Effect of Stability Context on Cutaneous Reflex Modulation during Treadmill Walking

by

Allen Lewis
BSc, University of Waterloo, 1987
BHSc, McMaster University, 1997

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Supervisory Committee

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Abstract

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Reflex control during walking has been shown to be specific to the behavioural context of a postural threat. Reflex modulation has been shown to be influenced by perturbations to the trunk, as well as by changes to arm activity that further affected the level of postural threat. The magnitudes of EMG responses in limbs and trunk to mechanical trip perturbations were differentially modulated depending on whether or not an earth- referenced railing was held. To further understand the neural control of limb and trunk muscles during walking contexts where changes to postural stability are solely linked to arm activity, we created 3 treadmill walking tasks each with the arms engaged differently to induce three levels of postural stability. Neurologically-intact participants walked on a treadmill using normal arm swing (NORMAL), holding a wheeled walker (WALKER), or holding the handrails (HANDRAIL). Subjects ranked the tasks according to degree of perceived challenge to stability; WALKER was ranked most challenging, followed by NORMAL and then HANDRAIL. Cutaneous reflexes were evoked via constant current stimulation (5 x 1.0 ms pulses at 300 Hz) of Superficial Peroneal (SP) nerve at the foot and Superficial Radial (SR) nerve at the wrist in separate trials during each walking task. EMG was recorded ipsilateral to nerve stimulation from arm and leg muscles and bilaterally from trunk muscles. Off-line analysis was conducted on eight phases of the step cycle after phase-averaging, contingent upon the timing of stimulation in the step cycle. The number of differences in bEMG and reflexes between tasks was graded with the proximity to the source of instability at the arms, progressively increasing from the legs to the arms. The gradient in bEMG differences suggests that the mechanical constraints of each task required different levels of muscle activation that was greatest for the arms, less for the trunk and least for the legs. The similar gradient seen for reflexes suggests functionally relevant changes in neural control of arm and trunk muscles in order to maintain postural stability during in each task. However, overall there were significantly fewer differences in reflexes between tasks compared to bEMG. We suggest that the mechanical constraints of the tasks yielded more significant changes in the muscle activation while requiring far fewer task-specific changes in reflex control suggesting a conservation of some elements of the neural control mechanisms across tasks.

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Acknowledgments

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Dedication

A very special thank you to Laurel, for without your unending patience and support, this would never have been possible.

CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW

Neural control of locomotion has been explored over the past hundred years since Sir Charles Sherrington identified the nature of reflexes (Sherrington 1906). Direct evidence of spinal circuitry responsible for locomotor control has predominantly come by way of reduced animal preparations (Grillner 1975; Grillner and Dubuc 1988; Grillner and Matsushima 1991). In such preparations, spinal central pattern generators (CPGs) have been shown to control rhythmic fore- (Yamaguchi 2004), and hind-limb (Grillner and Zangger 1984) movement. By necessity, investigation of neural control mechanisms of rhythmic movement in humans is both indirect and inferred. Bipedal human locomotion involves greater postural demands than quadrupedal locomotion and therefore requires precise integration of postural control with the rhythmic, alternating movement of arms and legs. Although bipeds and quadrupeds share common elements of locomotor control mechanisms, it is likely that the specific expression of such control is shaped by the unique postural constraints imposed on each. The control of posture during locomotion involves many subservient physiological systems supporting multiple, whole-body responses. This research project will examine the neural control of trunk and limb movement during walking tasks in different stability contexts by investigating how reflex modulation and muscle activation patterns are influenced by changes in the stability constraints of the task.

This literature review will examine neural control of locomotion, in the quadruped and the human biped. Specific focus will be given to the spinal central pattern generators (CPGs) and evidence to support their purported contributions to the regulation of rhythmic movement of upper and lower limbs as well as interlimb coordination during rhythmic movement. Finally, the neural control of arm, leg and trunk muscles during walking tasks that vary by degree of postural stability will be reviewed as well as the influence of arm activity on locomotor control.

I. Role of the Central Pattern Generator in Control of Rhythmic Movement

i. Evidence in Non-Human Animals

In 1906, Sherrington studied the scratch-reflex in the spinalized dog (Sherrington 1906) and subsequently investigated crossed-limb stepping reflexes in the presence and absence of sensory feedback in the spinalized and decerebrate cat (Sherrington 1910). T. Graham Brown (1911) furthered this research by demonstrating in the spinalized and deafferented cat model that within the spinal cord, a locomotor rhythmic motor output could be generated in the absence of afferent feedback and descending cortical input. From these and subsequent findings, Brown proposed the “half-centre” model, which included flexor and extensor interneurons that received a common excitatory drive. The ‘half-centres’ worked through reciprocally-inhibiting flexor and extensor interneurons which prevented simultaneous activity and allows for reciprocating out-of-phase activation. Subsequent models furthered this to suggest separate half-centres for each limb existed to control ipsi-, and contralateral flexor and extensor motorneuron output (Pang and Yang 2000). Brown suggested that the alternating limb activity observed during locomotion was a consequence of synaptic fatigue of each half-centre; as the firing of each half-centre slowed, its reciprocal inhibition onto the opposing half-centre was removed and the cycle would repeat itself (Brown 1914).

Since Brown's contribution, successive conceptualizations have been put forth to reflect a deeper understanding of the organization of spinal circuitry responsible for rhythmic locomotion (Miller and Scott 1977; Székely et al. 1969; Pearson 1995; Kriellaars et al. 1994; McCrea and Rybak 2008). Central pattern generators are now thought to involve complex spinal inter-neuronal networks comprised of integrated reflex pathways capable of generating repetitive, reciprocating movement patterns used to create purposeful behaviours such as walking, swimming and breathing (Zehr 2005).

Elements of rhythmic locomotion have been demonstrated across many species, including the stick insect (Borgmann et al. 2009), the moth (Manduca sexta), and in many other insect flight preparations (Vierk et al. 2009). Studies by Wolf & Pearson (1987) demonstrated rhythmic movement patterns in locust flight in the absence of sensory input, supporting the hypothesis of CPG-modulated rhythmic movement. CPGs have been demonstrated across many invertebrate species; the mollusk (Tritonia) has been shown to utilize CPGs to regulate swimming (Getting and Dekin 1985). The isolated spinal cord of the lamprey has been induced to produce undulating movements such as fictive swimming (Harris-Warrick and Cohen 1985; Parker and Grillner 2000). Similar rhythmic locomotor patterns appear conserved across other vertebrates (Samara and Currie 2008).

In various vertebrate animal models it has been demonstrated that within the spinal cord there exist neuronal linkages responsible for the coordinated nature of quadrupedal gait (Guertin 2009; Juvin 2005; Kiehn 2006). Rhythmic and reciprocating fore and hind-limb movements during quadrupedal locomotion have been demonstrated in cat (Chandler et al. 1984; Miller et al. 1975; Frigon et al. 2009; Yamaguchi 1992) and rat preparations (Cowley and Schmidt 1997; Kjaerulff and Kiehn 1996).

Although there is a relative abundance of evidence in support of CPG regulation of rhythmic movement patterns in lower animals, there is less direct evidence in primates. Especially in the human, it is difficult to demonstrate rhythmic, locomotor-like movements with no descending supraspinal contribution and in the absence of afferent input from the periphery. Fedirchuk et al. (1998) demonstrated fictive locomotor patterns in the decerebrate and spinalized marmoset monkey with the application of clonidine and excitatory amino acids. As well, rudimentary stepping movements have been shown in the squirrel monkey after complete spinal cord transection (Vilensky and O'Connor 1998). As New World monkeys, the marmoset and squirrel monkey are considered more primitive than the Old World primates, which include apes and humans. It has therefore been suggested that the difficulty in demonstrating fictive locomotion in Old World primate spinal or decerebrate preparations is due to the greater descending influence of the corticospinal tract during locomotion in these species (Vilensky and O'Connor 1998).

II. CPG Evidence in the Control of Human Lower limb Rhythmic movement

i. Infant Walking Patterns

It has been suggested that because the corticospinal tract remains largely unmyelinated at birth, descending supraspinal control in the human neonate is deficient, resulting in locomotor behaviours that may be compared to the decerebrate cat (Zehr and Duysens 2004). With significantly less input possible from the motor cortex, rudimentary stepping movements demonstrated in prenatal infants (de Vries et al. 1984) and supported neonates suggest that a spinal mechanism is responsible for control (Lamb and Yang 2000; Yang et al. 2004). In the human infant prior to independent walking, stepping responses can be initiated over ground or on a moving treadmill (Forssberg 1985; Thelan 1986; Yang et al. 1998; Lamb and Yang 2000; Pang and Yang 2000, 2002) and if gait is briefly blocked during swing, a bilateral response pattern is induced (Dietz et al. 1986). Forssberg (1985) compared gait patterns of human infants and children who had recently learned to walk and demonstrated that while the neonatal stepping reflex was possibly controlled exclusively by CPGs, adaptable locomotor patterns appeared only in later stages of ontogeny with further maturation of the CNS. Finally, in anencephalic human infants, no descending cortical input exists and yet the stepping response has been demonstrated, lending support to a spinal mechanism being responsible for such rhythmic movement patterns (Peiper 1963).

Taken together, the evidence suggests that in the human infant prior to the maturation of the descending influence of the motor cortex, spinal CPG circuitry exists that may assist in the neural control of stepping movements.

ii. Spinal Cord Stimulation

Although inferences have been made based on various animal preparations, direct evidence of CPG-mediated mechanisms of locomotor control in the human is limited. In some of the most compelling human CPG investigations to date, reciprocal, locomotor patterns with corresponding EMG activity were demonstrated in individuals with complete spinal cord injuries (SCI) with the application of tonic epidural electrical stimulation (20-60Hz) to the dorsal spinal cord (L2-L3) (Dimitrijevic et al. 1998; Minassian et al. 2007). Tonic electrical stimulation, acting as a proxy for descending input from supraspinal centres, initiated patterned locomotor muscle activity through isolated spinal circuitry (Dimitrijevic et al. 1998).

iii. Sleep-Related Periodic Leg Movements

Occurring unilaterally or bilaterally, involuntary rhythmic leg movements have been reported in both neurologically-intact (Coleman et al. 1980; Bixler et al. 1982) and complete SCI individuals (Lee et al. 1996). It has been suggested that removal of descending inhibition onto spinal circuitry responsible for rhythmic movement generation during sleep may be responsible (Lee et al. 1996).

