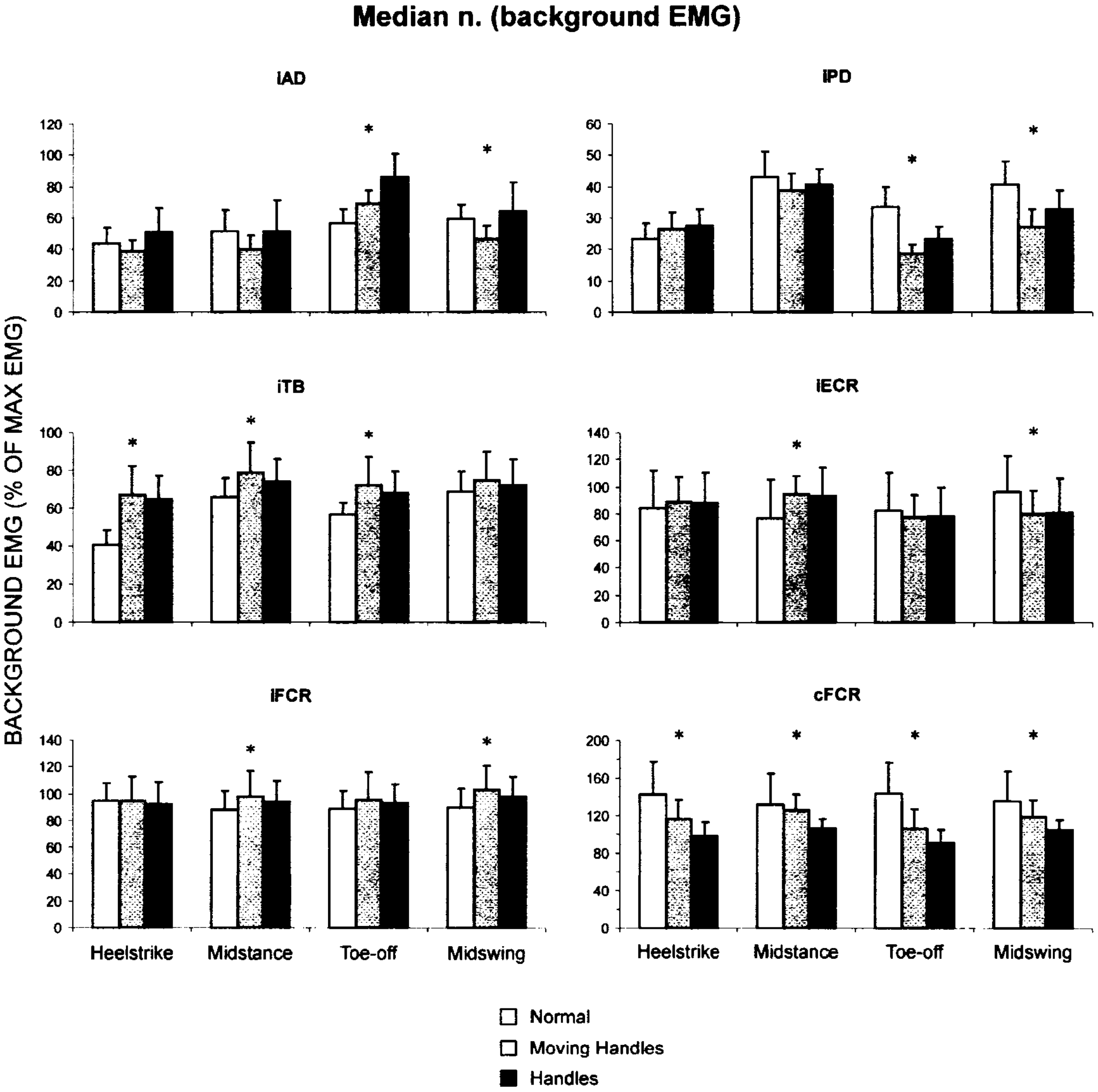
H conditions in iAD at toe-off. The reflex amplitude during the normal walking condition was significantly different than that for the H condition.

The corresponding background EMG for muscles that displayed significant differences in average cutaneous reflex amplitude values between conditions with median nerve stimulation are shown in Figure 5.5. The background EMG activity during conditions in which the median nerve was stimulated closely resembled that for muscles shown in Figure 5.3 (SR nerve). Thus, similar to that described during the SR nerve stimulation paradigm, significant differences in background EMG activity were generally observed between conditions involving in which the hands were engaged in balance control and normal walking. Greater background EMG activity was generally observed during the MH and H conditions for iTB at all points of the step cycle. Planned comparisons revealed that these differences were statistically significant. Significantly greater background EMG activity was also observed during the MH and H walking conditions for iAD, and iECR at certain points of the step cycle. In addition, significantly lower background EMG values were observed during conditions in which the handles were held compared to normal walking for cFCR at all points of the step cycle, as well as for iPD and iECR at points indicated on the Figure.

5.3.3 Influence of perturbations on cutaneous reflexes

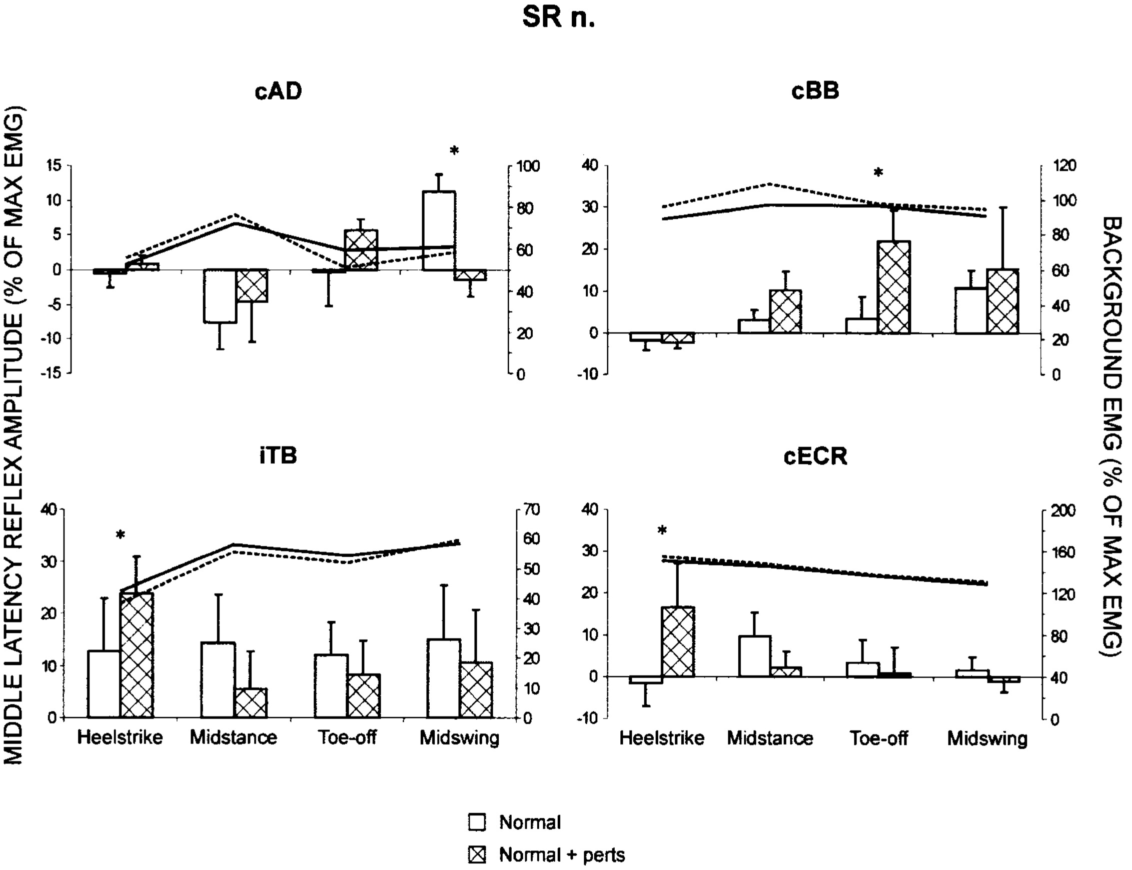
The threat of receiving a perturbation at the torso influenced the amplitude of cutaneous reflexes. This was observed for all three arm tasks (arms swinging freely, holding moving handles, holding stable handles) and for reflexes evoked

Figure 5.5: Group averaged data for background EMG activity during the median nerve stimulation paradigm for muscles in which a significant difference was found in cutaneous reflex amplitude values between conditions in which the arms were allowed to swing freely and conditions in which handles were held. The four points of the step cycle investigated are shown on the abscissa. Average middle latency interlimb cutaneous reflex amplitude values are depicted as open (N), grey (MH), and black (H) bars, with the standard error shown. Reflex values are normalized to the maximum EMG produced during normal, undisturbed walking. *: significant difference ($p < 0.05$) in middle latency interlimb cutaneous reflexes.