III. Reflex Studies- Further Evidence of CPG Control in Human Lower Limb Rhythmic Movement

Evoked spinal reflexes, whether by mechanical or electrical means, have been used as neural probes to investigate neural mechanisms responsible for the control of rhythmic movements such as locomotion (Burke 1999; Zehr and Duysens 2004). Sensory input has been demonstrated to have significant influence on the modulation pattern of motor output during rhythmic movements (Duysens and Pearson 1976; Duysens and Van de Crommert 1998; Zehr and Stein 1999). Reflex expression during static conditions has been shown to be tightly coupled with the background EMG activity of the muscle in which the reflex is evoked, referred to as “automatic gain compensation” (Mathews 1986). In contrast, during rhythmic movement conditions (e.g. walking), reflex amplitude has been demonstrated to be poorly correlated with bEMG across the movement cycle (Komiyama et al. 2000; Zehr and Haridas 2003). In addition to reflex amplitudes being independent of background EMG, reflexes evoked during rhythmic movement also present with characteristic features of task-, and phase-dependency. It has been suggested that these reflex modulation patterns may be the result of gating of afferent input by CPGs via alteration of spinal interneuron excitability (Duysens et al. 1990; Zehr 2005) and pre-synaptic inhibition of afferent pathways (Dubuc et al. 1988). In this way, reflex responses provide inferential evidence of CPG function in humans (Duysens and Van de Crommert 1998; Zehr 2005; Zehr et al. 2009).

i. Task-Dependent Reflex Modulation Patterns

Modulation patterns (amplitude and/or sign reversal) in reflexes have been shown to differ depending upon the behavioural context of the movement (task-dependent) (Zehr and Stein 1999). It is reasonable therefore to expect that reflexes should appropriately adapt to the movement context in order to provide flexible and functional locomotor responses (Zehr and Stein 1999). Task-dependent reflex modulation patterns in the legs during rhythmic movement have been reported previously (Brooke et al. 1997; Zehr and Duysens 2004). For example, cutaneous reflexes evoked in leg muscles have been shown to exhibit task-dependency in leg cycling vs. static contraction (Zehr et al. 2001), standing vs. walking (Komiyama et al. 2000) and standing vs. running (Duysens et al. 1993). Task-dependent modulation of Hoffmann (H) reflexes has also been demonstrated in leg muscles during leg-cycling conditions (Brooke et al. 1997), arm-cycling conditions (de Ruiter et al. 2010), and in reduced locomotor tasks (Mezzarane et al. 2011). H-reflexes in soleus muscle have shown task-dependent modulation, with increasing reflex amplitude suppression from standing, to walking, to running (Stein and Capaday 1988).

ii. Phase-Dependent Reflex Modulation Patterns

Modulation of evoked reflexes independent of background muscle activity (bEMG) has been attributed in part to the control of spinal CPGs. Cutaneous reflexes evoked with stimulation of the foot have been shown to be phase-modulated, dependent upon the phase of gait cycle in which they were elicited (Tax et al. 1995; Zehr et al. 1998; Van Wezel et al.1997; Haridas and Zehr 2003, 2005; Lamont and Zehr 2007; Duysens et al. 2008). Stimulation of the superficial peroneal (SP) nerve in the foot during a walking task elicited suppression of the tibialis anterior muscle during early swing phase, allowing the foot to avoid an obstacle. Suppression was observed again at the end of swing phase, near heel strike, to allow the foot to make stable contact with the ground; whereas throughout stance phase there was no effect on reflex amplitude (Duysens et al. 1990; Van Wezel et al. 1997; Zehr et al. 1997; Zehr and Stein 1999). Similarly, findings of task-, and phase-dependent reflex modulation have also been shown in leg-cycling paradigms (Sakamoto et al. 2006; Zehr et al. 2007a).

Reflex responses in the lower extremity have also demonstrated nerve-specificity, meaning responses were specific to the cutaneous innervation field stimulated. Stimulation of the superficial peroneal, sural and posterior tibial nerve afferent fibres of the foot each has been shown to elicit specific patterns. Stimulation of the superficial peroneal nerve on the foot dorsum resulted in a suppressive response in tibialis anterior muscle in early and late swing, while tibial nerve stimulation of the sole of the foot evoked facilitation of tibialis anterior muscle during early and mid-swing phase (Zehr et al. 1997). Stimulation of the sural nerve on the lateral aspect of the foot caused inhibition of tibialis anterior at late swing and early stance phase (Zehr et al. 1998).

IV. Evidence of Upper Limb CPG Control in Humans

The rhythmic movement of the arms during walking has been attributed to activation of shoulder muscles and not simply a passive, pendulous response (Elftman 1939; Ballesteros et al. 1965; Jackson 1983). Jackson (1983) suggested that during walking, human arm muscles were controlled by "rhythm generators", much the same as in other animal species. The walking human demonstrates reciprocating muscle activity of the opposing lower limbs coupled with diagonally out-of-phase activity of the upper limbs (Ballesteros et al. 1965; Wannier et al. 2001). During walking, EMG and reflex modulation of arm muscles has demonstrated phase-dependency across the gait cycle, similar to leg muscles (Zehr and Haridas 2003; Zehr et al. 2004). Cutaneous and H-reflexes evoked in human upper limbs were shown to be task-, and phase-dependent during arm-cycling movements (Zehr and Chua 2000; Zehr and Kido 2001; Zehr et al. 2003, Carroll et al, 2005; Zehr and Hundza 2005; Sakamoto et al. 2006). Interestingly, phase-dependent reflex modulation in arm muscles appears whether the arm-cycling task is forward or backward in direction (Zehr and Hundza 2005). During walking versus matched static positions, cutaneous reflexes in the arms have shown alterations in amplitude when equivalent phases of the gait cycle were compared (Zehr and Haridas 2003). In the arms, as in the legs, reflex amplitudes during rhythmic movements have been shown to be poorly correlated with bEMG, whereas in static conditions a relative high degree of correlation has been shown (Zehr and Kido 2001; Zehr et al. 2003; Zehr and Haridas 2003). Cutaneous reflexes of the upper limb have also been described in terms of nerve-specificity, in a manner similar to that seen in the legs (Zehr and Kido 2001). As in the legs, task-, and phase-dependent reflex modulation in arm muscles during rhythmic arm tasks has also been ascribed, in part, to contributions from spinal CPG mechanisms (Zehr and Haridas 2003; Balter and Zehr 2007).

During arm-cycling, it has been demonstrated that cutaneous reflex modulation was independent of contralateral arm activation whether active or passive (Carroll et al. 2005) suggesting a weaker neural circuitry between arms as compared to the legs (Zehr and Duysens 2004). In contrast, during rhythmic leg movement, either passive or active, the contralateral leg was shown to inhibit evoked reflexes in the ipsilateral leg (Collins et al. 1993). In review, Zehr and Duysens (2004) provided the explanation for the difference in strength of neural linkage between upper limbs versus lower limbs, attributing it to an evolutionary shift toward independent function of the upper limbs. A flexible, task-oriented neuronal coupling between cervical and lumbo-sacral CPG networks, it has been reasoned, would have provided early human ancestors with the freedom to use the arms for manipulative and grasping behaviours during bipedal locomotion (Zehr et al. 2009).

V. Inter-limb Coordination

Rhythmic motor tasks such as walking, crawling, cycling, swimming require coordination between reciprocally-moving upper and lower limbs. The findings of Wannier and colleagues (2001) demonstrated a fixed-frequency coupling of upper and lower limb rhythmic movements in human walking, swimming and creeping tasks. This coordination was preserved despite the slowing of leg movements by flippers. The authors hypothesized that such inter-limb coordination corresponded to coupled oscillators (CPGs) (Wannier et al. 2001).

It has been suggested that in the human, locomotor coordination between the limbs originates from neural linkages between cervical and thorocolumbar CPG networks (Dietz 2002; Zehr and Duysens 2004; Dietz and Michel 2009). Long projecting propriospinal neurons have been shown to connect cervical and lumbar enlargements in the cat (Miller et al. 1975), neonatal rat (Juvin 2005) and in the human spinal cord (Nathan and Smith 1955; Nathan et al 1996).

Inter-limb reflexes have been demonstrated during walking with perturbations to the foot (Dietz et al. 2001; Haridas and Zehr 2003) and hand (Haridas and Zehr 2003). Haridas & Zehr (2003) investigated inter-limb neural pathways using a treadmill walking paradigm in which cutaneous reflexes were evoked at the hand (superficial radial nerve) and foot (superficial peroneal nerve). The investigators found that inter-limb reflexes were modulated according to task (i.e. static vs. walking), and phase of the walking cycle. Mechanical accelerations and decelerations of the treadmill belt as well as electrical stimulation of the tibial nerve caused reflex responses in arm muscles during walking, but not during standing or sitting (Dietz et al. 2001).

Arm cycling has also been demonstrated to suppress the soleus H-reflex amplitude and that this inter-limb modulation was shown to be phase-, (de Ruiter et al. 2010) and task-dependent (Frigon et al. 2004; Loadman and Zehr 2007; de Ruiter et al. 2010), as well as dependent on frequency of arm-cycling (Hundza and Zehr, 2009). Combined arm and leg-cycling paradigms (i.e. ‘‘reduced’’ locomotion) have also been used to demonstrate inter-limb task-, and phase-dependent reflex modulation (Balter and Zehr 2007; Zehr et al. 2007a, b; Mezzarane et al. 2011).

VI. Postural Control During Walking

In human adult walking, the swing phase occurring on one side is temporally coordinated with stance phase in the contralateral limb (Dietz 1992). In studies where gait was perturbed during swing phase using a brief obstruction, a bilateral functionally relevant response pattern was evoked, thus indicating a coordinated response between legs (Dietz et al. 1986). Similar coordinated inter-limb responses in intact cats were proposed to be mediated at the spinal level given the short latency of the EMG responses (Gorassini et al. 1994). CPG-driven muscle activation was purported to be responsible for the coordinated patterning between lower limbs during human infant locomotion (Lamb and Yang 2000).

Locomotion is believed to be mediated through complex interactions within a tripartite system involving descending supraspinal input from the motor cortex, spinal networks (CPGs and associated interneurons) and sensory feedback from peripheral muscle and skin receptors (Zehr and Duysens, 2004). Forming an additional layer of the CPG, integrated interneuronal reflex pathways can be used to further shape the motor pattern for specific behaviours. Such neural circuits form the framework of inter-limb reflexes believed to play a role in the coordination of all four limbs during various rhythmic locomotor tasks (Dietz et al. 2001; Dietz 2002; Zehr and Duysens 2004). In order for locomotion to be functional and appropriate to the immediate context, sensory information serves to appropriately sculpt locomotor output, such as the velocity, amplitude and trajectory of limb swing (Zehr 2005).

i. Walking in Unstable Environments

Reflex control during walking has been shown to be related to the context in which the reflexes were elicited, thus demonstrating the flexibility of the CNS to utilize pertinent sensory input in order to create functional locomotor output. It was suggested that the gain of reflexes changes across the movement cycle as dictated by the functional context and that reflexes are therefore able to provide ongoing corrections to maintain progression of the movement (Zehr et al. 2004). Forssberg (1979) is credited with demonstrating the "stumbling corrective response" in the intact cat model in which electrical and tactile stimulation of the dorsum of the hind-limb paw elicited a functional phase-dependent response during walking. If the stimulus occurred during ipsilateral swing-phase, a reflex response of flexor muscles occurred, causing the perturbed limb to further flex over an obstacle placed in its path. In humans, physical perturbation on the foot dorsum during swing phase elicited excitation on knee flexor, biceps femoris, and inhibition of the ankle dorsiflexor, tibialis anterior (Eng et al. 1994). It was proposed that the functional significance of such a "stumbling corrective reaction" in both the cat and human was to provide a mechanism for maintaining stability and progression of forward locomotion in response to tactile stimuli provided by unanticipated perturbations (Forssberg, 1979; Van Wezel 1997; Zehr and Stein, 1999).

Haridas et al (2005) showed that cutaneous reflexes evoked with SP nerve stimulation were modulated according a postural threat created by whole-body perturbations applied at the waist with participant's arms held across their chest during treadmill walking. In a later study, postural threat was varied by having subjects walk with and without their arms crossed over their chest, and with and without the application of mechanical perturbations to the foot dorsum (Haridas et al. 2008). Cutaneous reflexes were evoked using SP nerve stimulation at set phases of the gait cycle and compared across conditions. The results from these experiments were interpreted to suggest that reflexes play a functional role in the in maintenance of stability during walking (Haridas et al. 2005, 2008).

Walking on slippery surfaces serves to provide an altered sensory context and poses a significant postural threat during locomotion. Under such conditions, it was proposed that the principal goal of the central nervous system was to maintain control of the body's centre of mass and its base of support (Marigold and Misiaszek 2009; Oates et al. 2005). Cappellini et al. (2010) compared human gait patterns when subjects walked on a slippery surface similar to an icy surface, as compared to a non-slippery surface. Walking on a slippery surface caused significant alterations in gait kinematics, kinetics and a general increase in muscle activation, including increased arm and trunk movements (Cappellini et al. 2010).

The effect of an absence of anticipated sensory input during walking was investigated by having subjects walk on a platform that was unexpectedly lowered (Van der Linden et al. 2007). In trials where heel contact was anticipated but absent, ipsilateral anti-gravity leg muscles were rapidly (47–69 ms) stimulated. The authors attributed this rapid response to the activity of subcortical or cerebellar pathways (van der Linden et al. 2007). While walking, adults were subjected to unanticipated floor translations in forward-backward and lateral directions (Perry et al. 2000). In addition, cutaneous sensation of the plantar aspect of the foot was decreased via hypothermic anesthesia and its effect on compensatory reactions evoked floor translations during gait was investigated. Findings included an impaired ability in sensing the body's centre of mass over the base of support which resulted in a delayed foot-lift in backward-directed stepping; more frequent use of multiple steps to recover equilibrium in forward-step reactions, and less frequent use of cross-over steps in lateral step reactions. (Perry et al. 2000).

ii. Effect of Activity of the Arms on Bipedal Locomotion

Arm activity has been shown to play a role in stabilizing reactions during standing and locomotion. For example, when faced with an unanticipated perturbation, arm muscles commonly react during gait **(**Dietz et al. 2001; Marigold et al. 2003; Misiaszek 2003) and standing (McIlroy and Maki 1995) by grasping for nearby objects or in sudden arm-raising actions. It has been suggested that these behaviours may be aimed at protection against a fall or re-establishing stability (Maki and McIlroy 1997; Misiaszek 2003). It has also been suggested that the arms function to mechanically affect the angular momentum of the body (Marigold and Patla 2002) or alter body dynamics during a fall (Marigold et al. 2003) or reduce forward centre of mass momentum which occurs when attempting to stop on a slippery surface (Marigold and Misiaszek 2009; Oates et al. 2005). Anticipation of a slippery surface has been shown to cause significant diminution in lower limb muscle activity and loading and even elimination of an arm reaction during locomotion leading some to suggest that cognitive factors may influence reactions to such perturbation, and as such, could be exploited in a rehabilitation setting (Marigold and Misiaszek 2009).

Previous work has demonstrated that holding a handrail to provide support during treadmill walking tasks with differing levels of postural challenge influences muscle activation and reflex control. Using a single-step tripping paradigm, Rietdyk and Patla (1998) altered the base of support to create two different support conditions; “unilimb” support during normal stance phase, and “trilimb” support provided by the addition of bilateral handrail support. “Balance-dependent” control was compared between these two conditions after an unanticipated obstacle was placed in the path of the swing leg during walking. The investigators found that the magnitudes of EMG responses in limb and trunk muscles to mechanical trip perturbations with and without use of a handrail were differentially modulated (Rietdyk and Patla 1998) demonstrating context dependent responses.

Findings of Lamont & Zehr (2007) also suggested that spinal reflexes can be modulated according to context and as such, may modify the full expression of balance reactions. The authors found that when holding onto an earth-referenced handrail, cutaneous reflex amplitudes were modulated in muscles across the entire body. Most interestingly, reflexes evoked with sural nerve stimulation at the foot were increased in arm extensor muscles. It was suggested that the degree of stability offered by the earth-referenced handrail during various walking tasks influenced inter-limb reflex pathways and that the facilitation of reflexes was greatest in muscles that were able to make use of handrails to restore balance (Lamont and Zehr 2007). Jeka and Lackner (1994) demonstrated that even if the stabilizing force of contact was minimal, an earth-referenced handrail effectively improved postural stability in standing.

The specific role of the arms during obstacle-avoidance stepping was studied through inter-limb reflexes evoked with electrical stimulation to the tibial nerve in the leg (Michel et al. 2008). The investigators found that during locomotion, reflex responses in ipsilateral leg muscles and proximal bilateral arm muscles were facilitated prior to obstacle-stepping compared to prior to normal stepping. In the contralateral arm flexors muscles the reflex amplitude was graded with the foot clearance. In addition, EMG activity in arm muscles mimicked the preceding reflex patterns. The observations suggest that an anticipatory interlimb coordination is involved in the acquisition and performance of a locomotor precision task (Michel et al. 2008).

Changes to arm activity have been incorporated to increase the level of postural threat during perturbations to the trunk and were found to influence reflex modulation (Haridas et al. 2005, 2006). While holding the arms across the chest during an unstable walking task, the investigators found an overall facilitation of reflexes evoked in arm muscles with stimulation to nerves in the foot, thus demonstrating the “context-dependency” of inter-limb reflexes (Haridas et al. 2006).

Similarly, Misiaszek and Krauss (2005) found that when the arms were restricted, evoked reflexes in leg muscles increased in amplitude during treadmill walking when participants were perturbed at the torso. Previously, it has been shown that responses in arms after backward perturbations to the trunk were highly variable across subjects, perhaps reflecting fewer constraints imposed upon the action of the arms compared to the legs during locomotion with normal arm swing (Misiaszek 2003).

Bateni et al. (2004) showed that holding an object significantly influenced upper-limb ‘reach-and-grasp’ reactions under conditions of unanticipated perturbation (Bateni et al. 2004). Holding an object such as a cane or cane top reduced early arm activation and considerably inhibited the tendency to grasp at a handrail for stabilization. The task of maintaining grasp onto the object was given higher priority regardless of its lack of task- or context-relevance and despite the prospect of falling as a consequence (Bateni et al. 2004).

VII. Summary

Rhythmic movements such as locomotion have been studied extensively and direct evidence from animals, both intact and reduced preparations, demonstrates that the central pattern generator provides neural control of motor output. As well, propriospinal neurons have been shown to connect cervical and lumbar enlargements in the cat (Miller et al. 1975), neonatal rat (Juvin 2005) and in the human spinal cord (Nathan and Smith 1955; Nathan et al. 1996). In the human, evidence of a spinal pattern generator responsible for rhythmic limb movements remains for the most part, inferential, and continues to be the focus of research efforts using indirect means.

Sensory input has been demonstrated to have significant influence on the modulation pattern of motor output during rhythmic movements (Zehr and Stein 1999). Therefore, evoked spinal reflexes have been used as neural probes to investigate the neural mechanisms of locomotion, including the relative contribution of afferent input from upper and lower limbs (Burke 1999; Zehr and Duysens 2004). Reflex control during different walking tasks has generally been shown to be specific to the context of postural threat and yet the extent to which the arms may play in providing stability remains unclear. Thus we sought to determine if neural control of limb and trunk muscles is altered between tasks where arm activity is the primary source of altered (reduced or increased) stability.

CHAPTER 2: MANUSCRIPT

I. INTRODUCTON

Reflex control during different walking tasks has generally been shown to be specific to the context of postural threat. Cutaneous reflexes were shown to be context-specific during mechanical perturbations applied to the top of the foot during walking (Haridas 2008). Haridas et al. (2005) showed that cutaneous reflexes evoked with SP nerve stimulation during walking were modulated according to the level of postural threat created by whole body perturbations applied at the waist. The results from these experiments were interpreted to suggest that cutaneous reflexes in the legs may assist in maintaining stability during walking. Similarly, walking on slippery surfaces compared to a non-slippery surface evoked responses integral to postural control (Cappellini et al. 2010). The arms may also play a role in balance reactions and holding an object significantly influenced the contributions of upper-limbs to balance reactions (Bateni et al. 2004). Previous work has evaluated the influence of holding an earth-referenced handrail to provide support during the walking tasks with differing levels of postural challenge (Haridas 2005, 2006; Rietdyk and Patla 1998; Lamont and Zehr 2007). The magnitudes of EMG responses in limb and trunk muscles to mechanical trip perturbations with and without holding a railing were differentially modulated in a complex manner which optimized a recovery strategy (Rietdyk and Patla 1998). It has also been shown that holding a rail may produce functionally relevant reflexes in arm muscles to make use of a supportive handrail for stability particularly during more challenging tasks of walking on an incline or climbing stairs (Lamont and Zehr 2007). In addition, changes to arm activity (e.g. arms crossed across chest) have been incorporated experimentally to increase the level of postural threat during perturbations to the trunk and were found to influence reflex modulation (Haridas et al. 2005; 2006). However, reflex modulation has never been examined with the source of instability originating solely from the activity of the arms.

Thus we sought to determine if neural control of limb and trunk muscles is altered between tasks where arm activity is the primary source of reduced or increased stability. We used 3 treadmill walking tasks where the leg activity was the same, while the arms were engaged differently in each to induce three levels of postural stability. Participants walked on a treadmill using normal arm swing, holding a handrail (context of increased stability) or holding a wheeled walker (context of decreased stability). In over-ground walking, a wheeled walker typically provides increased support; however, walking with a wheeled walker which must be steered as the wheels intermittently move off and on the moving belt of the treadmill created an unstable walking context. Using evoked cutaneous reflexes, the neural control of limbs and trunk muscles was probed during walking tasks with three different levels of postural instability related to arm function. We hypothesized that cutaneous reflex amplitude would be altered by the stability of the walking task in a fashion relevant to maintaining balance.