from both nerves. Shown in Figures 5.6 and 5.7 are the average cutaneous reflex amplitudes comparing the normal and NP walking conditions for muscles in which significant differences were found during the SR and median nerve stimulation protocols respectively. The average background EMG values are also displayed as the lines in each panel. With SR nerve stimulation, four of the twelve muscles recorded displayed significant differences in cutaneous reflex amplitudes between walking conditions (Figure 5.6). In general, lower reflex amplitudes during the NP condition were observed compared to normal walking for iTB and cECR for most points of the step cycle, except at heelstrike. At heelstrike, significantly larger reflex amplitudes were observed during the NP condition in iTB and cECR. In addition, cutaneous reflex amplitudes were generally larger during the NP walking condition in cBB across the entire step cycle, with the reflexes at toe-off being significantly larger compared to normal walking. The amplitude of the cutaneous reflex in cAD during the NP condition was significantly lower than that during the normal walking condition at midswing. In addition, a task-related reversal in reflex sign was noted for cAD and cECR at midswing and heelstrike respectively. That is, a facilitatory reflex observed in cAD at midswing during normal walking became an inhibitory reflex during the NP condition. For cECR, an inhibitory reflex at heelstrike reversed its sign to be facilitatory during the NP condition. Between the normal and NP conditions, reflex reversals were observed only with SR nerve stimulation. In all four muscles, background EMG activity was similar between walking conditions, with no significant differences observed.

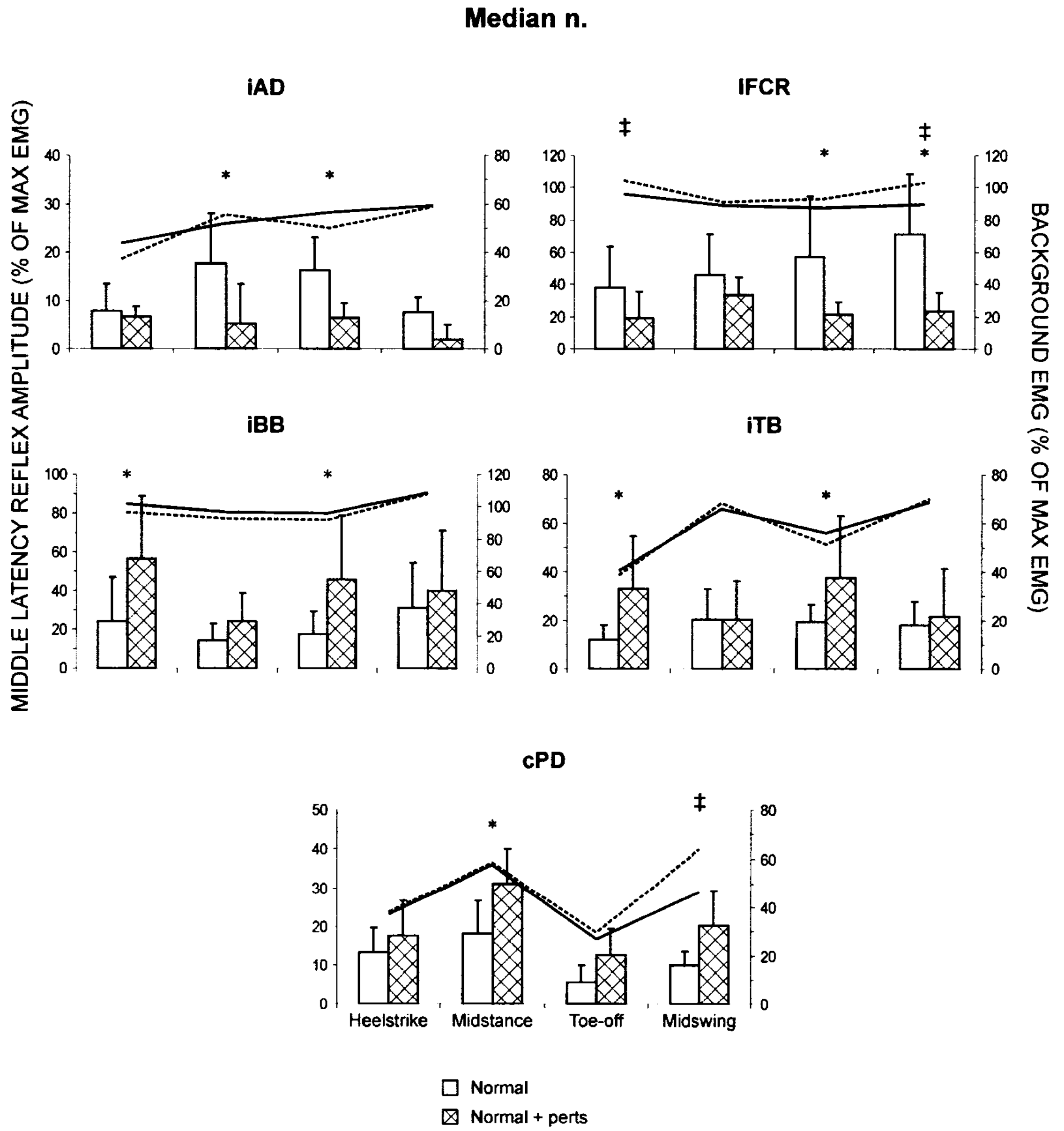
Figure 5.6: Group averaged data for middle latency interlimb cutaneous reflexes arising from SR nerve stimulation between conditions in which the arms were allowed to swing freely for muscles in which a significant difference was found. The four points of the step cycle investigated are shown on the abscissa. Average middle latency interlimb cutaneous reflex amplitude values are depicted as open (N) and hatched (NP) bars, with the standard error shown. Values for middle latency reflexes are shown on the left ordinate. Average background EMG is represented by the solid (N) and dotted (NP) black lines, with its values along the right ordinate. Both reflex and background EMG values are normalized to the maximum EMG produced during normal, undisturbed walking. *: significant difference ($p < 0.05$) in middle latency interlimb cutaneous reflexes.



Significant differences were also observed in cutaneous reflex amplitudes between walking conditions with median nerve stimulation (Figure 5.7). Cutaneous reflex amplitudes were generally greater during the NP walking condition compared to normal walking for iBB, iTB, and cPD across the step cycle. Planned comparisons revealed significantly greater cutaneous reflex amplitudes during the NP condition for iBB and iTB at heelstrike and toe-off, as well as for cPD at midstance. Also, smaller reflex amplitudes were generally observed for all points of the step cycle during the NP walking condition for iAD and iFCR. Significantly lower reflex amplitudes were noted during the NP condition compared to normal walking for iAD at midstance and toe-off, and for iFCR at toe-off and midswing. The corresponding background EMG activity between the normal and NP walking conditions were generally similar. Significant differences in EMG levels were observed for cPD at midswing, and iFCR at heelstrike and midswing. At these instances, the ongoing EMG activity during the NP condition was significantly higher than during normal walking.

Qualitatively, the threat of perturbations had a more robust influence on cutaneous reflexes when the hands were engaged in balance control. For example, Figures 5.8 and 5.9 display comparisons made between walking conditions in which the hands were similarly engaged in holding moving handles (MH, MHP). Significant differences in cutaneous reflex amplitudes were observed in half of the recorded muscles between comparable walking conditions for both nerve stimulation paradigms. With SR nerve stimulation, greater cutaneous reflex amplitudes were generally observed when walking in an environment in which

Figure 5.7: Group averaged data for middle latency interlimb cutaneous reflexes arising from median nerve stimulation between conditions in which the arms swung rhythmically for muscles in which a significant difference was found. The four points of the step cycle investigated are shown on the abscissa. Average middle latency interlimb cutaneous reflex amplitude values are depicted as open (N) and hatched (NP) bars, with the standard error shown. Values for middle latency reflexes are shown on the left ordinate. Average background EMG is represented by the solid (N) and dotted (NP) black lines, with its values along the right ordinate. Both reflex and background EMG values are normalized to the maximum EMG produced during normal, undisturbed walking. *: significant difference ($p < 0.05$) in middle latency interlimb cutaneous reflexes; ‡: significant difference ($p < 0.05$) in background EMG.



perturbations were delivered while the hands were holding onto moving handles (Figure 5.8). For iPD, iTB, and iFCR, reflex amplitudes during the MHP walking condition were greater than that for the MH condition at all points of the step cycle. A similar trend was also observed for iBB. Planned comparisons revealed significantly greater cutaneous reflex amplitude during the MHP waking condition for iPD at all points of the step cycle, iBB at toe-off, iTB at toe-off and midswing, and iFCR at midswing. In cECR, reflexes evoked at heelstrike were also significantly, and substantially larger during the MHP condition than the MH condition. This is in contrast to the general, though not significant, suppression of reflexes observed at the other points in the step cycle. One notable exception to the general finding that reflexes were larger during the MHP walking condition was found in cAD, in which a significantly lower reflex amplitude value was observed during the MHP condition at toe-off. Additionally, a reflex reversal was noted in iBB at midswing, where an inhibitory reflex amplitude value during the MH condition reversed in sign to become facilitatory during the MHP walking condition. The corresponding background EMG activity was similar between the MH and MHP walking conditions. Significantly greater ongoing EMG activity was observed during the MHP condition for iBB at heelstrike, iFCR at all points of the step cycle, cAD at toe-off, and iTB at midstance and midswing.