II. METHODS

i. Participants

Fifteen healthy adults free of documented neurological or metabolic impairment (7 males and 8 females between 21 and 48yrs; mean = 28.8yrs; SD = 8.4yrs) participated in this study with informed, written consent according to protocols approved by the

Human Research Ethics Board at the University Victoria and in accordance with the Declaration of Helsinki.

ii. Procedures

Participants walked on a treadmill (Life Fitness™) for approximately 6 min. for each of 6 walking trials assigned in random order. Each trial consisted of a combination of either superficial radial nerve (SRn) or superficial peroneal nerve (SPn) stimulation, plus one of three walking tasks (i.e. wheeled WALKER; NORMAL arm swing; holding bilateral HANDRAIL) at a self-selected pace (approx. 5km/hr) consistent across conditions. Data (120 sweeps per trial) was collected from each individual subject across all trials on the same experimental day. Following the experiment, participants were asked to rank the three tasks (i.e. NORMAL vs. WALKER vs. HANDRAIL) by degree of perceived postural challenge.

iii. Cutaneous Nerve Stimulation

Intra-limb nerve stimulation was used in order to provide the most robust reflex responses; SRn was stimulated to probe the upper limb muscles, while SPn was used to probe the lower limb and trunk muscles. In separate trials, right SRn was stimulated on the dorsum of the wrist just proximal to the ‘anatomical snuffbox’; right SPn was stimulated on the dorsum of the foot, using a Grass S88 stimulator connected in series with a SIU5 isolation unit and a CCU1 constant-current stimulation unit (Grass Instruments, Quincey, MA). Stimulation to nerves was delivered pseudo-randomly throughout the step cycle using flexible disposable surface EMG electrodes (Thought Technology, Montreal, QC, Canada) with trains of 1ms square-waved pulses (5 X 1.0 ms at 300 Hz) at approximately twice (2.1 ± 0.12 SD) the threshold at which a clear and full radiating paresthesia was perceived into the dorsum of the hand (Zehr et al. 1997; Zehr and Haridas 2003), and medial aspect of the foot (Haridas and Zehr 2003).

iv. Electromyography (EMG)

After the skin was cleaned with alcohol, disposable surface electrodes were applied to the skin over limb and trunk muscles. All muscles were recorded ipsilateral (i) to the site of stimulation (i.e. right side), except erector spinae, which was recorded bilaterally. Surface EMG recordings were obtained from anterior deltoid (iAD), posterior deltoid (iPD), flexor carpi radialis (iFCR), triceps brachii (iTB), erector spinae (iES; cES), vastus lateralis (iVL), biceps femoris (iBF), tibialis anterior (iTA), and medial gastrocnemius (iMG). Ground electrodes were applied over nearby electrically neutral tissue. EMG signals were amplified at X 5,000 and filtered from 100 to 300 Hz (Grass P511, Astro-Med Grass).

v. Data acquisition and EMG Analysis

Data was sampled at 1 kHz with a 12-bit A/D converter connected to a computer running custom-written LabView^{TM} software (National Instruments, Austin, TX). Sensors were applied to the participant’s right shoe insole in order to establish ipsilateral heel strike. Post-acquisition, the step cycle was separated into 8 bins of equal duration (phases of gait cycle) beginning with the initiation of stance at right heel strike. EMG data were full-wave rectified and low-pass filtered at 40 Hz with a dual-pass Butterworth filter. EMG from stimulated step cycles were averaged and then subtracted from non-stimulated (control) cycles to obtain subtracted reflex traces. Subtracted reflex amplitudes occurring at same portion of gait cycle were examined at middle latency (ML) occurring between 75 and 110 ms post-stimulation. Mean reflex responses and background EMG (bEMG) were expressed as percent of maximum bEMG during NORMAL task. Averaged reflexes were considered significant if the peak amplitude exceeded a 2 standard deviation (2SD) band outside the pre-stimulus mean level. Background EMG amplitudes for each muscle across each bin were averaged between SRn and SPn within each task.

vi. Statistics

Separately for SRn and SPn, a repeated measures ANOVA comparing tasks was conducted for separately background EMG and middle latency (ML) reflexes, at each phase of movement (STATISTICA^{TM}, StatSoft Inc.). Therefore in total, there were 16 separate RM-ANOVA tests conducted. Fischer's LSD test was used for *post hoc* analysis of significant main effects; statistical significance for all tests was set at $p \leq 0.05$. Correlation analyses were also performed between ML reflex amplitudes and bEMG at each phase during each task for each muscle.

III. RESULTS

Participants ranked walking tasks by degree of perceived postural challenge; unanimously, subjects reported that WALKER was the most challenging, followed by NORMAL, then HANDRAIL. Therefore in the present study, walking on a treadmill with a wheeled walker created an unstable task and provided a unique paradigm for studying the neural control of locomotion in different stability contexts.

i. Background EMG

Leg muscle activity (bEMG) was generally similar across walking tasks (Fig. 1). In the four leg muscles, significant differences in averaged bEMG between tasks were noted in four bins. In iTA, at heel-strike (bin 1), the amplitude of NORMAL bEMG exceeded WALKER ($p = 0.011$) and HANDRAIL ($p = 0.007$). In ipsilateral MG, at mid-stance (bin 4), bEMG HANDRAIL exceeded both NORMAL ($p = 0.026$) and WALKER tasks ($p = 0.029$). In iVL at heel-strike (bin 1) bEMG NORMAL exceeded WALKER ($p = 0.018$); and WALKER exceeded HANDRAIL ($p = 0.046$). At the end of gait cycle (bin 8), bEMG iVL HANDRAIL was less than WALKER ($p = 0.025$) and less than NORMAL ($p = 0.002$).

In two trunk muscles, averaged bEMG differed between tasks in 3 bins (Fig. 1). In iES, approaching the end of gait cycle (bin 7), bEMG iES WALKER was greater than HANDRAIL ($p = 0.001$) and NORMAL ($p = 0.003$), whereas at the end of the cycle (bin 8), bEMG iES WALKER was less than NORMAL ($p = 0.006$). For the contralateral trunk muscle, cES, during mid-stance of the ipsilateral leg (bin 3), bEMG WALKER exceeded NORMAL ($p = 0.004$) and HANDRAIL ($p = 0.007$).

As opposed to leg muscles where few differences in bEMG were noted across tasks, arm muscle activity differed markedly across the tasks (Fig. 1). Across the gait cycle, bEMG of the wrist flexor (iFCR) in HANDRAIL was greater than NORMAL ($p < 0.02$ across bins 1-8). As well, bEMG of iFCR for WALKER exceeded NORMAL ($p < 0.04$ across bins 1-8); however, no significant differences were observed in bEMG of iFCR between WALKER and HANDRAIL. In the arm muscle, iTB, bEMG also varied considerably according to the tasks (Fig. 1). For example, across all phases of the gait cycle bEMG NORMAL fell below both WALKER ($p < 0.0003$) and HANDRAIL ($p < 0.01$). At heel strike, bEMG iTB WALKER also exceeded that of HANDRAIL (bin 1, $p = 0.02$; bin 2, $p = 0.04$).

Background muscle activity of iAD, only differed across tasks at bin 8 where bEMG WALKER exceeded NORMAL ($p = 0.002$). Background muscle activity of iPD demonstrated considerable differences across tasks. WALKER bEMG exceeded HANDRAIL across all 8 bins ($p < 0.002$) and NORMAL during most of the cycle ($p < 0.02$, bins 1-6; $p = 0.0001$, bin 8). Only at one point in time (bin 6) did bEMG iPD NORMAL surpass HANDRAIL ($p = 0.03$).

ii. Middle Latency Reflexes

Single subject reflex traces plus background EMG (bEMG) of trunk, shoulder and arm muscles during the three different treadmill walking tasks across 8 bins (phases) are shown in Fig. 2. Reflex responses to SPn are shown for trunk muscles (iES, cES) on left, and reflexes following SRn stimulation are shown on right. Rectangular boxes highlight middle latency (ML) reflexes; bEMG traces appear oriented vertically. Facilitatory reflexes in trunk muscles (iES, cES) were present during WALKER compared to during NORMAL or HANDRAIL tasks. Reflexes in the shoulder muscle (iPD) and arm extensor (iTB) during WALKER were more suppressed than during NORMAL and HANDRAIL.

Group data for reflex responses across tasks are displayed in Fig. 3. In a fashion observed in bEMG for leg muscles, reflexes were similar across tasks. The only leg muscle that showed significant reflex differences across tasks was iMG, where WALKER exceeded NORMAL (bin 2, $p = 0.0016$).

In trunk muscles (iES), reflex amplitude in WALKER was greater than in HANDRAIL (bin 2, $p = 0.008$; bin 5, $p = 0.008$) during ipsilateral stance phase. For cES, during mid-stance ipsilateral to nerve stimulation reflex amplitude for WALKER was larger than HANDRAIL (bin 3, p = 0.003; bin 5, p = 0.004): also WALKER exceeded NORMAL at bin 3 (p = 0.003).

More differences in reflex responses were observed in arm muscles compared to the legs. A sign reversal was seen in several reflex responses between tasks. In iPD, reflexes during the WALKER task were inhibitory while they were excitatory in HANDRAIL during terminal stance (bin 5, p = 0.012) and terminal swing (bin 8, p = 0.013). In addition, in iPD at bin 8, reflexes during WALKER were inhibitory, while excitatory in NORMAL (p = 0.037); reflexes during HANDRAIL were excitatory, while in NORMAL they were inhibitory in stance (bin 2, p = 0.015) and during late-stance (bin 5, p = 0.006). Whereas in iAD NORMAL reflexes were excitatory, in both WALKER and HANDRAIL they were inhibitory at onset of swing (bin 6, p= 0.02 and p= 0.017, respectively). Finally, in iTB at terminal swing, WALKER reflexes were inhibitory whereas they were excitatory in NORMAL (bin 8, p = 0.012)

iii. Relationship between Background Muscle Activity and ML Reflexes

Pearson correlations were conducted to evaluate the extent to which reflexes from each tasks varied with the corresponding bEMG (see Table 1). Of the 30 correlations conducted, only 3 times were the correlations between reflex and bEMG amplitudes significantly coupled: during SRn in iAD during WALKER (r = -0.54); iTB during HANDRAIL (r = 0.58); iFCR during HANDRAIL (r = -0.56). In addition, there were generally a greater number of differences seen in bEMG amplitudes between tasks than for reflex amplitudes.

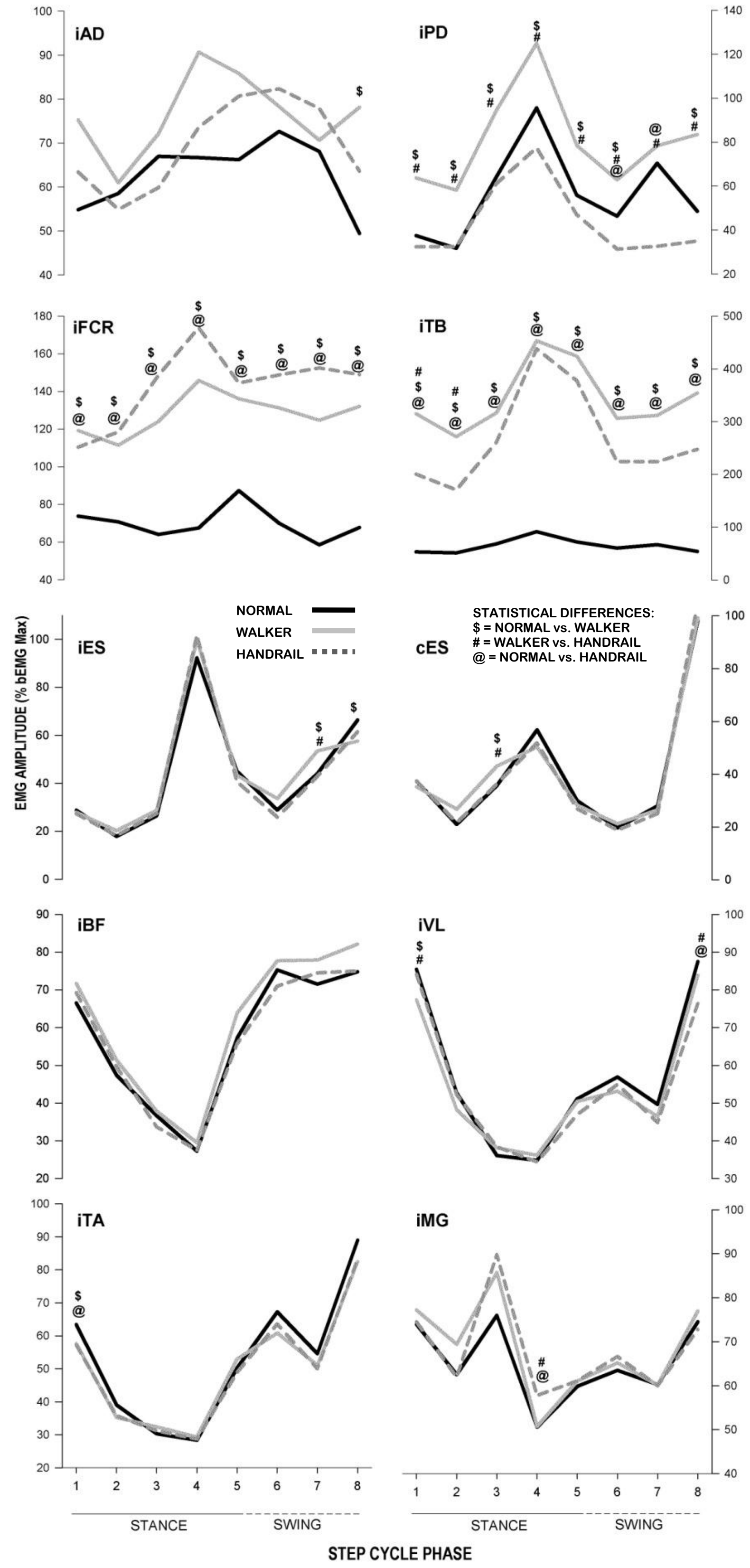

Figure 1. Group bEMG data averaged between SRn and SPn for individual muscles across tasks

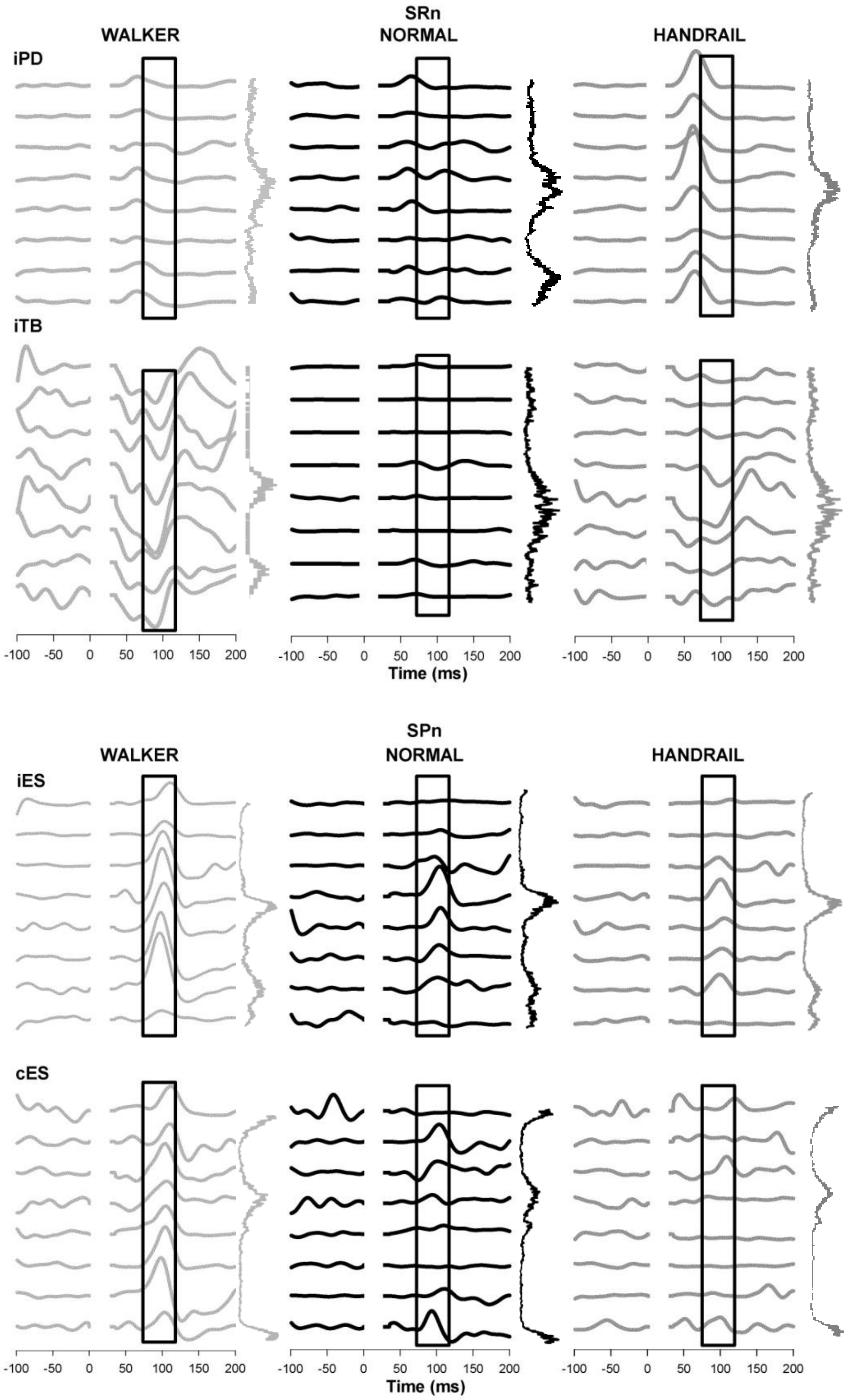

Figure 2. Single-subject subtracted reflex electromyographic (EMG) traces across 8 bins (phases) during SPn stimulation for trunk muscles, iES, cES; during SRn stimulation for arm muscles, iTB, iPD. Rectangular boxes highlight ML reflexes, bEMG traces oriented vertically.

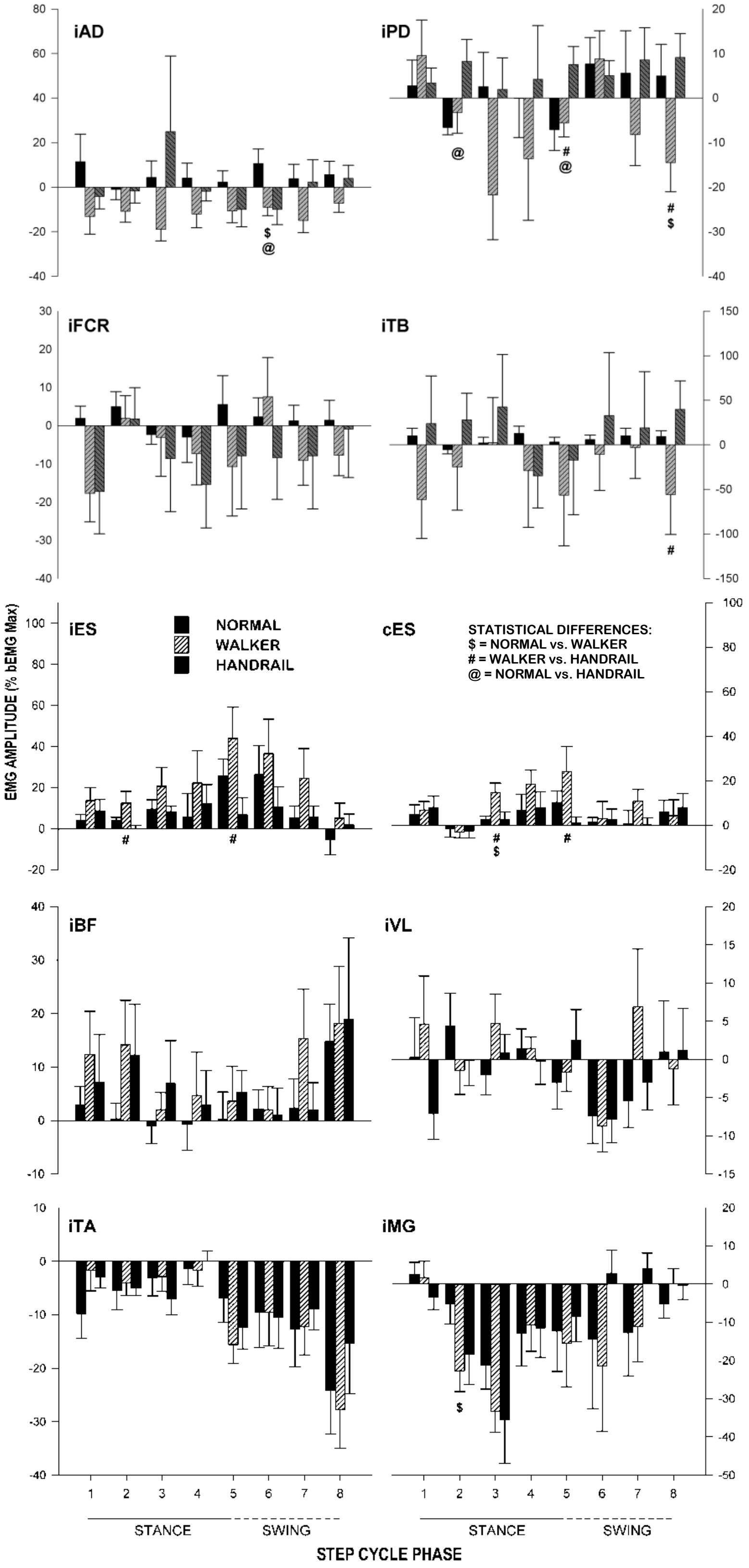

Figure 3. Group data for normalized middle latency (ML) reflexes across tasks during superficial radial nerve (SRn) stimulation in arm and shoulder muscles (iAD, iPD, iFCR, iTB) and during superficial peroneal nerve (SPn) stimulation in leg and trunk muscles (iES, cES, iBF, iMG)

Table 1. Correlation analysis between bEMG and ML reflex amplitude for all muscles; significant correlation noted in bold italics.