Differences in reflex amplitudes between the MH and MHP walking conditions were also observed with median nerve stimulation (Figure 5.9). Cutaneous reflex amplitudes were greater during the MHP walking condition for iECR at all points of the step cycle, and for cFCR at most points, except at

Figure 5.8: Group averaged data for middle latency interlimb cutaneous reflexes arising from SR nerve stimulation between conditions in which moving handles were held for muscles in which a significant difference was found. The four points of the step cycle investigated are shown on the abscissa. Average middle latency interlimb cutaneous reflex amplitude values are depicted as solid (MH) and hatched (MHP) grey bars, with the standard error shown. Values for middle latency reflexes are shown on the left ordinate. Average background EMG is represented by the solid (MH) and dotted (MHP) grey lines, with its values along the right ordinate. Both reflex and background EMG values are normalized to the maximum EMG produced during normal, undisturbed walking. *: significant difference ($p < 0.05$) in middle latency interlimb cutaneous reflexes; ‡: significant difference ($p < 0.05$) in background EMG.

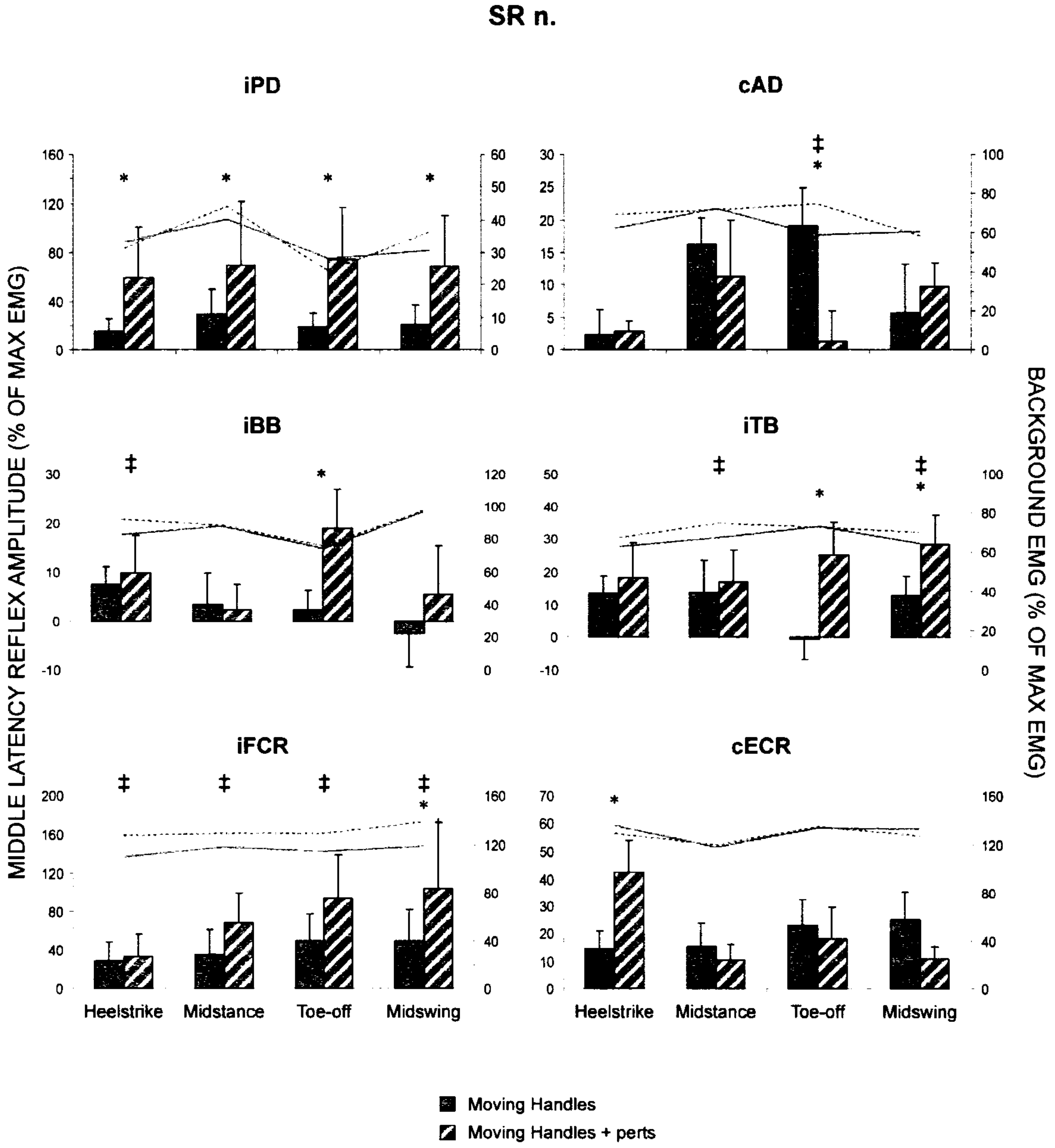
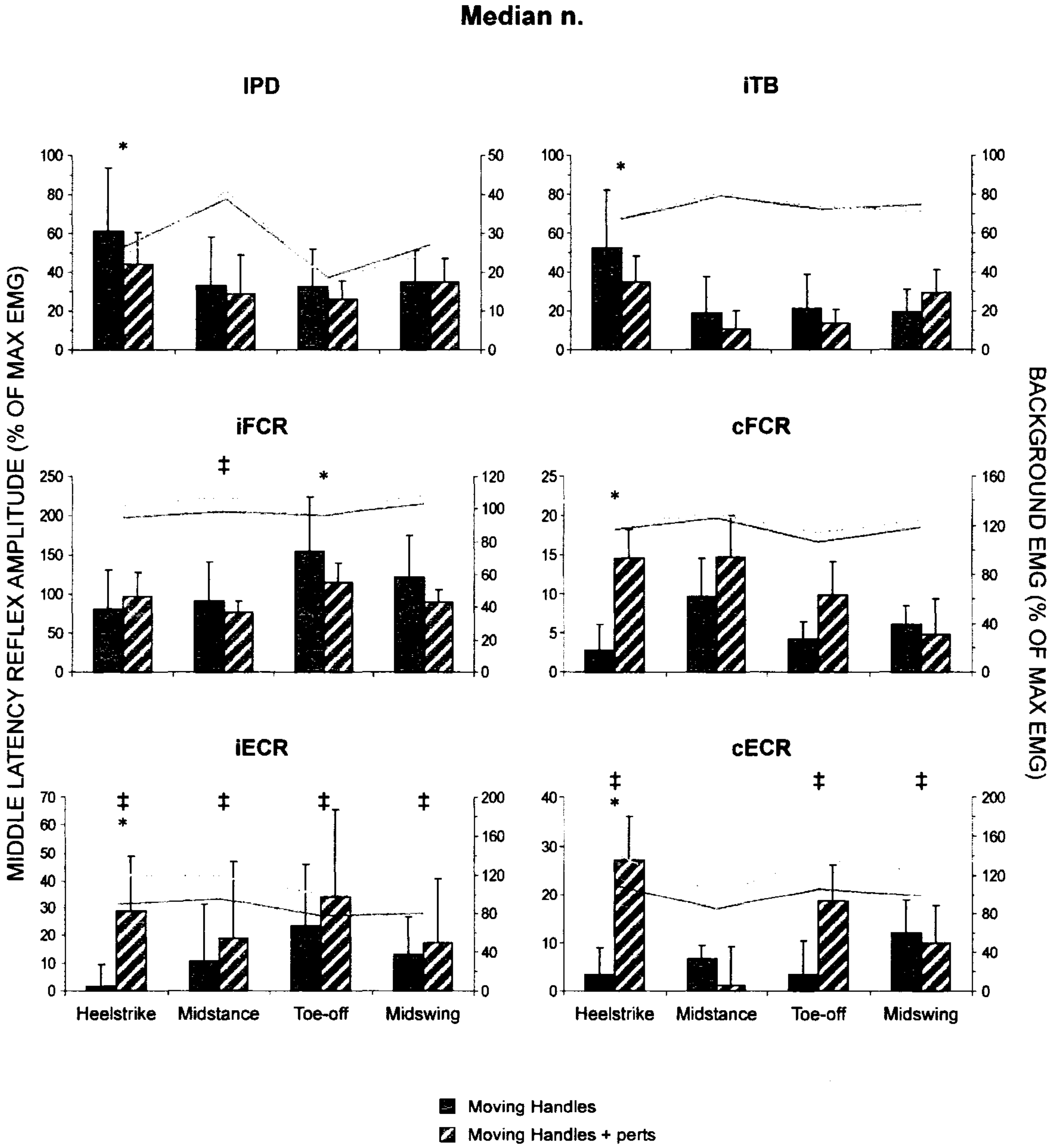