SPn	NORMAL	WALKER	HANDRAIL
ESR	0.12	0.19	-0.07
ESL	0.01	-0.13	0.10
VL	-0.06	0.03	-0.18
BF	-0.004	0.14	0.04
TA	-0.31	-0.41	-0.25
MG	-0.12	-0.12	-0.44
SRn			
AD	-0.09	***-0.54***	-0.12
PD	-0.07	-0.17	-0.09
TB	0.03	-0.42	***0.58***
FCR	0.18	-0.37	***-0.56***

IV. DISCUSSION

This study investigated the neural control of limb and trunk muscles during locomotion where differentially engaging the arms contextualized treadmill walking tasks within three levels of postural stability. There were three noteworthy findings. There was an upward gradient in the number of differences between the tasks in bEMG and reflexes with the largest number of differences found closest to the source of instability. Alterations in reflex control were shown between the tasks and may have functional relevance to maintaining stability during walking. In addition, there were fewer differences in reflexes as compared to differences in bEMG between the tasks.

Walking on a treadmill while steering a wheeled walker atop a moving belt with the wheels intermittently on and off the belt created a novel, unstable locomotor task, one in which the source of instability was related to arm function. Consequently, the walker did not play the typical role of an assistive device in providing increased stability during walking, but the converse. Participants qualitatively confirmed this by unanimously reporting that the WALKER task was the most challenging, followed by NORMAL, then HANDRAIL; further, muscle activation and reflex findings provided quantitative confirmation. This paradigm provided a unique framework for studying the neural control of limbs and trunk in stability contexts of both increased and decreased stability. Further, in both the most stable task (holding handrail) and the least stable task (holding the walker), the activity of the arms was similar in terms of bilaterally holding a device with the arms in a similar position, thus making the main difference between the two tasks the stability context.

i. Anatomical Proximity to Source of Instability Increases Effect on bEMG and Reflexes

There was a progressive increase in the number of differences in bEMG and reflexes across tasks in a caudo-cranial direction; the largest number of differences between tasks occurred in the arm muscles, anatomically closest to the source of instability. Haridas and colleagues (2008) found that reflex modulation during walking tasks was influenced by the relative proximity between a mechanical perturbation and the muscle in which a reflex response was observed. Our findings likewise highlight the relevance of the locus of a perturbation experienced during walking to limb and trunk muscle reflex modulation. Changing the activity of the arms within these walking tasks altered the stability context; however, this was reflected by minimal differences in both bEMG and reflex responses in leg muscles across different tasks. In contrast, the neural control of arm and trunk muscles was more affected. It is possible that such alterations were due to the closer proximity of these muscles to the source of instability, and therefore the destabilizing task had greater relevance to them in maintaining balance within the given context.

ii. Reflex Control Dependent on Context of Stability

We attempted to tease apart the effect of holding a device across motor tasks from the functional relevance of that device for providing stability. Although participants applied a similar grasp in both HANDRAIL and WALKER tasks, the device had opposite effects on stability in each tasks, increasing and decreasing, respectively. Specifically, in the WALKER task, not only was the contribution by the arms to stability limited during that task, the source of instability originated solely from the activity of the arms. Bateni et al. (2004) demonstrated that holding an object significantly influenced the involvement of upper limbs in balance reactions during unanticipated perturbations. This was seen in the extreme case of maintaining grasp even when an object was not useful in assuring stability.

In the present study, significant differences were found in expression of reflexes in arm muscles iPD and iTB. Reflexes were inhibitory during WALKER, but excitatory during HANDRAIL, thus showing not only a difference in amplitude, but also a sign reversal. Such differences in reflexes suggest a context-dependent access to neural circuitry that could make use of the more stable handrails in order that weight could be borne through extension of the elbow and shoulder during walking, while in contrast, inhibiting the use of the unstable walker. Interestingly, in those cases where NORMAL was significantly different from WALKER or HANDRAIL, WALKER was more inhibitory, whereas HANDRAIL was more excitatory. For example, in late swing phase (bin 8), NORMAL was excitatory while WALKER was inhibitory, whereas in bin 2 and 5, HANDRAIL was excitatory while NORMAL was inhibitory. This is consistent with the relative stability of the three tasks.

Findings in the present study were similar to those of Lamont and Zehr (2007), who observed increased activity of functionally relevant arm muscles when holding an earth-referenced handrail during walking tasks. Facilitatory effects were seen in posterior deltoid and triceps muscles when lightly gripping an earth-referenced handrail compared to holding a freely-moving cylinder (i.e. moving rail). In addition, similar reflex responses in iPD were seen during walking when holding a rail versus normal arm swing, with the largest differences seen during the most challenging task of incline-walking or stair climbing (Lamont and Zehr 2007). Such findings might suggest that enhanced arm reflexes indicate a pathway that could be accessed to make use of a supportive handrail for stability during gait. This may be the case, however, only if this stability could be assured since the same facilitated reflexes did not appear when the device was not earth-referenced (Lamont and Zehr 2007). The current findings are similar in that facilitated reflexes were seen iPD and iTB muscles during HANDRAIL when the stability was assured, while reflexes were inhibitory during WALKER where the device was the source of instability.

Rietdyk and Patla (1998) found that the magnitude of EMG responses in limb and trunk muscles during mechanical trip perturbations were differentially modulated, depending upon whether or not a handrail was held, which seemed to aid in a recovery strategy. The authors attributed the different responses to an increase in base of support when using a handrail. In our experiment, the wheeled walker likely could not offer a wider base of support because the arms were actively engaged in an unstable task--steering the walker on and off the moving belt. This locomotor context precluded the participant from using the walker as a viable option to provide stability.

Cutaneous reflexes evoked by stimulation to the foot were influenced by the level of postural threat introduced by perturbation to the trunk (Haridas et al. 2005, 2006). Further, alterations in arm activity during walking tasks were used to amplify the level of postural threat during perturbations to the trunk and were found to further influence reflex modulation (Haridas et al. 2005, 2006). These investigators found that cutaneous interlimb reflex responses during treadmill walking were larger when the arms were crossed over the chest, making the task more unstable. In contrast to the findings of Haridas et al. (2005), we did not find differences in leg muscle reflexes across tasks.

Previously, investigators have established reflex linkages connecting muscle and cutaneous receptors of the lower limb with erector spinae muscles in standing (Clair et al. 2009) and during walking (Lamont and Zehr 2007). Similar to previous findings (Lamont and Zehr 2007) differences in reflex modulation in trunk muscles was demonstrated across walking tasks with different contexts of stability. In the WALKER task, where the arms were not assisting in balance correction, the reflexes in arm muscles (iPD and iTB) that could potentially provide a weight-bearing role were reduced. In contrast, the reflex amplitudes observed in bilateral trunk muscles were enhanced in the WALKER task, perhaps suggesting an increased compensatory role by the trunk muscles for balance correction strategies. Regardless of the interpretation of functional relevance, differences in trunk muscle reflexes suggest an altered reflex control in trunk muscles across the tasks.

Differences in reflex control were shown to be independent from bEMG, as indicated by only three significant correlations between reflex and bEMG amplitudes across tasks (see Table 1). These observations suggest that neural mechanisms regulating cutaneous reflex modulation in arm muscles evoked with SRn stimulation and in trunk muscles evoked with SPn stimulation were not simply related to modifications in bEMG amplitude, but rather reflect differences in neural control.

iii. Fewer Differences in Reflexes than bEMG Suggest Conservation in Neural Control

Despite noting some key differences in reflexes across tasks, overall there were far fewer changes in cutaneous reflexes in comparison to many significant differences in bEMG. We suggest that limited task-specific changes to reflex control reflects conservation of some elements of the underlying neural control mechanisms across the tasks while relatively more changes seen in muscle activation reflects necessary changes in motor responses to accommodate the mechanical constraints associated with each task. In addition to there being far fewer differences in reflexes compared to bEMG, the differences in bEMG were often shown at a phase where there was no difference in reflexes or vice versa, differences in reflexes were shown with no difference in bEMG at a given phase. This independence of bEMG from reflex responses, also shown by the lack of correlation between them, corroborates the premise that muscle activation patterns respond to the unique mechanical nature of each task while reflex responses reflect the ability to respond to an electrical stimulus in each task. Previous findings of numerous changes in bEMG with minimal changes in reflex modulation across different arm cycling tasks were interpreted to suggest a conservation of neural control (Hundza and Zehr 2006). Similarly the neural regulation of arm and leg rhythmic movement during walking, arm and leg cycling, and arm-assisted recumbent stepping shared common neural substrates despite having different mechanical demands in each task (Zehr et al. 2007).

iv. Functional Implications

Context-dependent control of reflexes is related to the stability requirements of the walking task. Current results of enhanced reflexes in functionally relevant arm muscles indicate a pathway that could be accessed to make use of an earth-referenced supportive handrail for stability during gait. Conversely suppressed reflexes and sign reversed inhibited reflexes in functionally relevant arm muscles indicate a gating of pathways to limit use of an unstable walking aid. In addition, results suggest that enhanced trunk muscle reflexes indicate a pathway that could be accessed to increase the role of trunk muscles in maintaining stability in less stable tasks where a supportive handrail is not available. Results also suggest that the closer the proximity of the muscles to the source of instability the greater the expression of the reflex context-dependency.

References

Ballesteros ML, Buchthal F, Rosenfalck P (1965) The Pattern of Muscular Activity during the Arm Swing of Natural Walking. Acta Physiol Scand 63:296-310

Balter JE, Zehr EP (2007) Neural coupling between the arms and legs during rhythmic locomotor-like cycling movement. J Neurophysiol 97:1809-1818. DOI 10.1152/jn.01038.2006

Bateni H, Heung E, Zettel J, McLlroy WE, Maki BE (2004) Can use of walkers or canes impede lateral compensatory stepping movements? Gait Posture 20:74-83. DOI 10.1016/S0966-6362(03)00098-5

Bateni H, Zecevic A, McIlroy WE, Maki BE (2004) Resolving conflicts in task demands during balance recovery: does holding an object inhibit compensatory grasping? Exp Brain Res 157:49-58. DOI 10.1007/s00221-003-1815-8

Borgmann A, Hooper SL, Buschges A (2009) Sensory feedback induced by front-leg stepping entrains the activity of central pattern generators in caudal segments of the stick insect walking system. J Neurosci 29:2972-2983. DOI 10.1523/JNEUROSCI.3155-08.2009

Brooke JD, Cheng J, Collins DF, McIlroy WE, Misiaszek JE, Staines WR (1997) Sensori-sensory afferent conditioning with leg movement: gain control in spinal reflex and ascending paths. Prog Neurobiol 51:393-421

Brown TG (1914) On the nature of the fundamental activity of the nervous centres; together with an analysis of the conditioning of rhythmic activity in progression, and a theory of the evolution of function in the nervous system. J Physiol 48:18-46