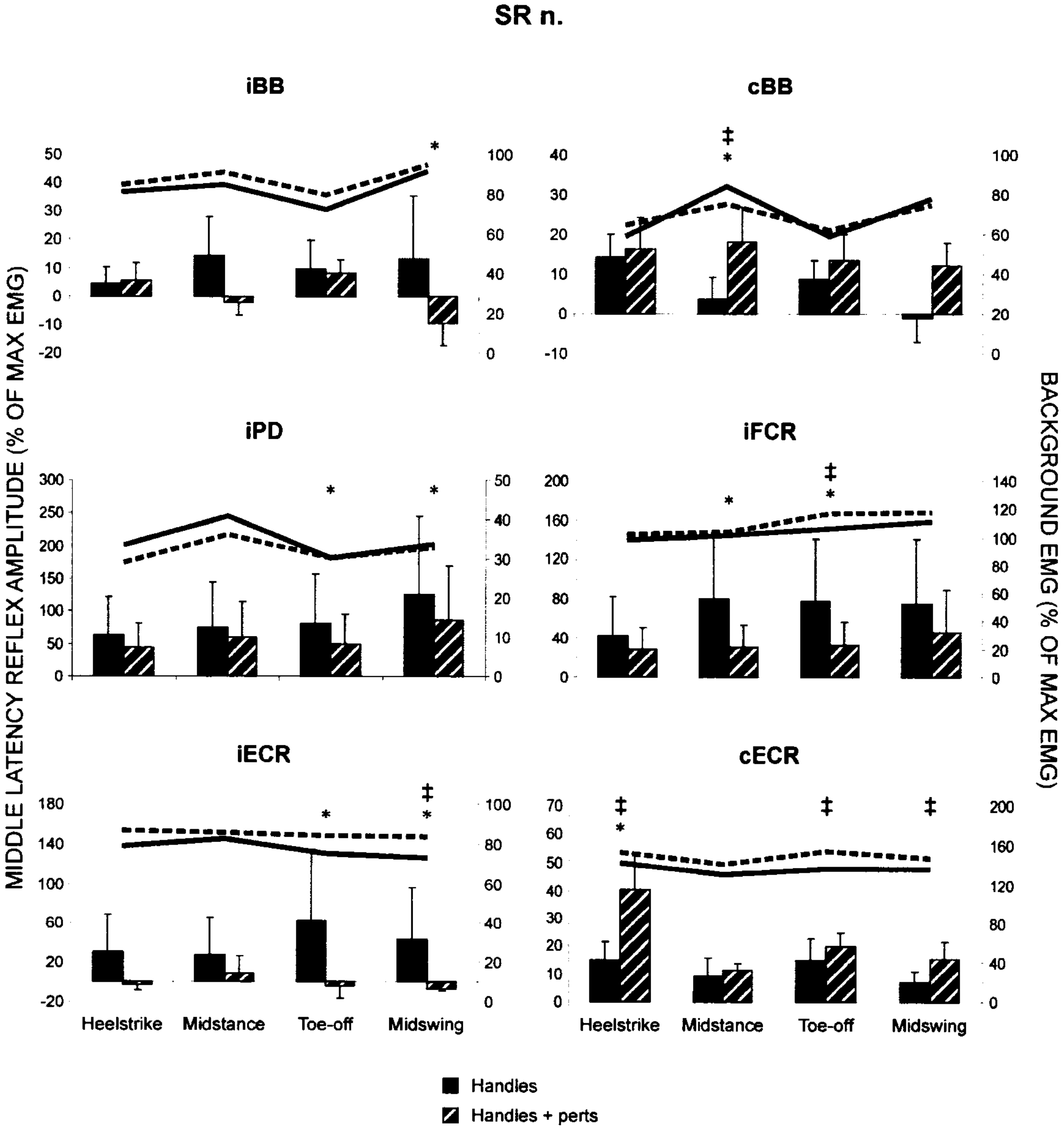
Figure 5.9: Group averaged data for middle latency interlimb cutaneous reflexes arising from median nerve stimulation between conditions in which moving handles were held for muscles in which a significant difference was found. The four points of the step cycle investigated are shown on the abscissa. Average middle latency interlimb cutaneous reflex amplitude values are depicted as solid (MH) and hatched (MHP) grey bars, with the standard error shown. Values for middle latency reflexes are shown on the left ordinate. Average background EMG is represented by the solid (MH) and dotted (MHP) grey lines, with its values along the right ordinate. Both reflex and background EMG values are normalized to the maximum EMG produced during normal, undisturbed walking. *: significant difference ($p < 0.05$) in middle latency interlimb cutaneous reflexes; ‡: significant difference ($p < 0.05$) in background EMG.



midswing. Significantly greater reflex amplitudes were observed during the MHP condition for iECR, cFCR, and cECR at heelstrike. Generally lower reflex amplitudes were observed during the MHP condition for iPD, iTB, and iFCR at most points of the step cycle, with planned comparisons revealing significantly lower reflex amplitude values compared to the MH condition for iPD and iTB at heelstrike, as well as for iFCR at toe-off. In all instances where the background EMG was significantly different between conditions, the ongoing EMG activity was significantly greater during the MHP walking condition compared to the MH condition. Significant differences were observed in iFCR at midstance, iECR at all points of the step cycle, and cECR for all points except at midstance.

When the hands were holding stable handles, significant differences were observed during both nerve stimulation protocols. With SR nerve stimulation, half the muscles recorded showed significant differences in reflex amplitudes between the H and HP walking conditions (Figure 5.10). There was a general trend towards lower cutaneous reflex amplitude values during the HP condition compared to the H walking condition. For instance, reflex amplitudes during HP walking were lower for iPD, iFCR, and iECR across all points of the step cycle. This trend was also generally observed in iBB, except at heelstrike. Planned comparisons revealed significant differences between conditions that followed the general trend described above, with significantly lower reflex amplitudes being observed during the HP condition for iPD and iFCR at midstance and toe-off, iECR at toe-off and midswing, and for iBB at midswing. Generally greater cutaneous reflex amplitudes were observed during the HP walking condition over

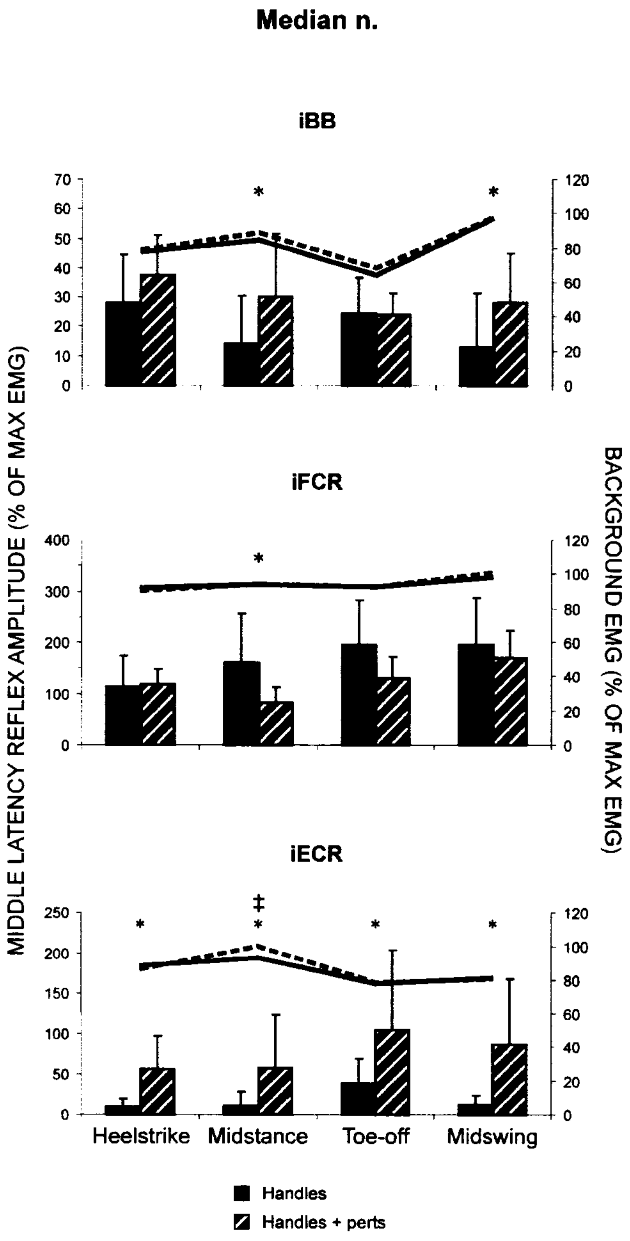
Figure 5.10: Group averaged data for middle latency interlimb cutaneous reflexes arising from SR nerve stimulation between conditions in which stable handles were held for muscles in which a significant difference was found. The four points of the step cycle investigated are shown on the abscissa. Average middle latency interlimb cutaneous reflex amplitude values are depicted as solid (H) and hatched (HP) black bars, with the standard error shown. Values for middle latency reflexes are shown on the left ordinate. Average background EMG is represented by the solid (H) and dotted (HP) thick black lines, with its values along the right ordinate. Both reflex and background EMG values are normalized to the maximum EMG produced during normal, undisturbed walking. *: significant difference ($p < 0.05$) in middle latency interlimb cutaneous reflexes; ‡: significant difference ($p < 0.05$) in background EMG.



all points of the step cycle compared to the H condition for cBB and cECR. Cutaneous reflex amplitudes were significantly higher during the HP condition for cBB at midstance and cECR at heelstrike. The corresponding background EMG activity was observed to be significantly higher during the HP walking condition compared to the H condition for iFCR at toe-off, iECR at midswing, and cECR at heelstrike, toe-off, and midswing. Significantly lower background EMG activity was observed during the HP walking condition for cBB at midstance. In addition, reflex reversals were observed for iBB at midswing, and iECR at toe-off and midswing. In all these occurrences, excitatory reflexes during the H walking condition were significantly different than inhibitory reflexes observed during the HP condition.

Qualitatively, there were fewer differences in cutaneous reflex amplitudes between the H and HP walking conditions with median nerve stimulation (Figure 5.11). During the HP walking condition, significantly higher cutaneous reflex amplitude values were observed for iBB at midstance and midswing, as well as for iECR across all points of the step cycle, compared to reflex values during the H walking condition. A significantly lower reflex amplitude value was observed during the HP condition for iFCR at midstance. The corresponding background EMG activity was similar between the H and HP walking conditions for all these muscles, with the only difference in background EMG activity between conditions identified for iECR at midstance. Furthermore, no reflex reversals were observed between the H and HP walking conditions with median nerve stimulation.

Figure 5.11: Group averaged data for middle latency interlimb cutaneous reflexes arising from median nerve stimulation between conditions in which stable handles were held for muscles in which a significant difference was found. The four points of the step cycle investigated are shown on the abscissa. Average middle latency interlimb cutaneous reflex amplitude values are depicted as solid (H) and hatched (HP) black bars, with the standard error shown. Values for middle latency reflexes are shown on the left ordinate. Average background EMG is represented by the solid (H) and dotted (HP) thick black lines, with its values along the right ordinate. Both reflex and background EMG values are normalized to the maximum EMG produced during normal, undisturbed walking. *: significant difference ($p < 0.05$) in middle latency interlimb cutaneous reflexes; ‡: significant difference ($p < 0.05$) in background EMG.



5.4 Discussion

Tactile information from the hands has been shown to assist in the ongoing regulation of stability during standing (Jeka 1997) and walking (Dickstein and Laufer 2004). Consequently, cutaneous reflexes elicited from the hands may be involved in compensatory reactions observed in the arms during walking. Corrective responses have been observed in the muscles of the upper limbs in response to perturbations during walking (Marigold and Patla 2002; Misiaszek 2003). This study examined the influence of engaging the hands in balance control on cutaneous reflexes evoked from stimulation at the hand during walking. We found that the amplitude of cutaneous reflexes in the upper limbs was influenced by the manner in which the hands were engaged in balance control, as well as the threat of balance disturbance during walking.

5.4.1 Nerve-specific responses

Significant differences in cutaneous reflex amplitudes between walking conditions were generally more prevalent with SR nerve, compared to median nerve stimulation. In addition, although instances were observed in which the same muscles displayed significant differences for each nerve, the responses within each of these muscles differed between nerves. This is likely an example of nerve-specificity, a characteristic previously reported for cutaneous reflexes evoked in the muscles of the legs during walking (Van Wezel et al. 1997; Zehr et al. 1997), and in the muscles of the upper limbs during arm cycling (Zehr and Kido 2001). In the lower limbs, nerve-specificity refers to observations of differential reflex modulation evoked with the stimulation of cutaneous nerves innervating different areas of the foot during walking. These different reflex responses are associated with different kinematic responses, which have been suggested to reflect the role of location-specific information from the foot during locomotion (Zehr and Stein 1999).

In this study, the difference in reflex responses between SR and median nerve stimulation may be due to the innervation areas for these nerves. For the median nerve, the innervation area comprises the palmar surface of hand. It follows that cutaneous reflexes elicited from the median nerve would be more susceptible to context-dependent modulation during conditions in which the hands were engaged in balance control. Since the palmar surface of the hand receives cutaneous information from contact with the handles, it is possible that cutaneous reflexes evoked by median nerve stimulation may not be as flexible to undergo context-dependent modulation, since the innervation area of the median nerve is already receiving cutaneous information. In contrast, cutaneous input from the dorsum of the hand (i.e. SR nerve stimulation) may indicate a disturbance to the hand that is holding onto the handle, which may be viewed as a threat to the stability provided by holding onto fixed handles. The innervation area for the SR nerve can serve a functional role by detecting obstacles during walking (Haridas and Zehr 2003). In turn, this may explain the greater number of muscles that displayed significant differences between the H and HP walking conditions. However when the handles are able to move, stimulation of cutaneous nerves innervating the hand may be interpreted as a threat to stability, regardless of which part of the hand the information is coming from. This may explain the similar number of muscles that showed significant differences in reflex amplitude between the two nerves stimulated during the MH and MHP walking conditions.

5.4.2 Reflex reversals

In addition to significant differences in reflex amplitude values, cutaneous reflex reversals were also observed between walking conditions. Moreover, reflex reversals were more prominent with SR nerve stimulation. In comparing cutaneous reflex amplitudes across conditions in which the hands were engaged in balance control (N, MH, H), six out of the nine muscles that showed significant differences in reflex amplitudes also contained reflex reversals between conditions with SR nerve stimulation, in comparison to only one of six muscles with median nerve stimulation. When reflexes were compared between conditions in which the arms were performing similar tasks (N vs. NP; MH vs. MHP; H vs. HP), there were no occurrences of reflex reversals with median nerve stimulation. This was not the case with SR nerve stimulation, as eight out of sixteen muscles that showed significant differences in reflex amplitudes between conditions also contained reversals. The observation of more occurrences of cutaneous reflex reversals with SR nerve, compared to median nerve stimulation has been previously reported for middle-latency cutaneous reflexes evoked during arm cycling (Zehr and Kido 2001).

We have previously noted interlimb cutaneous reflex reversals in the muscles of the arms between walking conditions with cutaneous nerve stimulation at the foot (Haridas et al. 2006). In humans, reflex reversals have been reported in the muscles of the leg between different tasks such as standing and walking (Komiyama et al. 2000), as well as between phases of the step cycle (Yang and Stein 1990; Van Wezel et al. 1997). Cutaneous reflex reversals have also been observed in the muscles of the arms with electrical stimulation of nerves at the wrist between arm cycling and static tasks (Zehr and Kido 2001). De Serres et al. (1995) suggested that cutaneous reflex reversals in humans may be due to parallel excitatory and inhibitory pathways converging onto the same motoneuronal pool to either facilitate or suppress ongoing muscle activity, and that each pathway was differentially weighted according to the phase of the step cycle. The reversals noted in the present study are likely mediated by a comparable mechanism.

5.4.3 Functional relevance

This study describes the influence of utilizing the hands in balance control on the amplitude of cutaneous reflexes in the muscles of the arms. Cutaneous reflexes evoked with SR and median nerve stimulation were generally observed to be greater in amplitude when the hands were engaged in balance control (MH, H), compared to conditions in which the arms were allowed to swing freely during walking (normal). In particular, reflex amplitudes were typically greatest when the hands were engaged in holding onto stable handles. The implication is that changes in postural set, as a result of how the arms are involved in the task, leads to associated adaptations in reflex amplitude.

The general increase in cutaneous reflex amplitudes evoked from the hands when engaging the hands in balance control may suggest a functional role for these responses. Holding onto handles allows the arms to act against them to increase stability during locomotion, similar to holding a handrail during stair climbing. Thus, the facilitation of upper limb cutaneous reflexes observed in the present study may assist the arms in the execution of corrective responses. A similar observation was recently documented for interlimb cutaneous reflexes evoked from the foot while holding onto a fixed rail during walking, which led to facilitated reflex amplitudes in iPD (Lamont and Zehr 2007). These responses were much smaller in amplitude when no rail was held. Thus, they suggested that the increased response is observed only when the arm is able to assist in balance control, by acting against an earth-referenced support. The observation of increased cutaneous reflex amplitudes in iPD when the hands were holding onto stable handles with both SR and median nerve stimulation (Figure 5.2 and 5.4) in the current study would agree with this suggestion, as this muscle could assist in balance control by facilitating a pulling action against the fixed handles.