Brown TG (1911) The Intrinsic Factors in the Act of Progression in the Mammal. Proceedings of the Royal Society of London.Series B, Containing Papers of a Biological Character 84:pp. 308-319

Burke D, Dickson HG, Skuse NF (1991) Task-dependent changes in the responses to low-threshold cutaneous afferent volleys in the human lower limb. J Physiol 432:445-458

Burke RE (1999) The use of state-dependent modulation of spinal reflexes as a tool to investigate the organization of spinal interneurons. Exp Brain Res 128:263-277

Cappellini G, Ivanenko YP, Dominici N, Poppele RE, Lacquaniti F (2010) Motor patterns during walking on a slippery walkway. J Neurophysiol 103:746-760. DOI 10.1152/jn.00499.2009

Carroll TJ, Zehr EP, Collins DF (2005) Modulation of cutaneous reflexes in human upper limb muscles during arm cycling is independent of activity in the contralateral arm. Exp Brain Res 161:133-144. DOI 10.1007/s00221-004-2050-7

Chandler SH, Baker LL, Goldberg LJ (1984) Characterization of synaptic potentials in hindlimb extensor motoneurons during L-DOPA-induced fictive locomotion in acute and chronic spinal cats. Brain Res 303:91-100

Clair JM, Okuma Y, Misiaszek JE, Collins DF (2009) Reflex pathways connect receptors in the human lower leg to the erector spinae muscles of the lower back. Exp Brain Res 196:217-227. DOI 10.1007/s00221-009-1849-7

Cowley KC, Schmidt BJ (1997) Regional distribution of the locomotor pattern-generating network in the neonatal rat spinal cord. J Neurophysiol 77:247-259

de Ruiter GC, Hundza SR, Zehr EP (2010) Phase-dependent modulation of soleus H-reflex amplitude induced by rhythmic arm cycling. Neurosci Lett 475:7-11. DOI DOI: 10.1016/j.neulet.2010.03.025

Dietz V (2003) Spinal cord pattern generators for locomotion. Clin Neurophysiol 114:1379-1389

Dietz V (2002) Do human bipeds use quadrupedal coordination? Trends Neurosci 25:462-467

Dietz V (1992) Human neuronal control of automatic functional movements: interaction between central programs and afferent input. Physiol Rev 72:33-69

Dietz V, Fouad K, Bastiaanse CM (2001) Neuronal coordination of arm and leg movements during human locomotion. Eur J Neurosci 14:1906-1914

Dietz V, Michel J (2009) Human bipeds use quadrupedal coordination during locomotion. Ann N Y Acad Sci 1164:97-103. DOI 10.1111/j.1749-6632.2008.03710.x

Dietz V, Quintern J, Boos G, Berger W (1986) Obstruction of the swing phase during gait: phase-dependent bilateral leg muscle coordination. Brain Res 384:166-169

Dimitrijevic MR, Gerasimenko Y, Pinter MM (1998) Evidence for a spinal central pattern generator in humans. Ann N Y Acad Sci 860:360-376

Dubuc R, Cabelguen JM, Rossignol S (1988) Rhythmic fluctuations of dorsal root potentials and antidromic discharges of primary afferents during fictive locomotion in the cat. J Neurophysiol 60:2014-2036

Duysens J, Beerepoot VP, Veltink PH, Weerdesteyn V, Smits-Engelsman BC (2008) Proprioceptive perturbations of stability during gait. Neurophysiol Clin 38:399-410. DOI 10.1016/j.neucli.2008.09.010

Duysens J, Pearson KG (1980) Inhibition of flexor burst generation by loading ankle extensor muscles in walking cats. Brain Res 187:321-332

Duysens J, Pearson KG (1976) The role of cutaneous afferents from the distal hindlimb in the regulation of the step cycle of thalamic cats. Exp Brain Res 24:245-255

Duysens J, Tax AA, Murrer L, Dietz V (1996) Backward and forward walking use different patterns of phase-dependent modulation of cutaneous reflexes in humans. J Neurophysiol 76:301-310

Duysens J, Tax AA, Trippel M, Dietz V (1993) Increased amplitude of cutaneous reflexes during human running as compared to standing. Brain Res 613:230-238

Duysens J, Trippel M, Horstmann GA, Dietz V (1990) Gating and reversal of reflexes in ankle muscles during human walking. Exp Brain Res 82:351-358

Duysens J, Van de Crommert HW (1998) Neural control of locomotion; The central pattern generator from cats to humans. Gait Posture 7:131-141

Elftman H (1939) The Function of the Arms in Walking. Human Biology 11:529

Eng JJ, Winter DA, Patla AE (1994) Strategies for recovery from a trip in early and late swing during human walking. Exp Brain Res 102:339-349

Fedirchuk B, Nielsen J, Petersen N, Hultborn H (1998) Pharmacologically evoked fictive motor patterns in the acutely spinalized marmoset monkey (Callithrix jacchus). Exp Brain Res 122:351-361

Forssberg H (1985) Ontogeny of human locomotor control. I. Infant stepping, supported locomotion and transition to independent locomotion. Exp Brain Res 57:480-493

Forssberg H (1979) Stumbling corrective reaction: a phase-dependent compensatory reaction during locomotion. J Neurophysiol 42:936-953

Frigon A, Barriere G, Leblond H, Rossignol S (2009) Asymmetric changes in cutaneous reflexes after a partial spinal lesion and retention following spinalization during locomotion in the cat. J Neurophysiol 102:2667-2680. DOI 10.1152/jn.00572.2009

Frigon A, Collins DF, Zehr EP (2004) Effect of rhythmic arm movement on reflexes in the legs: modulation of soleus H-reflexes and somatosensory conditioning. J Neurophysiol 91:1516-1523. DOI 10.1152/jn.00695.2003

Getting PA, Dekin MS (1985) Mechanisms of pattern generation underlying swimming in Tritonia. IV. Gating of central pattern generator. J Neurophysiol 53:466-480

Gorassini MA, Prochazka A, Hiebert GW, Gauthier MJ (1994) Corrective responses to loss of ground support during walking. I. Intact cats. J Neurophysiol 71:603-610

Grillner S (1975) Locomotion in vertebrates: central mechanisms and reflex interaction. Physiol Rev 55:247-304

Grillner S, Dubuc R (1988) Control of locomotion in vertebrates: spinal and supraspinal mechanisms. Adv Neurol 47:425-453

Grillner S, Matsushima T (1991) The neural network underlying locomotion in lamprey--synaptic and cellular mechanisms. Neuron 7:1-15

Grillner S, Zangger P (1984) The effect of dorsal root transection on the efferent motor pattern in the cat's hindlimb during locomotion. Acta Physiol Scand 120:393-405

Guertin PA (2009) The mammalian central pattern generator for locomotion. Brain Res Rev 62:45-56. DOI 10.1016/j.brainresrev.2009.08.002

Haridas C, Zehr EP (2003) Coordinated interlimb compensatory responses to electrical stimulation of cutaneous nerves in the hand and foot during walking. J Neurophysiol 90:2850-2861. DOI 10.1152/jn.00531.2003

Haridas C, Zehr EP, Misiaszek JE (2008) Adaptation of cutaneous stumble correction when tripping is part of the locomotor environment. J Neurophysiol 99:2789-2797. DOI 10.1152/jn.00487.2007

Haridas C, Zehr EP, Misiaszek JE (2006) Context-dependent modulation of interlimb cutaneous reflexes in arm muscles as a function of stability threat during walking. J Neurophysiol 96:3096-3103. DOI 10.1152/jn.00746.2006

Haridas C, Zehr EP, Misiaszek JE (2005) Postural uncertainty leads to dynamic control of cutaneous reflexes from the foot during human walking. Brain Res 1062:48-62. DOI 10.1016/j.brainres.2005.09.003

Harris-Warrick RM, Cohen AH (1985) Serotonin modulates the central pattern generator for locomotion in the isolated lamprey spinal cord. J Exp Biol 116:27-46

Heiden TL, Sanderson DJ, Inglis JT, Siegmund GP (2006) Adaptations to normal human gait on potentially slippery surfaces: the effects of awareness and prior slip experience. Gait Posture 24:237-246. DOI 10.1016/j.gaitpost.2005.09.004

Hogue RE (1969) Upper-extremity muscular activity at different cadences and inclines during normal gait. Phys Ther 49:963-972

Howell DC (2008) Fundamental statistics for the behavioral sciences. Thomson/Wadsworth, Belmont, CA

Hundza SR, Zehr EP (2009) Suppression of soleus H-reflex amplitude is graded with frequency of rhythmic arm cycling. Exp Brain Res 193:297-306. DOI 10.1007/s00221-008-1625-0

Hundza SR, Zehr EP (2006) Cutaneous reflexes during rhythmic arm cycling are insensitive to asymmetrical changes in crank length. Exp Brain Res 168:165-177. DOI 10.1007/s00221-005-0089-8

Jackson KM (1983) Why the upper limbs move during human walking. J Theor Biol 105:311-315

Jeka JJ, Lackner JR (1994) Fingertip contact influences human postural control. Exp Brain Res 100:495-502

Juvin L, Simmers J, Morin D (2005) Propriospinal circuitry underlying interlimb coordination in mammalian quadrupedal locomotion. J Neurosci 25:6025-6035. DOI 10.1523/JNEUROSCI.0696-05.2005

Kiehn O (2006) Locomotor circuits in the mammalian spinal cord. Annu Rev Neurosci 29:279-306. DOI 10.1146/annurev.neuro.29.051605.112910

Kjaerulff O, Kiehn O (1996) Distribution of networks generating and coordinating locomotor activity in the neonatal rat spinal cord in vitro: a lesion study. J Neurosci 16:5777-5794

Klimstra MD, Thomas E, Stoloff RH, Ferris DP, Zehr EP (2009) Neuromechanical considerations for incorporating rhythmic arm movement in the rehabilitation of walking. Chaos 19:026102. DOI 10.1063/1.3147404

Komiyama T, Zehr EP, Stein RB (2000) Absence of nerve specificity in human cutaneous reflexes during standing. Exp Brain Res 133:267-272

Kriellaars DJ, Brownstone RM, Noga BR, Jordan LM (1994) Mechanical entrainment of fictive locomotion in the decerebrate cat. J Neurophysiol 71:2074-2086

Lackner JR, Rabin E, DiZio P (2001) Stabilization of posture by precision touch of the index finger with rigid and flexible filaments. Exp Brain Res 139:454-464

Lamb T, Yang JF (2000) Could different directions of infant stepping be controlled by the same locomotor central pattern generator? J Neurophysiol 83:2814-2824

Lamont EV, Zehr EP (2007) Earth-referenced handrail contact facilitates interlimb cutaneous reflexes during locomotion. J Neurophysiol 98:433-442. DOI 10.1152/jn.00002.2007

Loadman PM, Zehr EP (2007) Rhythmic arm cycling produces a non-specific signal that suppresses Soleus H-reflex amplitude in stationary legs. Exp Brain Res 179:199-208. DOI 10.1007/s00221-006-0782-2