A functional role for the observed context-related differences in reflex amplitudes is further supported by the observation that cutaneous reflexes in the arms are influenced by walking in an environment in which perturbations were delivered. This result corroborates similar findings in our previous studies, showing the stability context of the locomotor environment influences the amplitudes of both cutaneous and H-reflexes in the legs (Haridas et al. 2005; Krauss and Misiaszek 2007) and interlimb cutaneous reflexes in the arms (Haridas et al. 2006). As suggested by Misiaszek (2003), this context-dependent reflex modulation corresponds to observations of context-dependent adaptation of corrective response evoked with perturbations during walking (Misiaszek et al. 2000; Misiaszek and Krauss 2005). In addition, Misiaszek (2003) noted that corrective responses in the lower and upper limbs evoked during normal walking differed with respect to consistency, with more variability observed with responses in the arms. Since the arms were allowed to swing freely, they could participate in corrective responses in several ways, thus leading to the increased variability. Similarly in this study, stimulation of cutaneous nerves in the hand evoked reflex responses during normal walking that did not follow a clear systematic trend based on the task performed. This variability in context-related cutaneous reflex responses is similar to previous reports describing interlimb cutaneous reflexes in the muscles of the arms (Haridas et al. 2006).

When the hands were engaged in balance control, differences in cutaneous reflex amplitudes were observed when walking in an environment in which perturbations were delivered. While holding onto moving handles, there was a general trend towards greater reflex amplitudes during the MHP walking condition in several muscles compared to the MH condition. This trend was not as evident between the H and HP conditions, with fewer muscles displaying significant differences in reflex amplitude values. The different manner in which cutaneous reflexes were modified between conditions in which the hands were similarly engaged (i.e. MH vs. MHP; H vs. HP) may take into account the specific properties of each type of support. When the handles are able to move, responses in the muscles of the arms would likely be larger when walking in a context of increased threat to stability, as it is known that the handles that are being held do not provide as stable a support as when locked in place. When holding onto fixed handles, walking in an environment in which perturbations are unexpectedly encountered may not be perceived as a viable threat to stability, as the locked handles are recognized to provide the greatest level of stability. An example of these types of supports exist in a subway car or bus, where there are overhead rails (fixed) as well as hanging handles that are allowed to move while attached to a rail (moving). While it is possible to act against the hanging handles to regain balance, the characteristics of that corrective response is likely different than that needed to act against a fixed reference. When holding onto a handles hanging off a rail, greater amplitude responses in the muscles of the arm are likely needed, compared to holding onto the fixed rail to compensate for the moving support, since the arm is now being relied on heavily to maintain stability. Thus, we suggest the difference in cutaneous reflexes between the MH-MHP and H-HP walking conditions suggests a context-specific modulation related to the properties of the support, similar to that reported recently by Lamont and Zehr (2007).

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Chapter 6 - General Discussion

6.1 Introduction

The main objective of this thesis was to investigate the context-dependency of cutaneous reflexes. Specifically, the context of stability was utilized to evaluate cutaneous reflex modulation during walking. This section summarizes the main findings of this thesis, and discusses the overall functional relevance of this reflex adaptation during locomotion.

6.2 Context-dependent modulation of cutaneous reflexes

Previously, cutaneous reflexes have been reported to modulate in both a task- and phase-dependent manner during movements of the upper (Zehr and Chua 2000; Zehr and Kido 2001; Zehr and Haridas 2003) and lower limbs (Duysens et al. 1990; Duysens et al. 1993; Van Wezel et al. 1997; Zehr et al. 1997; Brooke et al. 1999). The specific adaptation of these reflexes according to the performed behaviour and phase of the movement cycle has led to the suggestion that cutaneous reflex modulation contributes to the maintenance of stability during walking (Zehr and Stein 1999). Thus, cutaneous reflexes should also be modulated during walking in an environment in which stability is altered. In this thesis, a systematic examination was performed on locomotor cutaneous reflex modulation under varying postural demands.

The main finding from the work presented in this thesis was that cutaneous reflexes were modulated in a context-dependent manner during locomotion. In Chapter 2, I reported that reflexes evoked in the muscles of the lower limbs with electrical stimulation of cutaneous nerves innervating the foot were modulated in relation to the changing threat to stability, induced by restricting the use of the arms as well as delivering mechanical perturbations to the torso. That is, cutaneous reflex amplitudes were greater while walking in an environment in which existed a higher threat to stability. In contrast, cutaneous reflexes were suppressed when walking in the most stable environment. Following these findings, Chapter 4 focused on the influence of context-specific perturbations (with respect to the innervation area of the stimulated SP nerve) on cutaneous reflexes in the lower limbs. While walking in an environment in which context-specific mechanical perturbations were delivered to the cutaneous field innervated by the SP nerve, cutaneous reflexes normally associated with the stumbling corrective response (Van Wezel et al. 1997; Zehr et al. 1997) were suppressed during swing phase. Taken together, these findings suggest that cutaneous reflex responses in the lower limbs are capable of being adapted to the particular demands of a locomotor task.

Cutaneous reflexes in the muscles of the upper limbs during walking were the focus of Chapters 3 and 5. In Chapter 3, interlimb cutaneous reflexes evoked from electrical stimulation at the foot were found to be influenced by the level of stability and the task of the arms. When the arms were crossed, interlimb reflexes were facilitated when the threat to stability was greatest. However, when the arms were allowed to swing freely, interlimb reflex responses were suppressed while walking with an increased threat to stability. In Chapter 5, the influence of engaging the hands in balance control on reflexes evoked in the upper limbs by electrical stimulation of cutaneous nerves innervating the hand was investigated. It was found that cutaneous reflex amplitudes were influenced according to the manner by which the hands were engaged in balance control, as well as the threat to stability. Generally, holding onto handles resulted in greater amplitude reflexes compared to when the arms were allowed to swing freely during walking. These results suggest that cutaneous reflexes in the muscles of the upper limbs are regulated in a task-dependent manner during locomotion.

Therefore, cutaneous reflexes in both the lower and upper limbs were observed to be context-dependent during locomotion. In addition, the changes in cutaneous reflexes were not due to a generalized change in spinal circuit excitability, as reflex adaptations were targeted to specific cutaneous reflex pathways in a task-specific manner during locomotion. Furthermore, cutaneous reflex adaptation in the lower limbs was limited to specific points in the step cycle. These findings suggest a functional role for the context-dependent modulation observed.

6.3 Functional relevance of context-dependent reflex modulation

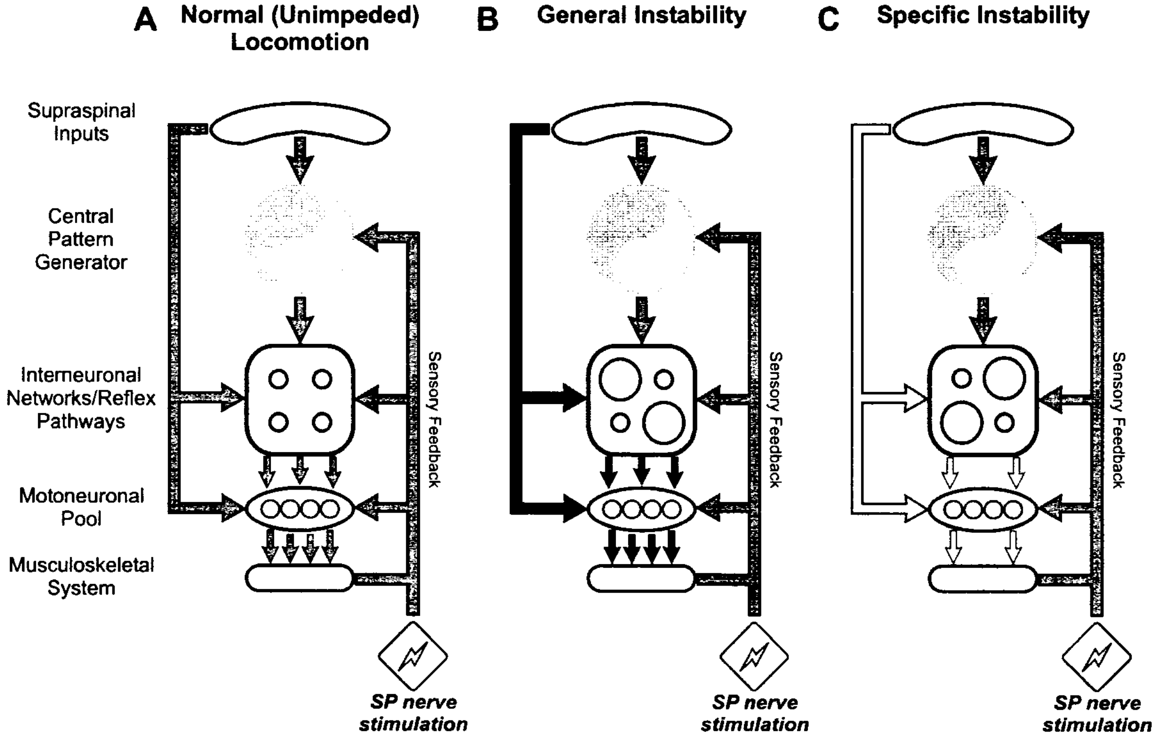
In Chapter 1, I proposed that cutaneous reflexes may serve to assist in the maintenance of balance during locomotion. Specifically, when encountering a perturbation during walking, these reflexes may assist in corrective responses that are elicited across the body. The observations of cutaneous reflexes undergoing context-dependent modulation in this thesis are consistent with this theory. However there are limitations with respect to this suggested functional role (see *6.4 Limitations*).