Maki BE, McIlroy WE (1997) The role of limb movements in maintaining upright stance: the "change-in-support" strategy. Phys Ther 77:488-507

Marigold DS, Bethune AJ, Patla AE (2003) Role of the unperturbed limb and arms in the reactive recovery response to an unexpected slip during locomotion. J Neurophysiol 89:1727-1737. DOI 10.1152/jn.00683.2002

Marigold DS, Misiaszek JE (2009) Whole-body responses: neural control and implications for rehabilitation and fall prevention. Neuroscientist 15:36-46. DOI 10.1177/1073858408322674

Marigold DS, Patla AE (2002) Strategies for Dynamic Stability During Locomotion on a Slippery Surface: Effects of Prior Experience and Knowledge. J Neurophysiol 88:339-353

McCrea DA, Rybak IA (2008) Organization of mammalian locomotor rhythm and pattern generation. Brain Res Rev 57:134-146. DOI 10.1016/j.brainresrev.2007.08.006

McIlroy WE, Maki BE (1995) Early activation of arm muscles follows external perturbation of upright stance. Neurosci Lett 184:177-180

Mezzarane RA, Klimstra M, Lewis A, Hundza SR, Zehr EP (2011) Interlimb coupling from the arms to legs is differentially specified for populations of motor units comprising the compound H-reflex during "reduced" human locomotion. Exp Brain Res 208:157-168. DOI 10.1007/s00221-010-2467-0

Michel J, van Hedel HJ, Dietz V (2008) Obstacle stepping involves spinal anticipatory activity associated with quadrupedal limb coordination. Eur J Neurosci 27:1867-1875. DOI 10.1111/j.1460-9568.2008.06145.x

Miller S, Scott PD (1977) The spinal locomotor generator. Exp Brain Res 30:387-403

Miller S, Van Der Burg J, Van Der Meche F (1975) Coordination of movements of the kindlimbs and forelimbs in different forms of locomotion in normal and decerebrate cats. Brain Res 91:217-237

Minassian K, Persy I, Rattay F, Pinter MM, Kern H, Dimitrijevic MR (2007) Human lumbar cord circuitries can be activated by extrinsic tonic input to generate locomotor-like activity. Hum Mov Sci 26:275-295. DOI 10.1016/j.humov.2007.01.005

Misiaszek JE (2003) Early activation of arm and leg muscles following pulls to the waist during walking. Exp Brain Res 151:318-329. DOI 10.1007/s00221-003-1501-x

Misiaszek JE, Krauss EM (2005) Restricting arm use enhances compensatory reactions of leg muscles during walking. Exp Brain Res 161:474-485. DOI 10.1007/s00221-004-2094-8

Nathan PW, Smith M, Deacon P (1996) Vestibulospinal, reticulospinal and descending propriospinal nerve fibres in man. Brain 119 (Pt 6):1809-1833

Nathan PW, Smith MC (1955) Spino-cortical fibres in man. J Neurol Neurosurg Psychiatry 18:181-190

Oates AR, Frank JS, Patla AE (2010) Control of dynamic stability during adaptation to gait termination on a slippery surface. Exp Brain Res 201:47-57. DOI 10.1007/s00221-009-2011-2

Pang MY, Yang JF (2002) Sensory gating for the initiation of the swing phase in different directions of human infant stepping. J Neurosci 22:5734-5740. DOI 20026544

Pang MY, Yang JF (2001) Interlimb co-ordination in human infant stepping. J Physiol 533:617-625

Pang MY, Yang JF (2000) The initiation of the swing phase in human infant stepping: importance of hip position and leg loading. J Physiol 528 Pt 2:389-404

Parker D, Grillner S (2000) Neuronal mechanisms of synaptic and network plasticity in the lamprey spinal cord. Prog Brain Res 125:381-398

Pearson KG (1995) Proprioceptive regulation of locomotion. Curr Opin Neurobiol 5:786-791

Peiper A (1963) Cerebral function in infancy and childhood. Consultants Bureau, New York

Perry SD, McIlroy WE, Maki BE (2000) The role of plantar cutaneous mechanoreceptors in the control of compensatory stepping reactions evoked by unpredictable, multi-directional perturbation. Brain Res 877:401-406

Rietdyk S, Patla AE (1998) Context-dependent reflex control: some insights into the role of balance. Exp Brain Res 119:251-259

Sakamoto M, Endoh T, Nakajima T, Tazoe T, Shiozawa S, Komiyama T (2006) Modulations of interlimb and intralimb cutaneous reflexes during simultaneous arm and leg cycling in humans. Clin Neurophysiol 117:1301-1311. DOI 10.1016/j.clinph.2006.03.005

Samara RF, Currie SN (2008) Location of spinal cord pathways that control hindlimb movement amplitude and interlimb coordination during voluntary swimming in turtles. J Neurophysiol 99:1953-1968. DOI 10.1152/jn.01087.2007

Sherrington CS (1910) Flexion-reflex of the limb, crossed extension-reflex, and reflex stepping and standing. J Physiol 40:28-121

Sherrington CS (1906) Observations on the scratch-reflex in the spinal dog. J Physiol 34:1-50

Stein RB, Capaday C (1988) The modulation of human reflexes during functional motor tasks. Trends Neurosci 11:328-332

Tax AA, Van Wezel BM, Dietz V (1995) Bipedal reflex coordination to tactile stimulation of the sural nerve during human running. J Neurophysiol 73:1947-1964

van der Linden MH, Marigold DS, Gabreels FJ, Duysens J (2007) Muscle reflexes and synergies triggered by an unexpected support surface height during walking. J Neurophysiol 97:3639-3650. DOI 10.1152/jn.01272.2006

Van Wezel BMH, Ottenhoff FAM, Duysens J (1997) Dynamic Control of Location-Specific Information in Tactile Cutaneous Reflexes from the Foot during Human Walking. J Neurosci 17:3804-3814

Vierk R, Pflueger HJ, Duch C (2009) Differential effects of octopamine and tyramine on the central pattern generator for Manduca flight. J Comp Physiol A Neuroethol Sens Neural Behav Physiol 195:265-277. DOI 10.1007/s00359-008-0404-5

Vilensky JA, O'Connor BL (1998) Stepping in nonhuman primates with a complete spinal cord transection: old and new data, and implications for humans. Ann N Y Acad Sci 860:528-530

Wannier T, Bastiaanse C, Colombo G, Dietz V (2001) Arm to leg coordination in humans during walking, creeping and swimming activities. Exp Brain Res 141:375-379. DOI 10.1007/s002210100875

Wolf H, Pearson KG (1987) Intracellular recordings from interneurons and motoneurons in intact flying locusts. J Neurosci Methods 21:345-354

Yamaguchi T (2004) The central pattern generator for forelimb locomotion in the cat. Prog Brain Res 143:115-122. DOI 10.1016/S0079-6123(03)43011-2

Yamaguchi T (1992) Muscle activity during forelimb stepping in decerebrate cats. Jpn J Physiol 42:489-499

Yang JF, Lam T, Pang MY, Lamont E, Musselman K, Seinen E (2004) Infant stepping: a window to the behaviour of the human pattern generator for walking. Can J Physiol Pharmacol 82:662-674. DOI 10.1139/y04-070

Yang JF, Stein RB (1990) Phase-dependent reflex reversal in human leg muscles during walking. J Neurophysiol 63:1109-1117

Yang JF, Stephens MJ, Vishram R (1998) Transient disturbances to one limb produce coordinated, bilateral responses during infant stepping. J Neurophysiol 79:2329-2337

Yang JF, Whelan PJ (1993) Neural mechanisms that contribute to cyclical modulation of the soleus H-reflex in walking in humans. Exp Brain Res 95:547-556

Zehr EP, Stein RB (1999) What functions do reflexes serve during human locomotion? Prog Neurobiol 58:185-205

Zehr EP (2006) Training-induced adaptive plasticity in human somatosensory reflex pathways. J Appl Physiol 101:1783-1794. DOI 10.1152/japplphysiol.00540.2006

Zehr EP (2005) Neural control of rhythmic human movement: the common core hypothesis. Exerc Sport Sci Rev 33:54-60

Zehr EP (2002) Considerations for use of the Hoffmann reflex in exercise studies. Eur J Appl Physiol 86:455-468. DOI 10.1007/s00421-002-0577-5

Zehr EP, Balter JE, Ferris DP, Hundza SR, Loadman PM, Stoloff RH (2007) Neural regulation of rhythmic arm and leg movement is conserved across human locomotor tasks. J Physiol 582:209-227. DOI 10.1113/jphysiol.2007.133843

Zehr EP, Carroll TJ, Chua R, Collins DF, Frigon A, Haridas C, Hundza SR, Thompson AK (2004) Possible contributions of CPG activity to the control of rhythmic human arm movement. Can J Physiol Pharmacol 82:556-568. DOI 10.1139/y04-056

Zehr EP, Chua R (2000) Modulation of human cutaneous reflexes during rhythmic cyclical arm movement. Exp Brain Res 135:241-250

Zehr EP, Collins DF, Chua R (2001) Human interlimb reflexes evoked by electrical stimulation of cutaneous nerves innervating the hand and foot. Exp Brain Res 140:495-504. DOI 10.1007/s002210100857

Zehr EP, Collins DF, Frigon A, Hoogenboom N (2003) Neural control of rhythmic human arm movement: phase dependence and task modulation of hoffmann reflexes in forearm muscles. J Neurophysiol 89:12-21. DOI 10.1152/jn.00416.2002

Zehr EP, Duysens J (2004) Regulation of arm and leg movement during human locomotion. Neuroscientist 10:347-361. DOI 10.1177/1073858404264680

Zehr EP, Haridas C (2003) Modulation of cutaneous reflexes in arm muscles during walking: further evidence of similar control mechanisms for rhythmic human arm and leg movements. Exp Brain Res 149:260-266. DOI 10.1007/s00221-003-1377-9

Zehr EP, Hesketh KL, Chua R (2001) Differential regulation of cutaneous and H-reflexes during leg cycling in humans. J Neurophysiol 85:1178-1184

Zehr EP, Hundza SR (2005) Forward and backward arm cycling are regulated by equivalent neural mechanisms. J Neurophysiol 93:633-640. DOI 10.1152/jn.00525.2004

Zehr EP, Kido A (2001) Neural control of rhythmic, cyclical human arm movement: task dependency, nerve specificity and phase modulation of cutaneous reflexes. J Physiol 537:1033-1045

Zehr EP, Klimstra M, Dragert K, Barzi Y, Bowden MG, Javan B, Phadke C (2007) Enhancement of arm and leg locomotor coupling with augmented cutaneous feedback from the hand. J Neurophysiol 98:1810-1814. DOI 10.1152/jn.00562.2007

Zehr EP, Komiyama T, Stein RB (1997) Cutaneous reflexes during human gait: electromyographic and kinematic responses to electrical stimulation. J Neurophysiol 77:3311-3325

Zehr EP, Stein RB, Komiyama T (1998) Function of sural nerve reflexes during human walking. J Physiol 507 (Pt1):305-314