Cutaneous reflex responses evoked in the lower limbs from electrical stimulation at the foot were observed to adapt to the demands of the task during walking. For instance, reflex responses evoked from SP nerve stimulation during normal walking has been shown to lead to a coordinated stumbling corrective response, consisting of an increase in knee flexion and plantar flexion at swing phase (Van Wezel et al. 1997; Zehr et al. 1997). In Chapter 2, responses in iSOL and iBF were facilitated during the most unstable walking condition, which would allow for the foot to clear an encountered obstacle, resulting in the normal progression of the step cycle. In the same walking condition, cutaneous reflexes were also facilitated in cTA and cMG during the contralateral stance phase. This facilitation could serve to increase the rigidity at the ankle of the stance limb while walking in an unstable environment. Cutaneous reflex changes in the legs evoked with SP nerve stimulation were also observed while walking in an environment in which context-specific perturbations were delivered (Chapter 4). However, it was shown that reflexes normally associated with a stumbling corrective response were suppressed in the ipsilateral leg during swing when walking in a specific instability context. At the same point of the step cycle, cutaneous reflexes in the contralateral ankle extensor were facilitated. These findings suggest that cutaneous reflexes from the foot serve an important functional role in coordinating corrective responses during locomotion.

The difference in findings between Chapters 2 and 4 are interesting, as it gives further insight into the manner by which cutaneous reflexes from the foot are specifically regulated according to the context of the locomotor environment.

Recently, Misiaszek (2006) suggested a model in which the convergence of the factors that select and weight the rules governing dynamic stability during walking likely occurs in interneuronal networks and reflex pathways. Shown in Figure 6.1 is an adapted model illustrating that information on the context in which locomotion takes place, presumably via supraspinal input, can modify the set of rules. This in turn modifies various interneuronal networks and reflex pathways (represented by circles of varying sizes) to produce different motor outputs. Figure 6.1A represents previous findings in which electrical stimulation delivered to the SP nerve during walking evokes a functionally-relevant stumble corrective response, which corrects swing limb trajectory and assists with the maintenance of forward progression (Van Wezel et al. 1997; Zehr et al. 1997; Haridas and Zehr 2003). While walking in a generalized instability context (Figure 6.1B), the weighting of the interneuronal networks and reflex pathways is altered by descending influences, to adapt the contralateral portion of the stumble correction responses but leaves intact the ipsilateral response evoked by SP nerve stimulation (Chapter 2). However in Chapter 4, (see Figure 6.1C), SP nerve stimulation failed to evoke a stumble correction response while walking in a targeted and specific instability context (i.e. mechanical perturbations at the foot dorsum affecting swing leg trajectory directly). This suggests that in this context, the stimulus is not associated with a threat to stability and therefore the stumble corrective response may not be appropriate, given the particular context of the locomotor environment. Rather, the interneuronal networks and reflex

Figure 6.1: Schematic model (adapted from Misiaszek 2006), illustrating the role of supraspinal input in modulating motoneuronal output in response to electrical stimulation of the SP nerve (represented by ↯) during swing phase. A: Sensory information attained from stimulation of the SP nerve, along with feedback regarding limb position, is integrated with information on the context in which locomotion takes place in interneuronal networks/reflex pathways and motoneuron pools. The resulting motoneuronal output is a functionally-relevant stumbling corrective response (Zehr et al. 1997; Haridas and Zehr 2003). B: While walking in an environment in which a context of generalized instability exists, supraspinal input modulates interneuronal network and reflex pathway components to produce facilitated compensatory responses (Chapter 2). C: In Chapter 4, walking was performed in an environment in which a targeted instability was present (i.e. mechanical perturbations to the dorsum of the foot). Supraspinal input regarding the nature of the perturbation modulates interneuronal network and reflex pathway components to suppress a stumble corrective response, as this response is now inappropriate to the forward progression of the swing limb.



pathways are reorganized so that the motor response better suits the needs of the task (Figure 6.1C).

Supraspinal input likely plays an important role in regulating compensatory responses, by modulating components within interneuronal networks and reflex pathways. This input may originate from cortical areas associated with visual and vestibular systems, as well as from subcortical areas which could provide information regarding the context of the environment. A functional example of the expression of the responses for generalized instability can be considered when walking on a pitching boat or moving subway car. There is a generalized effect on stability, but it is still relevant to correct the swing leg motion to avoid stumbling (Chapter 2). By contrast, when walking in an environment where tripping and stumbling is likely, such as through dense underbrush or deep snow, continuous expression of the stumble correction response may conflict with the overall goal of forward progression and is consequently suppressed as shown in Figure 4.6. Overall the reflex networks are finely tuned to allow appropriate function to assist with locomotor progression in each context.

Context-dependent cutaneous reflex modulation was also observed in the upper limbs. As mentioned in the previous section, interlimb cutaneous reflex responses in the muscles of the arms evoked from the foot were generally facilitated when the arms were restricted from moving while walking in an environment with a higher threat to stability (Chapter 3). Since the arms were restricted in assisting in balance control, they would first have to be uncrossed. The facilitated reflexes during this arm task could function to assist in this standard corrective response. When the arms were allowed to swing freely, there are many ways in which the upper limbs can contribute to corrective responses. This likely contributed to the similar reflex responses observed with the arms free when walking in a higher instability context. When the arms are engaged in balance control by holding onto handles, cutaneous reflexes in the upper limbs evoked from the hand were observed to be generally facilitated compared to normal walking (Chapter 5). Cutaneous sensation from the hands evoked with electrical stimulation of cutaneous nerves may potentially indicate obstacles during walking (Haridas and Zehr 2003). As the handles can be used to increase stability by acting as a stable support, facilitation of upper limb cutaneous reflexes could serve to assist in corrective responses. This is similar to recent observations that reflexes in the upper limbs were facilitated only when the arm was capable of assisting in balance control (Lamont and Zehr 2007). Together, these findings indicate that cutaneous reflexes in the upper limbs may serve a functional role in coordinating corrective responses during walking.

In conclusion, the data presented in this thesis provides evidence that cutaneous reflexes are capable of being modulated during locomotion according to the context of the surrounding environment. The specific reflex changes observed support the view that cutaneous reflexes may serve to assist in coordinating whole-body corrective responses. The overall results contained in this thesis give further understanding to the overall function of cutaneous reflexes during locomotion.

6.4 Limitations

6.4.1 Operational definitions

As with most experimental designs, there were inherent limitations that existed in conducting the experiments described in this thesis. One such limitation of my studies concerns the term 'context-dependency'. In all projects, the walking conditions used were described as being varied with respect to stability, which was indicative of a change in the context of the locomotor environment. Following this, changes in cutaneous reflex amplitudes were said to be due to the context of the walking condition. However, the variable that I mention as being varied (stability) was not actually measured in all of the studies performed. An example of a variable that could have given a measure of stability for each walking condition would be the centre of mass, and its movement throughout the step cycle. In addition, responses evoked with mechanical perturbations, which were observed to alter the normal ongoing gait pattern, were not recorded during any of the walking conditions. Thus, we cannot conclude that the walking conditions used were different with respect to the level of stability.

In addition, it was also mentioned that walking conditions varied in terms of the level of postural threat. Similar to stability, the level of postural threat was not definitively measured. This variable could have been measured using an ordinal score provided by subjects on a scale from no perceived threat to great perceived postural threat (Carpenter et al. 2004). Alternatively, a more quantitative measure of threat could have been achieved by measuring galvanic skin conductance (GSC), which is used to evaluate the level of physiological arousal under certain conditions (Brown et al. 2002). Different levels of GSC between walking conditions could be interpreted as a change in arousal due to the experimental condition (Maki and McIlroy 1996). Therefore, a definitive definition of 'context-dependency' would have allowed for a stronger argument that the cutaneous reflex modulation observed was in fact due to the level of perceived postural threat associated with a given walking condition.

6.4.2 Functional relevance

Throughout this thesis, I suggest that the differences in cutaneous reflex responses observed between walking conditions in each experiment are indicative of a functional role during locomotion. Specifically, I suggest that the cutaneous reflex responses could serve to assist in balance control during walking. However, it is incorrect to simply conclude that cutaneous reflexes serve a functional role based on the context-dependent modulation of these responses. Previously, cutaneous reflexes have been suggested to serve a functional role during locomotion, based on their task- and phase-dependent modulation during the step cycle, as well as correlated changes in kinematics (Zehr and Stein 1999). To serve a functional role, cutaneous reflexes should ultimately be able to generate responses that are capable of generating sufficient torque to produce an observable corrective response. In this thesis, no measurement of forces generated was made.

However, investigating the functional role of cutaneous reflexes during locomotion was not the purpose of the work presented in this thesis. Rather, I used cutaneous reflexes as a probe to investigate the state of spinal circuitry during walking conditions, and observed the changes in reflex amplitude under various locomotor environments. From the results reported in my thesis, it can be concluded that varying the context of the locomotor environment influences the amplitude of cutaneous reflexes. Further, these changes in reflex responses are isolated to specific cutaneous reflex pathways at specific points in the step cycle. Based on the direction of the change in reflex amplitude, along with the current mechanical state (e.g. arms crossed, arms holding handles), I made inferences as to the functional relevance of the cutaneous reflex responses observed.

6.4.3 Source of context-dependent modulation

As suggested in the model presented in Figure 6.1, interneuronal networks and spinal reflex pathways are predicted to be the locus at which integration of sensory information attained from cutaneous receptors with supraspinal information regarding the locomotor environment takes place. This is indicated by the different sized circles within the interneuronal network/reflex pathway level for each type of locomotor environment (generalized instability, specific instability). This integration results in a reweighing of the interneuronal networks and specific reflex pathways to produce a modified motor output. However, this model can only predict the locus of the context-dependent modulation observed in this thesis. In order to definitively determine the locus of context-dependent cutaneous reflex modulation, the activity of interneurons and reflex pathways must be recorded. At present, it is not known which particular interneurons contribute to reflex modulation. In addition, no method exists to record interneuronal activity in humans during locomotion. Until such methods are developed, we can only predict the source of the context-dependent modulation observed. It may be more feasible to perform this type of research using animal models.

More evidence can be provided to determine that changes in interneuronal networks and reflex pathways contribute to the results reported in this thesis by using transcranial magnetic stimulation (TMS) over the motor cortex to evoke motor evoked potentials (MEP) in muscles of the extremities. This type of stimulation activates interneurons in the brain that synapse with corticospinal tract neurons, which have a monosynaptic connection to muscles in the arms and legs. Using TMS would therefore bypass the interneurons in the spinal cord, and if these spinal interneurons are responsible for the context-dependent modulation observed in this thesis, it would be expected that the evoked MEPs should not change in amplitude between different walking conditions. While this type of experiment can provide further evidence to the suggested role of interneurons during locomotion, it still cannot be concluded that these interneurons are responsible for the modified motor output observed in this thesis.

6.5 Future directions

6.5.1 Cutaneous contribution to dynamic balance control

The results from Chapters 2 and 3 indicate that whole-body cutaneous reflexes evoked from the foot are able to be modulated during walking according to the context of the surrounding environment. This modulation was also only observed in certain muscles at specific points of the step cycle, which provides further evidence to the suggestion that cutaneous reflexes may serve a functional role in assisting in the maintenance of balance during locomotion (Zehr and Stein 1999). However, the findings presented in these chapters, along with previous observations of task- and phase-dependent modulation of cutaneous reflexes only provide indirect evidence to the aforementioned suggested functional role.

One approach that would directly explore the functional role of cutaneous reflexes would be to investigate the influence of modifying cutaneous information on whole-body corrective responses elicited by mechanical perturbations during walking. This could be done by eliminating cutaneous sensation from the soles of the feet via anesthesia (e.g. nerve block), which has previously been done in studies investigating the role of plantar cutaneous information on quiet stance (Asai et al. 1990; Magnusson et al. 1990; Meyer et al. 2004b) as well as corrective responses elicited from a standing position (Do et al. 1990; Horak et al. 1990; Perry et al. 2000; Meyer et al. 2004a). In these studies, a reduction in cutaneous sensation from the plantar surface of the feet was associated with an increase in postural sway and impaired compensatory stepping reactions in response to unexpected perturbations. Reducing plantar sensation has also been shown to reduce gait velocity over a compliant surface (McDonnell and Warden-Flood 2000). However, the influence of diminished cutaneous information from the soles of the feet on corrective responses elicited by perturbations during locomotion has not yet been investigated. Studies examining the relationship between cutaneous information from the plantar surface of the feet and dynamic balance control would elucidate the role of cutaneous afferents in coordinating corrective responses. If cutaneous information is important for dynamic balance control, it would be expected that corrective responses elicited by unexpected perturbations during walking would be affected, such as a delayed onset of muscle activity.

6.5.2 Mechanism of context-dependent cutaneous reflex adaptation

In Chapter 4, cutaneous reflexes normally associated with a stumbling corrective response (Zehr et al. 1997) were modulated during walking conditions in which context-specific perturbations were delivered to the dorsum of the foot. This finding is associated with recent findings by McVea and Pearson (2007), who observed hindpaw hyperflexion in intact cats after repeated exposure to mechanical perturbations delivered to the dorsum of the hindpaw at early swing during treadmill locomotion. Interestingly this hyperflexion, characteristic of the stumbling corrective response in cats (Forssberg 1979), was only observed in the same locomotor context in which perturbations were delivered and not in other walking environments. The authors suggested this context-dependent hyperflexion to be indicative of a learned response. In turn, the context-dependent modulation of cutaneous reflexes observed in Chapter 4 may be representative of a learned reflex response.

From this, one area of research that could follow from the work presented in Chapter 4 is to investigate the mechanism regulating the context-dependent modulation of cutaneous reflexes. As McVea and Pearson (2007) noted, the dependency of the hyperflexion response on the context of the locomotor environment suggests cortical influences onto spinal circuitry. However, a recent study by Heng and de Leon (2007) showed that in the absence of descending influence, the lumbar spinal cord in rats is capable of producing corrective responses in the hindlimbs through repetitive exposure to an external perturbation during walking. Therefore, spinal reflex pathways may contribute to learned corrective responses during locomotion. This may have implications for rehabilitation strategies currently employed for gait training. As there is evidence that spinal circuits are capable of modifying locomotor activity in response to perturbations (Timoszyk et al. 2002; Edgerton et al. 2004), and the recent findings that spinal circuits are able to correct hindlimb stepping patterns via prior experience (Heng and de Leon 2007), cutaneous reflexes could be potentially used as a medium to induce plasticity in spinal circuits associated with generating locomotion.

6.5.3 Facilitation of cutaneous sensation in the hands

In Chapter 5, engaging the hands in balance control during locomotion led to an increased facilitation of cutaneous reflexes evoked in the upper limbs by electrical stimulation at the hand, compared to when the arms were allowed to swing freely. This suggests that cutaneous reflex pathways to the muscles of the upper limbs can be modulated according to the task of the arms. Therefore, increasing cutaneous sensation at the hand may lead to improvements in dynamic balance control. For example, corrective responses in the muscles of the arms may be facilitated by increasing cutaneous sensation at a contact surface such as the handle of a cane, which in turn could benefit dynamic balance control. Thus, increasing cutaneous sensation at the hand may have beneficial effects on balance control during walking. This area of research would be important to those who use assistive devices (e.g. canes, walkers) during walking to aid in balance control.

However, using an assistive device over a long-term period may lead to a continuous facilitation of cutaneous reflex pathways in the arms, which in turn could lead to an over-reliance on corrective responses in the arms. An over-reliance on assistive devices was reported by Bateni et al. (2004), who observed a persistence in maintaining contact with an assistive device in response to unexpected perturbations, which led to impaired compensatory stepping responses compared to having the hands free. Thus, holding onto assistive devices may impair dynamic balance control, as corrective responses in the muscles of the legs may not be utilized to the same extent. Holding onto a stable support during walking results in a suppression of corrective responses in the legs compared to normal walking (Misiaszek et al. 2000). As well, the work presented in Chapter 2 showed a suppression of cutaneous reflexes in the legs when holding onto stable handles, a finding also reported with the H-reflex during walking (Krauss and Misiaszek 2007). Future research on the influence of enhancing cutaneous sensation in the hands on dynamic balance control is needed, which in turn could lead to improvements in the design and development of next-generation assistive devices.

6.5 References

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